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Identifying efficient clinical parameters in diagnose of liver disease

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Abstract

Background: liver is one of the vital organs of human body. Automatic classification methods as a diagnostic tool help to reduce the working load of doctors. However, choosing the wrong factors cause the system classify error detection and to be complex. The purpose of this research is to identify efficient clinical parameters in diagnose of liver disease. Intelligent diagnosis models used in this research are QUEST, C5.0, CRT, CHAID, Genetic Algorithm, Chi Square, Gain Ratio, and Symmetrical Uncertainty.

Materials and Methods: Data were collected from the records of 583 patients in the North East of Andhra Pradesh, India. Data were registered at the University of California in 2012. All models were compared by the sensitivity, accuracy and area under ROC curve.

Results: The best classification accuracy which belongs to Genetic Algorithm is 73.07.

Conclusion: Genetic Algorithm and QUEST models were considered as the best model with the highest precision. Therefore, these models are proposed to identify the efficient features. This paper is invaluable in terms of research activities in the field of health, and it is especially important in the allocation of health resources for risky people.

Key words: Liver disease, Feature selection, QUEST, C5.0, CRT, CHAID, Genetic Algorithm, Chi Square, Gain Ratio, and Symmetrical Uncertainty.

1. Introduction

The liver is a vital organ and it is essential for human survival. Due to some problems such as, excessive alcohol consumption, inhalation of harmful gases, using too much unhealthy food and drugs, patients with liver problems are increasing day by day. One of the major health problems in the world is diseases that have the most resources and facilities of all and liver diseases belong to these diseases.

Liver has a main role in our metabolism. Liver diseases are usually caused by the inflammation or injury to liver cells. This disease is known as one of the world's top killer diseases. Liver cancer is the third leading cause of death in worldwide, approximately 560,000 new cases per year [1]. Problems which are associated with liver-diseased patients are not detectable in the early stages. It should be noted that even when the injury to the liver is small, it makes liver work improperly. Therefore, early diagnosis of liver injuries is one of the important steps in treatment of these patients [2]. Early diagnosis of this disease increases the survival rate of patients. Classification models which are completely non-parametric are increasingly applied in the different fields of science. The main objective of this model is to identify effective variables, the relationship between them, predication and estimation, this subject is very important in the medicine and health data analysis because of its data type [3]. Classification technique is one of the automatic tools for prediction and diagnosis in medical affairs. The intelligent models can help the

medical community to diagnose and predicate the liver diseases. However, the most important issue is determination of effective factors in recognizing the disease. The improper choice of the recognition factors or accessing the ineffective factors leads to errors in the recognition and also makes the classification system complex. Liver diseases can be identified by measuring various items of blood. For example, liver disease can be identified by analyzing enzyme levels [4]. Data presented in this paper includes different items to diagnose this disease. Data used in this research were collected from the records of 583 patients in the North East of Andhra Pradesh, India. Data were all registered at the university of California in 2012 [5]. The data set was used by the different methods of feature selection, i.e., QUEST, C5.0, CRT, CHAID, Genetic Algorithm (GA), Chi Square, Gain Ratio, and Symmetrical Uncertainty. The selected subsets of feature by these models were compared in terms of sensitivity, the area under ROC curve and accuracy of classification and, the best model of feature selection was introduced. In section 1, an introduction was impressed about the liver disease. In sections 2, 3 and 4, procedure, results, discussion and conclusion are discussed respectively.

2. Materials and Methods

In our research, we used the decision tree models to identify efficient features in diagnose of liver disease. Decision trees are supporting tools which apply a tree-like graph (model of decisions) in their approach. Identifying efficient features in diagnose of livers disease using a decision tree is a method commonly used in data mining. The goal is to create an intelligent model which can identify efficient features in diagnosis of liver disease. In this method, learning is like a tree in a way that each internal node is related to one of the input features and each edge is related to the values of the input features. Each leaf represents a feature value of the target variables in terms of the characteristics value of the input, from the root to the leaf.

A tree can be divided into subsets based on the characteristics value of each test. This process is repeated on each subset in a recursive method called recursive partitioning. In this method, termination occurs when each subset contains

the same number of nodes of the target variable. The top-down procedure of the decision tree [6] is like the greedy algorithms which are known as one of the most famous strategies in the learning process of decision trees. Recently, some developed methods can do this procedure in a bottom-up process [7]. In our study we used four tree models (QUEST, C5.0, CRT and CHAID) and GA, Chi Square, Gain Ratio, and Symmetrical Uncertainty to identify efficient features in diagnose of liver disease. In addition; these tree models have been compared and evaluated furthermore.

2.1. C5.0 Feature Selection Tree Model

This classifier produces a decision tree or a rule set. This model works by dividing instances base on information at each level. The goal criterion in this model should be in a batch. This classifier allows more than two division groups. A new generation of machine learning based on the decision trees is the C5.0 algorithms [8]. C5.0 is the upgraded version of C4.5 and is widely used as a classification tool. This classifier has some advantages to its previous version [9]. Production rules of this classifier are more exact and its run time is slow. Some new techniques of this classifier are highlighted below:

- Several decision trees are combined to enhance prediction
- Misclassification costs are reduced
- It supports new items like date, time, comparison and discrete features
- It supports null and missing date
- It supports sampling and cross validation

C5.0 classification is made of a simple command line which is used in the production of decision trees, rules and classified tests. Detailed information regarding C5.0 is provided in reference [10].

2.2. QUEST Feature Selection Tree Model

This tree was introduced by Loh and Shih [11] and it is the abbreviation of the word “Quick, Unbiased, Efficient and Statistical Tree”. To speed up, this algorithm chooses an input variable for division before a search has been conducted. As a result, the time needed for search is omitted.

This classifier provides a binary classification method for building decision trees. This method has been devised to reduce the processing time in huge analyses. Reducing bias in favor of the classification in tree allows numerical ranges for split features, but it should be a set for target variables. In this classifier all splits are binary.

2.3. CRT Feature Selection Tree Model

CRT is a classification and regression tree [12]. This decision tree allows the prediction and classification of future observations. This method uses a recursive division of the data to reduce its impurity at each stage. In this tree, a node is considered as a net if all samples of that node relates to the target variable. The target variable can be numerical or a set. All the splits are binary.

2.4. CHAID Feature Selection Tree Model

This model uses chi-square distribution to provide favorable divisions. In probability theory and statistics, the chi-square distribution (distribution) with K degrees of freedom is the distribution of the sum of squares of K independent standard normal random variables. Unlike CRT, QUEST and CHAID; this classifier can produce non-binary trees. This means that each node division can have more than 2 branches. The target variable can be numerical or a set [13].

3. Results

Data used in this research were collected from the records of 583 patients in the North East of Andhra Pradesh, India. These data were all registered at the university of California in 2012 [14]. Data includes 416 and 167 files related to liver-diseased and non-liver-diseased patients respectively. The target variable is divided into two groups of liver disease and non-liver disease. Therefore, in terms of gender, 441 male and 142 female constitute the population. The database used, had 10 variables for the diagnosis of liver which are presented in table 1.

Table 1. Clinical parameters of samples used in this study

Number	Clinical parameters	Frequencies
1	Age	44.746±16.19
2	Gender	
	Female	142
	Male	441
3	Total Bilirubin	3.2996.21±
4	Direct Bilirubin	1.486±2.808
5	Total proteins	6.483±1.085
6	Albumin	3.142±0.796
7	A/G ratio	0.947±0.318
8	SGPT	80.714±182.62
9	SGOT	109.911±288.919
10	Alkphos	290.576±242.938
11	Class (output)	
	liver-diseased	416
	non-liver-diseased	167

3.1. Performance Evaluation Setup

By considering that in each classification, P and N were given to the number of samples which belong to liver-diseased and non-liver-diseased class, respectively, the following definitions were presented:

FP = the samples which belong to the liver-diseased group and they were not predicted, accurately.

TP = the samples which belong to the liver-diseased group and they were predicted, accurately.

TN = the samples which belong to the non-liver-diseased group and they were predicted, accurately.

FN = the samples which belong to the non-liver-diseased group and they were not predicted, accurately

As a result, the equations (1), (2), and (3) will be defined:

$$\text{True positive rate} = \frac{TP}{P} \dots\dots\dots (1)$$

$$\text{False positive rate} = \frac{FP}{N} \dots\dots\dots (2)$$

$$\text{Accuracy of classification} = \frac{TP+TN}{P+N} \dots\dots\dots (3)$$

- *k*-Fold Cross Validation

For evaluating the accuracy of five model algorithm, Cross validation was used. In the suggested method, the Cross validation of *K*-Fold and also Leave one out types were used. In the type of *K*-Fold, data is directed to *K* subset which is being used for validation as well *k*-1 is being used for learning. This *K* procedure repeats and all data, *K*-times, are used for learning and also for validation. At the end, the final average of this *K*-times validation is being selected as a final estimation. Certainly, the other methods can be used for combining the results. As usual, the Cross validation, 10-fold is being used. In the Leave one out method, based on its name, in each stage, one of the data leaves out for validation and the other is being used for learning. This method is in fact *K*-Fold method in which *k* equals the number of data. This method in terms of calculation is expensive because the learning process and validation are being repeated for several times.

- Receiver Operating Characteristic (ROC)

In the theory of signal recognition, ROC curve is a graphical design which shows the performance of a binary classification system. Based on figure 1, this curve shows true positive rate to false positive rate. True positive rate was called Sensitivity and the false positive rate was called Specificity.

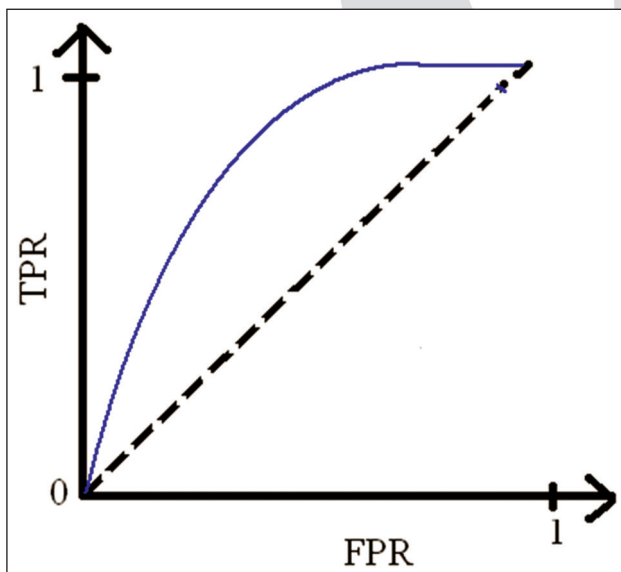


Figure 1. A sample of ROC curve

- Result validation

We use accuracy of 1 nearest neighborhood classifier (1NN) for evaluation of feature selection methods. This algorithm is a statistical pattern recognition method which is being used for determining the class of considered algorithm, from 1 similar pattern in the learning samples (1-nearest neighbors) as well their distance to the considered algorithm is being calculated by using the weighted Euclidean distance. In this method, by accessing the determined vector, 1-nearest vectors in the learning data were found by using the criterion of weighted Euclidean distance. The number of considered pattern is being defined based on the branches of 1-nearest neighbors algorithm and the frequency.

3.2. Performance of suggested models

The liver database uses different methods to identify efficient features in diagnose of liver disease. In table 2, the efficient features which have selected by four trees models, i.e. CHAID, QUEST, CRT and C5.0 and the other renowned methods, i.e. GA (GA) [15], Chi Square [16], Gain Ratio [17], and Symmetrical Uncertainty [18] were presented. The selected set was evaluated by 1-NN classifier and the results were presented in tables 3. The comparisons in this table are based on sensitivity, the area under ROC curve and accuracy of classification. In this table, the best value in terms of accuracy of classification was highlighted. In addition, QUEST is evaluated as the best models in decision tree models. Totally, GA is the best model among all algorithms.

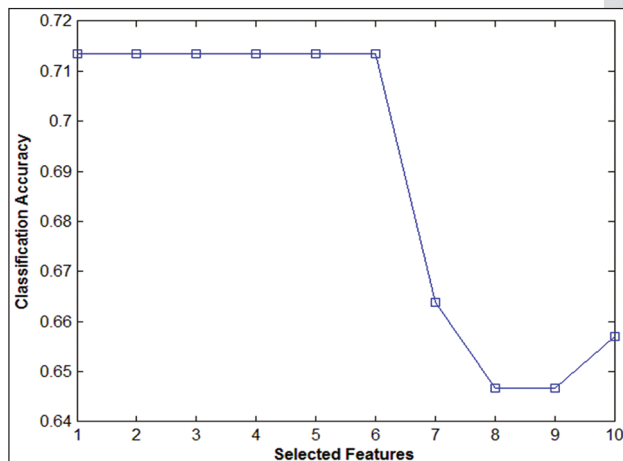
Chi Square, Gain Ratio and Symmetrical Uncertainty find efficient features by rank features (Figure 4 rank feature by proposed methods). Moreover, these methods weight the features by specific measure and rank them. After that, the features in the highest position which cause to improve classification accuracy are selected as final optimal subset. As you can see in Figure 2, this point for Chi Square, Gain Ratio and Symmetrical Uncertainty are 6, 5 and 6, respectively.

Table 2. Selected features by feature selection models.

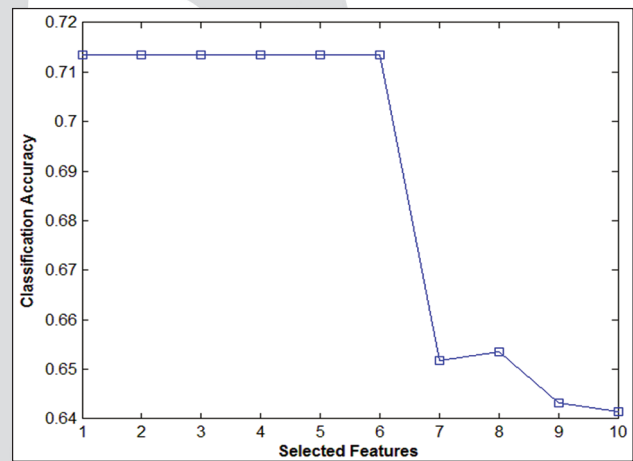
Feature selection tree models	Selected features
CHAID	DB, AGE, ALKPHOS
QUEST	DB, AGE, ALKPHOS, SGOT
CRT	SGOT, AGE, SGPT, ALKPHOS, TB, A/G Ratio
C5.0	Total Bilirubin , Direct Bilirubin, Total Proteins, Albumin, A/G ratio, Gender, SGPT, SGOT Alkphos, AGE,
GA	Age, Gender, TB, DB, Alkphos, A/G Ratio
Chi Square	Sgpt, TB, DB, Alkphos, Sgot, A/G Ratio
Gain Ratio	DB, TB, Sgot, Alkphos, Sgpt
Symmetrical Uncertainty	DB, TB, Sgot, Sgpt, Alkphos, A/G Ratio

Table 3. Performance of feature selection models (classifier evaluator is INN)

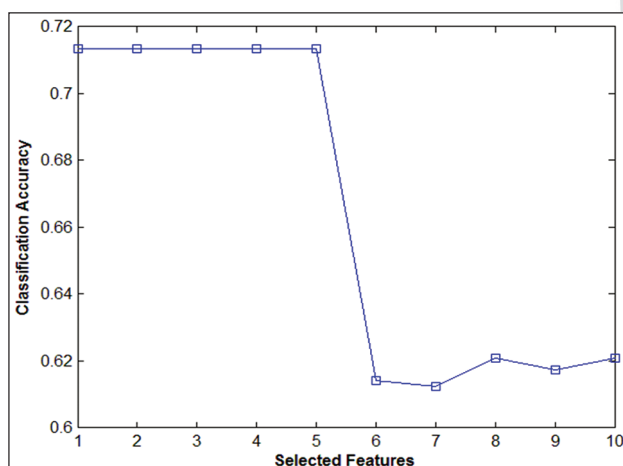
Feature selection tree models	ROC curve	Accuracy of classification (%)	Sensitivity
CHAID	0.64	70.33	0.78
QUEST	0.65	71.01	0.79
CRT	0.60	66.38	0.76
C5.0	0.60	64.49	0.71
GA	0.67	73.07	0.81
Chi Square	0.65	69.64	0.76
Gain Ratio	0.60	67.41	0.77
Symmetrical Uncertainty	0.65	69.64	0.76



(a) Chi Square



(c) Symmetrical Uncertainty



(b) Gain Ratio

Figure 2. Classification accuracy of feature subsets based on their rank

Figure 3 is demonstrated the optimal tree model for feature selection (QUEST decision tree). As you can see in this tree, nodes are selected features and the edges are the value of each feature. When an optimal tree is built, each terminal node is associated with a set of rules. Table 8 summarizes the 7 rules extracted from the optimal tree (QUEST). The rules have been evaluated and approved by doctors for designing proper diagnosis. As indicated in Table 3, the result of the validation sample obtained using the QUEST analysis is 71.01%.

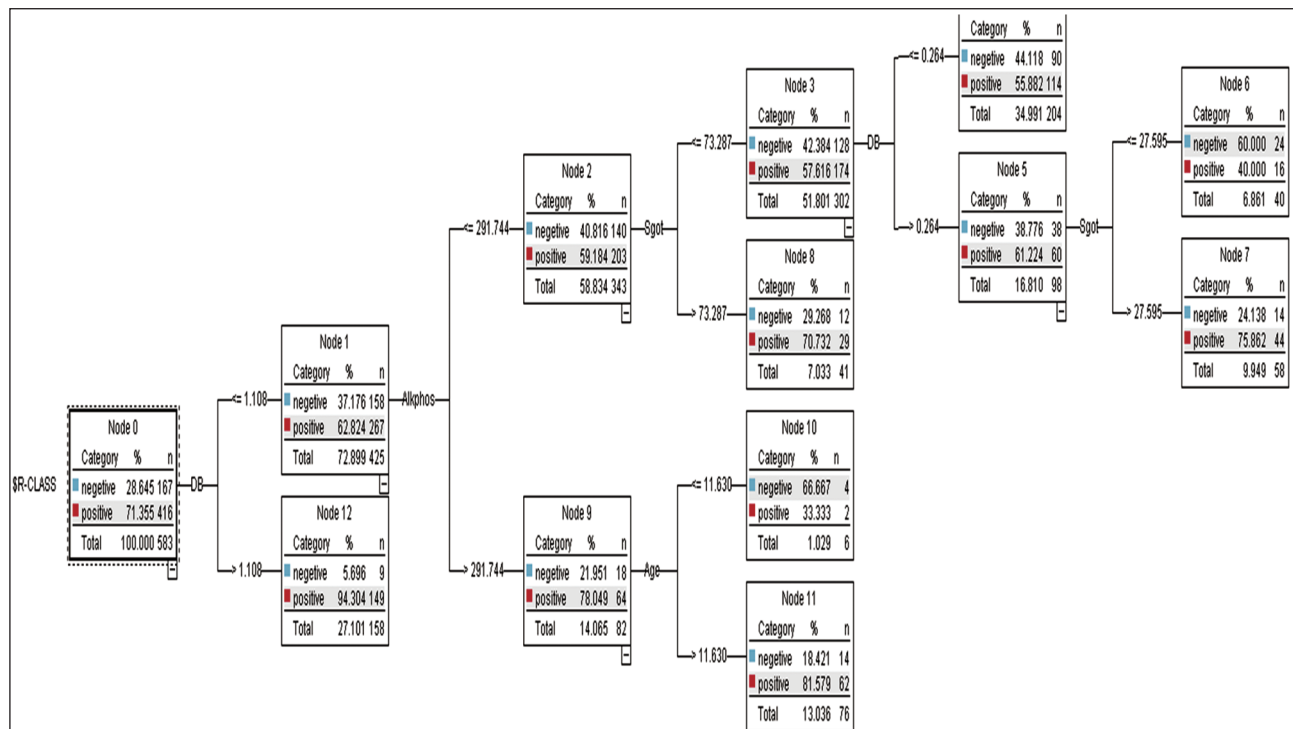
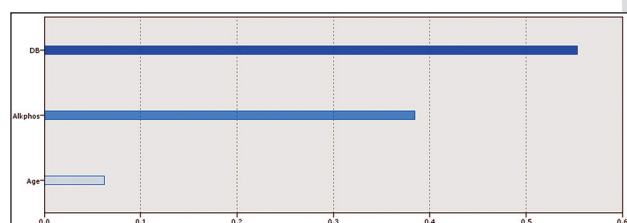


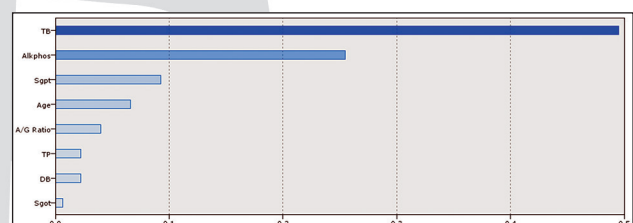
Figure 3. QUEST decision tree for selecting efficient features in liver disease

Table 4. The rule set of QUEST tree model with selected features for diagnose of Liver diseases

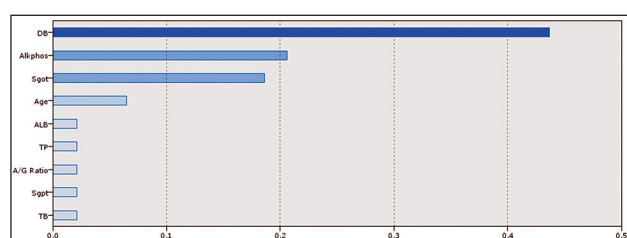
Rule number	Rule
1.	IF DB \leq 1.108 and ALKPHOS \leq 291.744 and SGOT \leq 73.287 and DB \leq 0.264 THEN liver-diseased.
2.	IF DB \leq 1.108 and ALKPHOS \leq 291.744 and SGOT \leq 73.287 and DB $>$ 0.264 and SGOT \leq 27.595 THEN non-liver-diseased
3.	IF DB \leq 1.108 and ALKPHOS \leq 291.744 and SGOT \leq 73.287 and DB $>$ 0.264 and SGOT $>$ 27.595 THEN non-liver-diseased
4.	IF DB \leq 1.108 and ALKPHOS \leq 291.744 and SGOT $>$ 73.287 THEN liver-diseased.
5.	IF DB \leq 1.108 and ALKPHOS $>$ 291.744 and Age \leq 11.63 THEN non-liver-diseased.
6.	IF DB \leq 1.108 and ALKPHOS $>$ 291.744 and Age $>$ 11.63 THEN liver-diseased.
7.	IF DB $>$ 1.108 THEN liver-diseased.



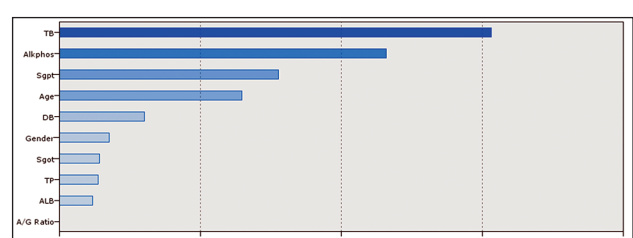
(a) CHAID



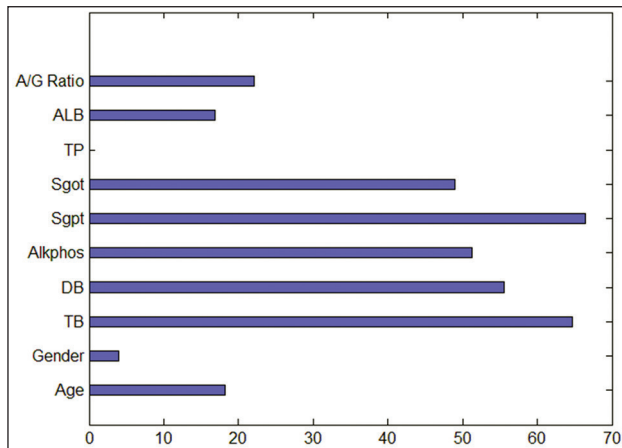
(c) CRT



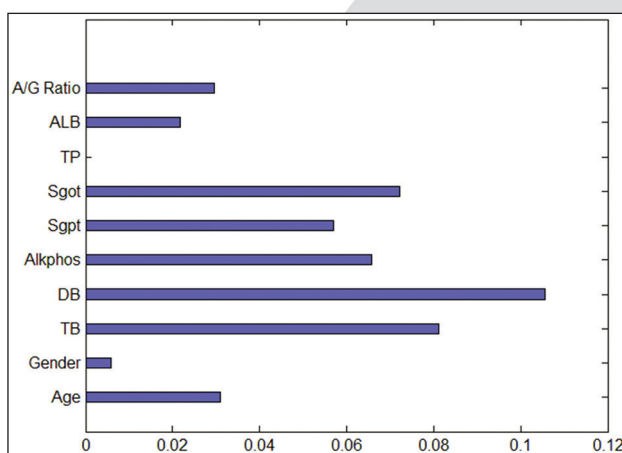
(b) QUEST



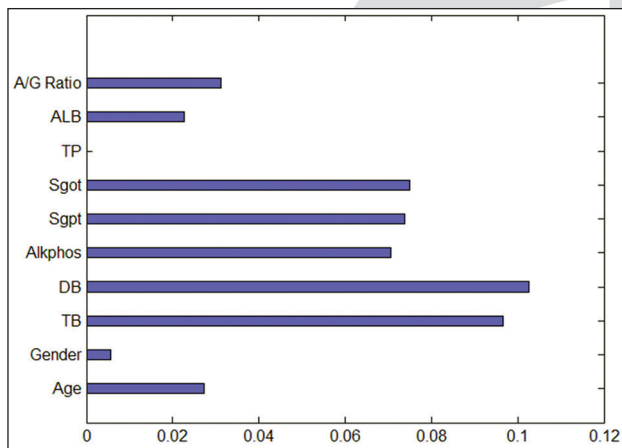
(d) C5.0



(e) Chi Square



(f) Gain Ratio



(g) Symmetrical Uncertainty

Figure 4. Ranking of clinic pathological features by weighting

4. Discussion and conclusion

Liver is one of the supporting organs of human lives. Although it plays a pivotal role in our survival, it is known as one of the world's top ten killer

diseases. Liver cancer is the third cause of death in the world. The main concern is that this disease is not easily detected and different causes are suggested for it. Early diagnosis of liver injury is one of the important steps in its treatment. Therefore, the goal of this research is to identify efficient features in diagnose of this disease. Four tree models (Quest, C5.0 CRT and CHAID) and GA, Chi Square, Gain Ratio, and Symmetrical Uncertainty are applied to aim this end. CHAID tree considered find DB, AGE and ALKPHOS parameters to diagnose this disease, effectively, and the other parameters are considered ineffective. With respect to this model, if a person's DB is more than 4, it can be said that this person is definitely affected by a liver disease. Both DB and AGE are effective parameters for people whose DB is between 9 and 4.1, if DB is less than 9, ALKPHOS is the effective parameter. For QUEST tree, DB, AGE ALKPHOS and SGOT are the only effective variables. If DB of a person is more than 1.08, the person is much likely (94%) affected by liver disease. DB is the only effective parameter in disease, when DB is more than 1.08. If DB of a person is less than 1.108, his/her ALKPHOS is more than 291.744 and her/his age is over the 11, the person is very likely (80%) affected by liver disease. If he/she is under the age of 11, he/she is not very likely affected by liver disease. This issue shows that ALKPHOS, DB and AGE are effective parameters in disease diagnosis for DB which is less than 108.1 and the other parameters are ineffective. In CRT tree, SGOT, AGE, SGPT, ALKPHOS and TB A/G Ratio are the only effective parameters. In this tree, if someone's TB is more than 65.1, the person is much likely (90%) affected by liver disease and the other factors are ineffective; If his/her DB is less than this amount and his/her ALKPHOS is less than 5.211, the person is very likely affected by the disease. All parameters are effective in C5.0 tree. In this tree, if a person's PB is more than 1.2 and his/her SGOT is more than 32, the person is very likely (98%) affected by the disease. These two factors are effective in disease diagnosis. If his/her SGPT is less than 32 and he/she is over 42 years, the person is certainly affected by disease. Considering the GA and QUEST models, which are known as efficient models, there are some common effective factors in them. The-

refores, it can be said DB, AGE, ALKPHOS be effective in disease diagnosis. Totally, with respect to GA, Age, Gender, TB, DB, Alkphos, A/G Ratio is determinant to diagnose of liver disease.

References

1. Bendi Venkata Ramana, M. Surendra Prasad Babu, N. B. Enkateswarlu. "A Critical Study of Selected Classification Algorithms for Liver Disease Diagnosis". In *Proceedings of the International Journal of Database Management Systems (IJDMS)*, May 2011, Vol. 3, No.2, 101- 114.
2. Rong-Ho Lin. *An intelligent model for liver disease diagnosis. Artificial Intelligence in Medicine*, 2009; 47: 53-62.
3. Biglarian A, Hajizadeh E, Kazemnejad A. Comparison of artificial neural network and Cox regression models in survival prediction of gastric cancer patients.
4. *Schiff's Diseases of the Liver*, 10th Edition Copyright ©2007 Lippincott Williams & Wilkins by Schiff, Eugene R, Sorrell Michael F, Maddrey Willis C.
5. Bache K, Lichman M. *UCI Machine Learning Repository*. Irvine, CA: University of California, School of Information and Computer Science, 2013, [<http://archive.ics.uci.edu/ml/>].
6. Quinlan JR. *Induction of Decision Trees*. Machine Learning, 1986; 1: 81-106, Kluwer Academic Publishers.
7. Barros RC, Cerri R, Jaskowiak PA, Carvalho ACPLF. A bottom-up oblique decision tree induction algorithm. *Proceedings of the 11th International Conference on Intelligent Systems Design and Applications (ISDA 2011)*.
8. *Information on See5/C5.0 - RuleQuest Research Data Mining Tools*, 2011. [Online]. Available: <http://www.rulequest.com/see5-info.html>
9. *Is See5/C5.0 Better Than C4.5*, 2009. [Online]. Available: <http://www.rulequest.com/see5-comparison.html>
10. *C5.0: An Informal Tutorial*, 2011. [Online]. Available: <http://www.rulequest.com/see5-unix.html>
11. Loh W, Shih Y. "Split Selection Methods for Classification Trees," *Statistica Sinica*, 1997; 7: 815-840. Introduces the QUEST algorithm. Refer to <http://www.stat.wisc.edu/~loh>
12. Breiman L, Friedman JH, Olshen RA, Stone CJ. *Classification and Regression Trees*, Wadsworth, Belmont, CA, 1984.
13. Kass GV. An exploratory technique for investigating large quantities of categorical data. *Appl. Statist.* 1980; 29: 119-127.
14. *ILPD Liver Disorders Dataset*. UCI repository of machine learning databases. Available from [http://archive.ics.uci.edu/ml/datasets/ILPD+\(Indian+Liver+Patient+Dataset\)](http://archive.ics.uci.edu/ml/datasets/ILPD+(Indian+Liver+Patient+Dataset)).
15. Oh IS, Lee JS, Moon BR. Hybrid genetic algorithms for feature selection. *Pattern Analysis and Machine Intelligence, IEEE Transactions on*, 2004; 26(11): 1424-1437.
16. Yiming Yang, Jan O. Pedersen. A Comparative Study on Feature Selection in Text Categorization. In *Proceedings of the 14th International Conference on Machine Learning (ICML)*, 1997; 412-420.
17. Karegowda AG, Manjunath AS, Jayaram MA. Comparative study of attribute selection using gain ratio and correlation based feature selection. *International Journal of Information Technology and Knowledge Management*, 2010; 2(2): 271-277.
18. Jiang BN, Ding XQ, Ma LT, He Y, Wang T, Xie WW. A hybrid feature selection algorithm: Combination of symmetrical uncertainty and genetic algorithms. In *The Second International Symposium on Optimization and Systems Biology*, 2008; 152-157.

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Brazilian and international guidance on breastfeeding for infants of HIV - infected mothers

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Abstract

Introduction: the moment of breastfeeding becomes one of the first contacts between mother and infant. Breastfeeding in infants of mothers living with AIDS is oriented divergently from the United Nations Children's Fund (UNICEF) and the Ministry of Health of Brazil, regarding the current information provided by the World Health Organization.

Objective: To describe adopted practices in the process of breastfeeding for infants exposed to vertical transmission of HIV.

Methods: A search has been conducted for articles and materials on breastfeeding in infants exposed to HIV. Information has been collected from Medline, Lilacs, Cochrane Library databases, and direct research in guidebooks distributed in the health services in Brazil. The keywords used were: breastfeeding, AIDS, monitoring maternal-infant health.

Results: the information collected indicates that breastfeeding can contribute effectively to the vertical transmission depending on the conduct adopted in relation to the use of antiretroviral therapy, length of medication and level of maternal viral load.

Conclusion: it will be up to the health professionals involved and the government policy adopted the direction to be followed on the issue of breastfeeding for neonates and infants exposed to vertical HIV transmission.

Key words: breastfeeding, child development, AIDS, vertical transmission of infectious disease, infant.

Introduction

From the moment that a mother brings the newborn baby close to her breast for the very first time, she will instinctively know that the loving messages that come along with breastfeeding are so important to the well-being, as the milk itself. Without these messages, the food would not be enough to stimulate the child emotional and even physical development¹. The timing of breastfeeding becomes one of the first contacts between mother and infant, strengthening the bond started during pregnancy. According to Brazelton, child development ends up depending heavily of this connection.

In the cases of mothers living with AIDS, such practice is guided not to occur by UNICEF and the Ministry of Health of Brazil. And the current orientation of World Health Organisation² is having exclusive breastfeeding until six months of life with the use of antiretroviral therapy for mother and infant.

This lack of mother-infant contact involves essentially important issues concerning AIDS and the family relationship, such as: bond formation, the practical and nutritional issue guaranteed by the offering of maternal milk, social deprivation not to share this moment in public nappy-changing facilities and the self-realization of the mother to continue serving the infant nutritionally beyond the nine months of pregnancy.

Additionally, it is worth mentioning the growing concern about the increasing rate of HIV/AIDS infection among women, which is called phenomenon of "feminisation"¹⁰, having the representation of this group been highlighted in recent years and appears as one of the focuses of the current study.

Specifically in 1985 it was reported the first case of HIV in children by the Ministry of Health^{3,4,5}. Over the recent years there has been no significant increase in mortality due to the prevention and combating of the virus. According to the São Paulo State Secretary of Health-Brazil⁶, considering data from SEADE - Foundation State System of Data Analysis, the transmission of AIDS in São Paulo state decreased by 64.4% in the last decade.

Aiming at gathering information on the subject matter, breastfeeding and AIDS, the current study has the objective to describe conducts adopted in the process of breastfeeding for infants exposed to HIV vertical transmission.

Methods

It is a manuscript in the form of data synthesis. Major international databases have been searched: Medical Literature Analysis and Retrieval System Online (Medline), Latin American and Caribbean Health Sciences (Lilacs), Scientific

Electronic Library Online (SciELO), Cochrane Library and direct research has been made in guide books distributed by the health service in Brazil.

The search has covered the years 1994 to 2014, using the keywords: breastfeeding, AIDS, monitoring of infants and maternal and child health. These descriptors (DECs) were investigated in the Virtual Health Library (Biblioteca Virtual em Saúde - BVS) of the Regional Library of Medicine (Biblioteca Regional de Medicina - BIREME).

As inclusion criteria were considered: the representativity of the samples, scientific journals, objective answered in the conclusion, clarity of the data provided and references for guidelines.

Results

The articles and chapters gathered together to compose this article follow in the table below, describing brief summaries of the topics addressed by the mentioned authors.

The Petra¹⁶	Experimental results provide strong evidence that during childbirth and postpartum, ARV ZDV/3TC and NVP early prophylaxis can reduce substantially the VT of HIV among populations who breastfeed.
Nolan M L et al¹⁷	The substantial decrease in maternal viral load and / or changes in viral load in breast milk may decrease the risk of transmission during breastfeeding.
Bulterys M et al¹⁸	The prolonged breastfeeding contributes substantially to the HIV-1 transmission, even in the presence of an effective early intervention with intensive counseling and continuous support by the research team.
Miotti PG et al¹⁹	Suggest that without antiretroviral drugs the rate of transmission attributable to breastfeeding is higher in the first weeks after birth and, then, declines at a constantly low or regressive rate.
Leroy V et al²⁰	There is an important finding of a strong relationship between maternal disease stage and viral load in breast milk.
Embree JE et al²¹	High power antiretroviral therapy allows the continued promotion and support for the practice of breastfeeding for all women (including the majority of women infected with HIV) and reduces morbidity and mortality.
WHO²²	All women who choose to breastfeed should be encouraged to breastfeed exclusively for the first six months of the infant life. Since the study results suggest that breastfeeding should occur in a guided way and with effective antiretroviral intervention to reduce VT and promote the survival of the infant.
Jones et al²³	According to the Division of Policy and Planning of UNICEF, the interventions needed to achieve the millennium development goal of reducing child mortality by two thirds by 2015 are available but are not being provided to the mothers and children who need them.
Brito et al¹⁸	Suggest a favorable response to the implementation of intervention policies for the prevention of vertical transmission of HIV in Brazil, as it occurred in other parts of the world.

Matida et al²⁴	This Brazilian analysis shows to be possible for a developing country to establish an effective system of free and universal access to antiretroviral therapy, even with regional difficulties for the organization of an ideal infrastructure for health, resulting in a significant increase in survival .
Brazelton¹	If food is fundamental to survival, the infant's future quality of life also depends on the affection that he receives from parents along with the food.
Ministério da Saúde do Brasil¹⁵	Current rates and guidance regarding breastfeeding being contraindicated in cases of maternal HIV.
Organização Mundial da Saúde²	Current rates and information on breastfeeding and HIV
UNICEF¹³	Current rates and information on breastfeeding and HIV
Maturana et al³, Moodley⁵	The first reported case of AIDS in Brazil was in 1985 and that, according to the Ministry of Health of Brazil, the period between 1980 and 2006 the route of vertical transmission was responsible for 78.1% of cases in children of less than 13 years.
Newell⁴	The persistence of high rates of perinatal and neonatal mortality in many developing countries reinforces the need to improve perinatal care in homes and major local public health centers.
Silva et al⁷	The clinical and hematological aspects of children exposed to vertical transmission of HIV-1 and comparison between the infected and the seroreverting children.
Herdy et al⁹	The HIV-infected child who receives a combination of antiretroviral drugs has better progress than those receiving isolated medication.
Veloso et al¹⁰	The intimate relationship between prevention of vertical transmission of HIV and prenatal and childbirth care requires joint action to be implemented by STD/AIDS and Women's Health programs at the federal, state and municipal levels.
Marques et al¹¹	It is suggested a routine of clinical-laboratory monitoring during the first 18 months and then annually until the end of adolescence.
Horvath et al²⁸	Complete avoidance of breastfeeding is efficacious in preventing vertical transmission, but this intervention has significant associated morbidity (e.g., diarrheal morbidity if formula is prepared without clean water). If breastfeeding is initiated, two interventions 1). exclusive breastfeeding during the first few months of life; and 2) chronic antiretroviral prophylaxis to the infant (nevirapine alone, or nevirapine with zidovudine) are efficacious in preventing transmission.

Discussion

HIV infection in developing countries, especially in the Latin American countries, spreads more strongly among women, a process called “feminization” of the epidemic¹² and, consequently, leads to an increased possibility of cases of vertical transmission from mother to child.

The Vertical Transmission (VT) or maternal-infant may occur during intrauterine life, at birth, and in the postpartum through breastfeeding⁷, current focus of this review. Statistics indicate that about 65% of the cases of vertical transmission occur during labor and childbirth itself, 35% occur in the womb, especially during the last weeks of pregnancy and breastfeeding represents an additional risk of transmission of 7% to 22%⁸.

In Brazil, approximately 90% of children living with AIDS were vertically infected⁹. This type of contamination presents bimodal clinical course, early, with a median age of onset of symptoms at four months and later, at age six. It is estimated that 20% of infants in the absence of effective antiretroviral therapy have early progression of the disease.

Considering the growth of the epidemic in the female population, and, consequently, the possibility of increasing the rate of vertical transmission, the Ministry of Health of Brazil published in 1995, specific regulations on the prevention of vertical transmission, establishing it as a priority by the STD and AIDS National Program¹⁰. After the publication of the regulation, the state of São Paulo has created the first adaptations for the implementation of Protocol ACTG-076.

However, the use of injectable AZT as an indicator of this prophylactic practice implementation, demonstrated that this procedure was performed with only 40% of HIV positive pregnant women expected for the year 1998¹¹. Such fact has occurred because of a protocol implementation problem in the institutions.

Aiming at the strengthening of this control action, another strategy to assess the implementation of the vertical HIV transmission prophylaxis protocol was the inclusion of monitoring the HIV positive pregnant and children exposed to diseases of compulsory notification since 2000 (Ordinance MS Nr. 993/2000)⁸.

After the implementation of these epidemiological measures and the supply of milk (infant formula), it was observed a decrease of about 70% of cases of vertical transmission⁹. Significant changes in the clinical prognosis of the children were also observed decreasing the index of morbidity and mortality by opportunistic infections.

Given the number of children living or cohabiting with HIV, the issue of breastfeeding has been receiving attention and new guidelines since December 2009.

According to WHO², the new guidelines to improve health and save lives have recommended, for the first time, breastfeeding for infants of mothers with AIDS to make use of antiretroviral therapy during breastfeeding to prevent vertical transmission. This guidance is directed primarily to places where there is no distribution of infant formula and the possibility of death due to malnutrition or diarrhea is very high.

"These new recommendations are based on the most current data available," said Hiroki Nakatani, Assistant General Director for HIV / AIDS, tuberculosis, malaria and neglected tropical diseases in the World Health Organization "The widespread adoption will help more people in areas with a high incidence of the virus have long and healthy lives", adds Nakatani.

Among the new guidelines is the use of antiretroviral therapy earlier in pregnancy from the 14th week until the end of breastfeeding².

The breastfeeding time is raised until the infant complete 12 months of age under the condition that both are on antiretroviral therapy. According to WHO surveys, this process will reduce the risk

of HIV transmission and improve the infant's chance of survival.

"In the new recommendations, we are sending a clear message that breastfeeding is a good option for the baby, even those with HIV positive mothers, when they have access to antiretroviral drugs," said Daisy Mafubelu, general director of Family and Community Health, World Health Organization.

National health authorities are encouraged by WHO to identify the most appropriate feeding practices of infants (breastfeeding with antiretroviral or use of infant formula) for their communities. The chosen practice should be used as the unique standard of care.

According to the UNICEF¹³ guidance, the infant formula should be offered. There is no cost and its supply to the infant may occur with the emotional commitment that would happen in a situation of exclusive breastfeeding. Moreover, it provides for the pregnant women living with AIDS the "Practical Guide to Food for Children under 12 months who cannot be breastfed", offering suitable options for full nutrition of infants.

It still guides that the breastfeeding by infected mother should be inhibited postpartum by bandaging or the use of lactation inhibitor, as soon as it happens to preserve the mother's emotional state at the very moment. It also emphasizes the importance of the aid by the medical team and family in supporting this decision without discrimination.

As for the Ministry of Health of Brasil¹⁵, in order to achieve the maximum reduction in the rate of vertical transmission, together with the State Program for STD/AIDS in São Paulo, the guidance is for the breastfeeding does not occur, but the replacement by the infant formula distributed free of charge, after counseling, thereby ensuring an adequate nutritional development.

There is also contra-indication for mixed breastfeeding, crossed breastfeeding (breastfeeding by another woman), so that the child is not exposed to other infectious agents, or home pasteurization of human milk because this milk is not tested.

When considering global data, especially in the regions most affected by the infection, the reducing of the number of deaths by infections among breastfed children reinforces the many factors that encourage breastfeeding exclusively²². Approximately 13% of deaths of children fewer than five years

can be avoided²³. “No other single strategy achieves the impact that breastfeeding has in reducing deaths of children under five years.” According to information by the World Health Organisation² and UNICEF¹³, six million children’s lives are being saved every year because of the increasing rates of exclusive breastfeeding in children with HIV.

The alarming rates of malnutrition are among the 30 poorest countries in the world, where at least 21 are African. In this region, unfavorable economic conditions, state of disrespect for the rights of the child and lack of protection for their development and growth, reflect an exposure to HIV virus more strongly¹³.

The latest international estimates that more than 25% of the population lives on less than US\$ 1.25 per day, being one of the most unequal situations in the whole world²⁵. In 2007, approximately 18% of adults between 15 and 49 years old lives with HIV. The young people represent 4% of the men and 13% of the women between 15 and 24 years. Teenage girls are likely two to 4.5 times of becoming infected with AIDS, when compared to boys, because of their anatomy.

Regarding children, 1.4 million children under 18 years, 8% located in South Africa have been orphaned by one or both parents due to AIDS. Approximately 20% of them are not registered at birth, which hinders access to basic services.

In the current situation, the rights to survival, development and health are affronted daily in environments lacking sufficient resources to social welfare and health of this population. This region is among the only ones that possessed the mortality rate of children under five years above 50 per thousand live births in 2008.

UNICEF¹³ data confirm that over 90% of children live in Africa and Asia, with one third of deaths in infancy of this group is due to malnutrition. Compared to the risk of vertical HIV transmission through exclusive breastfeeding, 7-22%⁸, the survival of infants prevails when receiving milk through the mother, ensuring their nutrition. Moreover, the access to antiretroviral drugs decreases the risk of further vertical transmission, what justifies the WHO guidance for its global operation.

Bulterys’ data¹⁸ state that prolonged breastfeeding contributes substantially to HIV transmission, even in the presence of an effective early in-

tervention, intensive counseling and continuous support by the research team. Miotti¹⁹ suggests that without antiretroviral drugs the rate of transmission attributable to breastfeeding is higher in the first weeks after birth and, then, declines at a consistently low or decreasing rate.

Embree²¹ underlies that the high potency antiretroviral therapy allows the continued promotion and support to the breastfeeding practice for all women (including the majority of women infected with HIV) and reduces morbidity and mortality associated with the use of formulas.

On this same theme, in Brazil, studies that evaluated mortality of children vertically infected have verified that there was a decrease of approximately 67% in the mortality rate of these children, parallel to an increase in the use of antiretroviral drugs between 1998 and 2002^{16,17-24,29}.

After the compulsory notification, the services have been able to provide more information about the exams, practices and care of mothers for their infants. Among this guidance is the artificial breastfeeding and nutritional status.

The distribution of the “Guide to Clinical Treatment of HIV Infection” to all pediatricians in the Public Health Network helps access to information. They are prepared based on the knowledge in the literature on viral dynamics, intervention guidelines (in countries like the United States and others in Europe) and the experience of professionals involved in their elaboration.

The referral services provide follow-up for mothers and children. It is performed during pregnancy through monthly visits in the first year of life of the infant, following on a yearly basis, according to each case individually. Children receive kits of infant formula, ensuring nutrition and protection to their exposure to HIV. Justifying the guidelines of the Ministry of Health, since in Brazil there is the possibility to offer and ensure the kit formula for all children.

As for the support and explanations given to the mother to understand the decision of the local health services and their recommendations, it can be emphasized the unique moment of attention and emotional commitment during the feeding of infants, by offering the breast or the formula.

According to Brazelton¹, as previously mentioned, “The food would not be enough if there was

no affection in the act of breastfeeding". That is, the time of breastfeeding can be broken in the act of sucking (the chest or in this case, the bottle), in visual contact with the mother when breastfeeding the infant, the approach with the mother's body (sensing temperature, texture, heartbeat and breathing) and mother-infant interaction by speaking or singing.

The quality of life of infants and their interaction with adults rely on previous enjoyable experiences. Allowing an infant to look an adult, let be packed and snug when being fed, makes him stop playing behind or avoid eye contact with people. From this point on infants gain weight and have a healthy development. If food is fundamental to survival, quality of future life also depends on the affection that he receives from parents along with food¹. Either being exclusive breastfeeding or bottle with infant formula.

Both counseling situations are based on different justifications related to the rate of HIV transmission increased through breastfeeding, which may give protection to the infant with the formula and nutritional process in economically disadvantaged countries without guaranteed access to health services and infant formula.

With the share of under-five deaths during the neonatal period rising in every region and almost all countries, neonatal health will need to be addressed more effectively. Systematic action by governments and partner organizations is needed to reach women and babies with effective care. Highly cost-effective interventions are feasible even at the community level, and most can be linked with preventive and curative initiatives for mothers and babies²⁹.

In this way, it will be for the health professionals involved and the government policy adopted the direction to be followed on the issue of breastfeeding in newborns and infants exposed to HIV through vertical transmission.

References

1. Brazelton TB. *Momentos decisivos do desenvolvimento infantil*. São Paulo: Martins Fontes. 1994; 1: 347-52.
2. UNICEF. Net. NY. 2013. *Children and AIDS: Third stocktaking report*, p. 16. Disponível em <www.unicef.org>. Acesso em: mar 2014.
3. Maturana AP, Rizzo CV, Vasquez DF, Cavaleiro N, Holzer S, Morais VS. *Avaliação da assistência ao parto em gestantes infectadas pelo HIV*. Arq Med ABC. 2007; 32(1): 11-6.
4. Newell ML. *Reducing childhood mortality in poor countries*. Transactions of The Royal Society of Tropical Medicine and Hygiene. 2003; 97: 22-4.
5. Moodley D, Moodley J. *HIV-1 infection: an indication for caesarean section?* International Journal of Obstetric Anesthesia. 2000; 9: 221-4.
6. Secretaria do Estado de Saúde, 2011.
7. Silva EB, Grotto HZW, Vilela MM. *Aspectos clínicos e o hemograma em crianças expostas ao HIV-1: comparação entre pacientes infectados e soro-reversores*. Jornal de Pediatria 2001; 77(6): 503-511.
8. Brito AM, Sousa JL, Luna CF, Dourado I. *Tendência da transmissão vertical de Aids após terapia anti-retroviral no Brasil*. Rev Saúde Pública 2006; 4: 18-22.
9. Herdy GVH, Pinto CAM, Lopes VGS, Ribeiro RP, Gomes IM, et al. *Study of the cardiac alterations in hiv-infected children consequent to the anti-retroviral therapy: prospective study of 47 cases*. Arq Bras Cardiol 2003; 80(3): 316-20.
10. Veloso GL; Vasconcelos AL; Grinsztejn B. *Prevenção da transmissão vertical no Brasil*. Bol Epidemiol Aids 1999; 12(3).
11. Marques HHS. *Avaliação crítica dos efeitos adversos do tratamento anti-retroviral no feto, recém-nascido e lactente*. Rev Bras Ginecol Obstet. 2006; 28(7): 424-30.
12. *Programa Nacional de DST/AIDS do Ministério da Saúde 2010 – Secretaria de Vigilância Sanitária em Saúde*; 1-81.
13. Brasil. Ministério da Saúde. *Guia prático de preparo de alimentos para crianças menores de 12 meses que não podem ser amamentadas*. Brasília: Ministério da Saúde, 2004; 50.
14. Machado MMT, Galvão MTG, Kerr-Pontes LRS, Cunha AJLA, Leite AJM, et al. *Acesso e utilização de fórmula infantil e alimentos entre crianças nascidas de mulheres com HIV/AIDS*. Rev. Eletr. Enf. [Internet]. 2007; 9(3): 699-11.
15. UNICEF. Net. 2013. *Situação mundial da infância*. Disponível em <www.unicef.org>. Acesso em: 20 fev 2014.

16. The PETRA study team. Efficacy of three short-course regimens of zidovudine and lamivudine in preventing early and late transmission of HIV-1 from mother to child in Tanzania, South Africa and Uganda (PETRA study): a randomised, double-blind, placebo-controlled trial. *Lancet* 2002; 359: 1178-1186.
17. Nolan ML, Greenberg AE, Fowler MG. A review of clinical trials to prevent mother-to-child HIV-1 transmission in Africa and inform rational intervention strategies. 2002; 16(15): 1991-9.
18. Bulterys M, Nolan M, Jamieson D, Dominguez K, Fowler MG. Advances in the prevention of mother-to-child HIV-1 transmission: current issues, future challenges. *AIDS Science* 2002; 2.
19. Miotti PG, Taha TE, Kumwenda NI, et al. HIV transmission through breastfeeding. A study in Malawi. *JAMA* 1999; 282: 744-749.
20. Leroy V, Karon J, Alioum A, et al. 24-month efficacy of a maternal short-course zidovudine regimen to prevent mother-to-child transmission of HIV-1 in West Africa: A pooled analysis of two randomized clinical trials. *AIDS* 2002; 16: 631-641.
21. Embree JE, Njenga S, Datta P, et al. Risk factors for postnatal mother-child transmission of HIV-1. *AIDS* 2000; 14: 2535-2541.
22. WHO Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality. Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: a pooled analysis. *Lancet* 2000; 355: 451-455.
23. Jones G, et al. How many child deaths can we prevent this year? *Lancet*, [S.l.], 2003; 362: 65-71.
24. Matida LH, Ramos AN, Moncau JEC, Marcopito LF, Marques HHS, et al. AIDS by mother-to-child transmission: survival analysis of cases followed from 1983 to 2002 in different regions of Brazil. *Cad. Saúde Pública* 2007; 23(3): s435-s444.
25. Mirochnick M, Fenton T, et al. for the Pediatric AIDS Clinical Trials Group Protocol 250 Team. Pharmacokinetics of nevirapine in HIV type 1 infected pregnant women and their neonates. *J Infect Dis* 1998; 178: 368-374.
26. Musoke P, Guay LA, Bagenda D, et al. A phase I/II study of the safety and pharmacokinetics of nevirapine in HIV-1 infected pregnant Ugandan women and their neonates. *AIDS* 1999; 13: 479-486.
27. Comitê Assessor das Recomendações para Profilaxia da Transmissão Vertical do HIV e Terapia Antirretroviral em Gestantes. *Recomendações para profilaxia da transmissão vertical do HIV e terapia antirretroviral em gestantes – 2010.*
28. Horvath T, Madi BC, Iuppa IM, Kennedy GE, Rutherford G, Read JS. Interventions for preventing late post-natal mother-to-child transmission of HIV. *Cochrane Database Syst Rev*. 2009 Jan 21; (1): CD006734. doi: 10.1002/14651858.CD006734.pub2.
29. Atrash HK. Childhood mortality: still a global priority. *Journal of Human Growth and Development*. 2013; 23(3): 257-260.

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Using the Health Belief Model to predict Pap smear test performance in Iranian women

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Abstract

Purpose: Despite the benefits of regular Pap smear test for early detection of breast cancer, only a small number of women are engaged in this action. Objectives of this study were to characterize the modifying and cognitive factors associated with their Pap smear performance.

Method: In this cross-sectional study, 350 women referred to health centers selected through the convenience sampling. The data collected by a self-administered questionnaire and standard Health Belief Model Scale. In data analysis by SPSS version 18 used suitable tests such as independent T test, Chi square test, logistic and linear regression model.

Results: The results showed that 40.9% of the women had the history of Pap smear performance. Among the subscales perceived barrier ($p=0.00$), seriousness ($p=0.03$), benefits ($p=0.05$), and health motivation ($p=0.00$) were significantly associated to Pap smear performance, however only perceived barriers ($OR=0.23$, 95% CI: 0.14, 0.38) were significant predictors.

Conclusion: Knowledge had direct and indirect effect in Pap smear performance. Increasing knowledge about cervical cancer, and eliminating barriers especially in low literate and women with low pregnancy, are necessary.

Key words: Cervical cancer; Health Belief Model; Pap smear test; Women.

Introduction

In the last 50 years, regular Pap smear test caused a dramatic decrease in mortality and incidence of cervical cancer in developed countries (Brotto et al, 2008), but in developing countries due to inadequate screening, cervical cancer is the sec-

ond biggest cause of female cancer with approximately 530,000 new cases and a 0.6% annual rate of increase. Cervical cancer is the most common gynecological cancer in Iran. However, since there is no lucid system to document the data on cancers, there are no clear reports of incidence and prevalence of cervical cancer in Iran (Pirzadeh & Amidi Mazaheri, 2012). In one study in Shiraz (Iran), the prevalence of HPV was 4.5% in women aged between 20-40 years and 20% in the older age group (50-59). The prevalence of high-risk HPV (HPV 16) was around 2% (Safaei et al, 2010).

Cancers imposes a lot of costs to the family and society including costs related to treatment, care and absence from work (Keshavarz et al, 2011).

Despite the creation of a cervical cancer screening program, this cancer killed 200,000 women in 2010 (McFarland, 2013; Forouzanfar et al, 2011). Death due to cervical cancer can be prevented with regular Pap smear tests, because it detects cervical lesions in early stage, when they can be effectively treated (Young & Davis, 2004).

Early detection of cervical cancer through Pap smear reduce mortality and morbidity of cervical cancer (WHO, 2005; Mosavel et al, 2009). Despite the advances in the past decade in screening and treatment, pelvic cancer is one of the major health problems among Iranian women. In one study, the rate of regular Pap smear performance in Iranian women was 31.8% (Hajializadeh et al, 2013).

One of the major goals related to health is to reduce mortality due to cancer, and attainment of it depends to effective public screening programs. Accordingly, it is important to have a better understanding of cervical cancer screening behaviors and the factors that may influence them.

The frameworks of many theories of change behavior suggest that beliefs have a significant

role in explaining and determining health behavior (Rosenstock et al, 1988). Health Belief Model (HBM) is a cognitive model that can be used to identify the beliefs influencing screening behaviors (Noroozi & Tahmasebi, 2011). The applicability of the HBM is reflected by its effectiveness for assessing educational needs (in terms of the beliefs described by its cognitive components) that are very significant for the implementation of different educational and preventive strategies (Rosenstock et al, 1988). According to this model, individual's decision to take screening is influenced by four beliefs: perceived susceptibility, perceived severity, perceived benefits, and perceived barriers (Noroozi & Tahmasebi, 2011).

Perceived susceptibility refers to the individual's belief that he or she is at risk for a particular disease, such as cervical cancer. Perceived severity is the individual's belief in depth of the risk and seriousness of the disease complications. Perceived benefits refer to the belief that screening performance have positive results from avoiding exposure to a disease. Perceived barriers refer to obstacles for taking preventive action. Health motivation was later added to the original HBM. This construct refer to the beliefs and behaviors related to the state of general concern about health. These beliefs along with demographic factors are effective in shaping behavior. Demographic factors include socio-demographic variables and structural factors such as knowledge about the disease that can play a role in shaping behavior in the direct or indirect (through behavioral belief) ways (Glanz et al, 2008).

In the several studies, demographic factors (such as age, level of education, income, and ethnicity), poor knowledge (Allahverdipour & Emami, 2008; Rezaie-Chamani et al, 2012; Lee et al, 2007) and beliefs related to cervical cancer screening were important determinants of Pap smear performance (Brotto et al, 2008; Allahverdipour & Emami, 2008; Rezaie-Chamani et al, 2012; Lee et al, 2007; Paskett et al, 2004; McMullin et al, 2005; McFarland, 2009).

Although level of cervical cancer screening test is unacceptable in Iran, few studies have been carried out to determine why women do not refer to participate in Pap smear test (Pirzadeh & Amidi Mazaheri, 2012). Also, Results of several studies show wide variation in terms of participation, knowledge

and beliefs about cervical cancer and Pap smear (Allahverdipour & Emami, 2008; Rezaie-Chamani et al, 2012; Keshavarz et al, 2011). Needs assessment in any society is essential to any plan to promote health behavior in this area (Rezaie-Chamani et al, 2012; Paskett et al, 2004).

Therefore, the purpose of the current study was to investigate effect of HBM constructs and demographic factors in Pap smear performance and also to assess the predictor factors of this model. Researchers strongly believe that the findings of this research will help health providers in design educational programs and potentially increase screening behaviors.

Method

Sample

In this cross sectional study, 375 women 18 to 65 years old referred to general health centers in Bushehr city (Iran) were recruited through convenience sampling procedure. Four out of 10 centers in the city was selected by the lottery. The aim of the study was verbally explained in Persian language for women with include criteria referred to these health centers. Then they were asked if they agreed to participate in the investigation. The participants were told that they could withdraw from the study at any time and that all information would be kept secret and anonymous. They were also requested to choose the answer that best described their beliefs and opinions. In this study, data were collected for five months from July to November 2013.

Exclusion criteria for this study were the diagnosed cervical cancer, hysterectomy, mental health problems, physical disabilities and illiteracy. From the total of 375 requested participants, 24 women refused to complete questionnaires, four women submitted imperfect data questionnaire, so they were excluded from the study. None of the requested participants were illiterate. The final sample included in the analysis was 347, yielding a 92.5% response rate.

Instruments and Measures

A self-administered questionnaire and standard Health Belief Model Scale (Guvenc et al, 2010) were used as the data collection instrument. Self-administered questionnaire included socio-demo-

graphic variables and knowledge questions for evaluation of demographic factors. The socio-demographic variables included age, current marital status, level of education, age of marriage, contraception method used, number of pregnancy, and having a family history of cervical cancer. Cancer knowledge questions included 18 questions, of which, 12 questions were about risk factors of cervical cancer and six others about the Pap smear test performance. The answers for risk factor questions were yes=1 and no=0. The answers for Pap smear performance questions had four items, these questions were re-coded into dichotomous variables by coding false=0 and true=1.

Five subscales of Health Belief Model Scale were used for evaluating the participants' cervical cancer beliefs. They included perceived susceptibility (3 items), perceived seriousness (7 items), perceived benefits (4 items), perceived barriers (14 items), and health motivation (7 items). All items in the five subscales had a 5-point Likert scale ranging from strongly disagree (1-point) to strongly agree (5 points). Higher ranking indicates greater agreement with the health beliefs that were assessed. All of the subscales were positively related to the screening behavior, except for the barriers, which were negatively associated.

For content validity of knowledge questions and Health Belief Model Scale, the researcher invited six Iranian experts in health education and midwifery. The experts assessed each item using a 3-point Likert-type scale: 1= essential, 2= useful but unessential, and 3= unessential and calculated content validity ratio. A CVR score of .80 or higher indicates good content validity (Lawshe, 1975). Total CVR score of knowledge questions was calculated 0.94 and CVR for questions of Health Belief Model Scale was 0.8 that were acceptable. All of the subscales were reliable and the ranges of Cronbach's alpha coefficients were 0.67 (health motivation) to 0.80 (perceived benefit). Kuder-Richardson 20 was 0.67 for knowledge questionnaire.

The dependent variable, Pap smear performance, was assessed by self reported response of the participants to Pap smear performance. All analyses compared women who had ever had a Pap test ("ever") with women who had never had a Pap test ("never").

Data analysis

The data obtained from the total of 347 completed questionnaires were coded and entered into the SPSS version 18.0. Descriptive statistics were used to examine the socio-demographic variables. Then the participants for each of Pap smear test performance were divided into two groups. Pap test group 1, the women who reported to perform Pap smear test and Pap test group 2, the women who did not perform Pap smear. Differences between the two groups were assessed by t-test (for qualitative variables such as Knowledge and HBM components) and chi square test (for categorical or qualitative variables). Logistic regression analysis was conducted to assess the direct effect of demographic factors and HBM components in Pap smear performance. In these models, the dependent variable was Pap smear performance, and independent variables were demographic factors (socio-demographic variables and knowledge) or HBM components. Multiple linear regression analysis was conducted to assess the indirect effect of demographic factors. In this regression model, the dependent variable was HBM component that was significant in logistic regression model, and independent variables were demographic factors. In all tests, the level of significance was 0.05.

Results

Overall, 347 Iranian women aged 18 to 65 years old with mean age of 31.98 (SD= 8.13) were recruited in this study. The majority of the women (54.2%) were in the age range of 25 to 35 years. Most of the women had husband (98%) and 45.2% of the respondents (n= 157) were graduated from high school, 23.9% (n= 83) had obtained college degree. The majority of the women (36.3%) had two children. Age of marriage in most of the women (51.9%) was in the age range of 20 and 30 years. Among the 340 married women, the most commonly used methods were condom (46.7%), coitus interruptus (20.5%), oral contraception (14.7%), sterilization (6.1%), and the intra-uterine device (3.5%).

A family history of cervical cancer was reported by 2.3% (n= 8) of the participants. Any participants didn't have smoking history. Approximately half (52.6%) the women interviewed had heard about the cervical cancer.

One hundred and forty two women (40.9% equal N= 142) reported that they had performed Pap smear test, of which 44.4% (N= 63) had pap smear test more than three years ago, 26.8% (N=38) had performed Pap smear in past year, 9.8% (N=14) and 19% (N=27) respectively had performed two and three years ago.

Associations of demographic factors with ever or never had Pap smear

The sample characteristics of the Pap test groups are shown in Table 1. Among demographic variables, Pap smear test performance was significantly related to older age, increasing gravidity,

using of sterilization methods for contraception, and having heard/read about cervical cancer. No significant associations were identified between performing Pap smear test and other variables.

Knowledge had significant differences between the two groups ($p < 0.001$). The means and standard deviations of knowledge in the women who had Pap smear and those who had not were 9.6 ± 2.1 and 8.9 ± 1.7 respectively.

Logistic regression analysis was used to assess the predictors of those variables that demonstrated significant association with ever having a Pap smear. The women who had three or more than three children were over four times more likely to per-

Table 1. Relation between the socio-demographic variables and Pap smear test

Variables	Pap smear Yes	Pap smear No	χ^2	P value
Age				
<25	9 (15.8%)	48 (84.2%)	28.330	0.000
25-35	74 (39.4%)	114 (60.6%)		
35-45	38 (54.3%)	32 (45.7%)		
> 45	21 (65.6%)	11 (34.4%)		
Education				
Secondary	24 (42.1%)	33 (57.9%)	2.131	0.712
High school	68 (43.3%)	89 (56.7%)		
College	50 (43.6%)	83 (56.4%)		
Married status				
Married	141 (41.5%)	199 (58.5%)	2.097	0.148
Widow/Divorcee	1 (14.3%)	6 (85.7%)		
Heard/read about CC				
Yes	92 (50.5%)	50 (30.5%)	14.348	0.000
No	90 (49.5%)	114 (69.5%)		
Contraception				
Modern	33 (46.5%)	38 (53.5%)	17.434	0.001
Barrier/ withdrawal	90 (38.1%)	146 (61.9%)		
Sterilization	16 (76.2%)	5 (23.8%)		
Not use	3 (15.8%)	16 (84.2%)		
Marriage age				
<16	8 (42.1%)	11 (57.9%)	3.765	0.288
16-20	65 (46.1%)	76 (53.9%)		
20-30	68 (37.8%)	112 (62.2%)		
> 30	1 (16.7%)	5 (53.3%)		
Gravidity				
No child	5 (15.2%)	28 (84.8%)	48.129	0.000
1	30 (24.6%)	92 (75.4%)		
2	62 (49.2%)	64 (50.8%)		
≥ 3	45 (68.2%)	21 (31.8%)		
Family history				
Yes	6 (75%)	2 (25%)	3.934	0.068
No	136 (40.1)	203 (59.9%)		

form Pap smear test than those who had not any children (OR= 4.44, 95% CI: 1.13, 17.49). The women who had heard/read about cancer were 72% more likely to perform Pap smear test than those who had not (OR= 1.72, 95% CI: 1.06, 2.8). The odds ratio for knowledge about cancer and pap smear test was 1.23, indicating that the women who had knowledge about cancer were 23% more likely to perform Pap smear than those who had not knowledge about cancer (OR= 1.23, 95% CI: 1.08, 1.48). The women with 45 years old or more were four times more likely to perform Pap smear test than those who had less than 25 years old (OR= 4.34, 95% CI: 1.23, 15.32) the odds ratio for women 35-45 years old and 25-35 years old was 3.31 (OR= 3.31, 95% CI: 1.22, 8.94), and 2.62 (OR = 2.62, 95% CI: 1.1, 6.23), respectively.

The other demographic factors were not significant predictors for Pap smear performance (Table 2).

Associations of HBM component with Pap smear performance

The HBM components of the Pap test groups are statistically compared in Table 3. Significant differences between the two groups were observed

for the subscales of benefits ($p= 0.05$), barriers ($p= 0.00$), seriousness ($p= 0.03$), and health motivation ($p= 0.00$). There were no significant differences in susceptibility ($p= 0.39$) between the two groups.

Logistic regression was conducted for those subscales that demonstrated significant association with ever having a Pap smear. In this analysis, one component of HBM had significant odds ratios. The results revealed that the women with lower perceived barriers were somewhat more likely to perform Pap smear than those with greater perceived barrier (OR= 0.23, 95% CI: 0.14, 0.38). The other components of CHBMS were not significant predictors for BSE performance (Table 4).

Indirect effect of demographic factors in Pap smear performance

Demographic factors include socio-demographic variables and knowledge had also indirect effect in behavior. In this study, multiple linear regression analysis was used to assess the indirect predictors of performing Pap smear. In this model, perceived barrier was dependent variable and demographic factors (socio-demographic variables and knowledge) were independent variables.

Table 2. Associations of demographic factors with Pap smear performance

	B	S.E.	OR	95% C.I. for OR		P
Age						0.048
25-35	0.962	0.442	2.616	1.099	6.227	0.030
35-45	1.197	0.507	3.309	1.224	8.942	0.018
> 45	1.469	0.643	4.345	1.232	15.318	0.022
Contraception						.314
Modern	1.213	0.744	3.365	0.782	14.473	0.103
Barrier/withdrawal	1.155	0.709	3.174	0.791	12.734	0.103
Sterilization	1.616	0.883	5.031	0.892	28.388	0.067
Heard/read about CC	0.542	0.249	1.719	1.055	2.802	0.030
Knowledge	0.209	0.068	1.232	1.079	1.407	0.002
Gravidity						0.037
1-2	0.604	0.597	1.829	0.567	5.898	0.312
≥ 3	1.490	0.700	4.439	1.127	17.489	0.033

Table 3. Relation between HBM components and Pap smear test

Subscale	Pap smear Yes Mean (SD)	Pap smear No Mean (SD)	t	P value
Perceived susceptibility	2.13 (0.83)	2.21 (0.87)	-0.855	0.393
Perceived seriousness	3.11 (0.99)	3.31 (0.76)	-2.139	0.033
Perceived benefits	4.54 (0.51)	4.47 (0.54)	2.007	0.046
Perceived barrier	2.04 (0.54)	2.52 (0.60)	-7.726	0.000
Health motivation	4.62 (0.37)	4.47 (0.46)	3.393	0.001

Table 4. Predictor factors of HBM component for Pap smear performance

HBM Components	B	S.E.	OR	95% C.I. for OR		P
Barrier	-1.472	0.252	0.229	0.140	0.376	0.000
Benefit	-0.193	0.259	0.825	0.497	1.369	0.456
Susceptibility	0.189	0.154	1.208	0.892	1.634	0.222
Severity	-0.049	0.153	0.952	0.705	1.285	0.747
Motivation	0.442	0.317	1.555	0.836	2.894	0.163

Knowledge ($p=0.001$), number of pregnancy, and level of education were determinant factors of barrier and had indirect effects on Pap smear test. In this way, one unit change in knowledge scores decreased the amount of perceived barrier to 0.69 ($B= -0.69$, $P < 0.001$). Also having college education ($B= -0.369$, $P= 0.002$) and three or more than children ($B= -0.409$, $P= 0.021$) decreased the amount of perceived barrier.

Discussion

According to the findings, the Iranian women seem to have moderate rates of Pap smear test (40.9%). Pap smear test among Iranian women is less than the studies performed in other countries, where it ranges from 77% to 84.7% (McFarland, 2013; Leyva et al, 2006; Lee-Lin et al 2007; Byrd et al, 2007). The rate of performing Pap smear found here was nearly identical to other studies in Iran (Hajializadeh et al, 2013; Allahverdipour & Emami, 2008) and previous studies conducted in the Muslim community of Turkish and Jordanian women (Amarin et al, 2008; Reis et al, 2012). Therefore, the rate of cervical cancer screening behaviors among Iranian women is moderate and recognition of effective factors for improving behaviors is necessary.

Some demographic factors including having heard/read about cervical cancer, using of sterilization contraception methods, having knowledge about cervical cancer, increasing gravidity and age were significantly associated to Pap smear performance. Also, all of the factors except contraception method were the predictors of Pap smear performance.

Having knowledge about cervical cancer, increasing gravidity, and holding higher education degree were the indirect predictor of Pap smear performance through decrease of barriers.

Consistent to the other studies (Leyva et al, 2006; Amarin et al, 2008) in the present research, the wo-

men with higher children more likely to perform Pap smear. These women have a regular health care provider for children's care who frequently informed them about the importance of early detection of cancer. Also, these results support previous findings that well-educated women (McFarland, 2013; Leyva et al, 2006) are more likely to perform Pap smear. High education increases the knowledge and the Knowledge can increase the participation in screening behavior (Hajializadeh et al, 2013; Allahverdipour & Emami, 2008). In this study, knowledge about cervical cancer was found to have direct and indirect effect (through barrier) in performing Pap smear in Iranian women. It has been revealed that as knowledge increase self-reliance, and self-respect and decrease barrier as well (Amarin et al, 2008; Avci, 2008; McFarland, 2003; Abotchie & Shokar, 2009; Allahverdipour & Emami, 2008; Keshavarz et al, 2011). Lack of knowledge about cervical cancer impress perceived barrier, this result support previous findings (Hajializadeh et al, 2013; Amarin et al, 2008; Austin et al, 2002; Keshavarz et al, 2011). Also these findings suggest the urgent need for increasing women's knowledge about cervical cancer and Pap smear test.

Concerning the HBM, the mean score of perceived severity, benefits, and health motivation in the women with history of Pap smear performance was higher than the women without history of this test. The results of the study are consistent with the several studies (Hajializadeh et al, 2013; Leyva et al, 2006; Abotchie & Shokar, 2009; Barata et al, 2008). The mean score of the perceived barriers in the women with the history of Pap smear performance was lower than the women without the history. This finding is consistent with this of other studies (Hajializadeh et al, 2013; Leyva et al, 2006; McFarland, 2003; Allahverdipour & Emami, 2008).

Among the subscales only perceived barriers predicted Pap smear performance. This finding is

consistent with other studies, as many studies have found perceived barriers as the most powerful predictor of Pap smear test (Hajializadeh et al, 2013; Austin et al, 2002; Amarin et al, 2008; Abotchie & Shokar, 2009; Allahverdipour & Emami, 2008; Chesun et al, 2012; Keshavarz et al, 2011). But, in contrast to HBM and consistent with the findings of other studies, perceived seriousness (Hajializadeh et al, 2013; Leyva et al, 2006), perceived susceptibility (McFarland, 2003; Austin et al, 2002), perceived benefits (Leyva et al, 2006; Chesun et al, 2012) didn't predict Pap smear performance. In a meta-analysis, perceived barrier was a stronger predictor of screening behaviors than perceived susceptibility and perceived benefits. One explanation for these findings may be this fact that many women understand that Pap smear successfully detects cervical cancer early and consider cervical cancer generally as a serious condition because it is fatal but they do not see themselves at risk and vulnerability to cervical cancer (Austin et al, 2002). Many researchers have not included health motivation in cervical cancer screening research because this variable has been recently added to the HBM. Most of the women perceive the test as beneficial and important for early detection of cervical cancer, even who had never Pap smear test believed that the test is beneficial and expressed the desire to be tested (Leyva et al, 2006; McFarland, 2003; Chesun et al, 2012).

In conclusion, for cancer education, more efforts to increase knowledge about cervical cancer, and eliminate the important barriers such as feeling embarrassment, fear of the test, lack of privacy, and painful Pap smear test, especially in low literate and women with low parity, are necessary.

The findings of this study may not be generalized to all Iranian women because this study was based on a convenience sampling, therefore community-based programs should be administered to different Iranian women groups to assess the actual rate of Pap smear performance and valid factors on them. Also, data completed by self report, inaccurate recall might adversely affect self-reports of Pap smear performance, which sometimes tend to be overestimated, nonetheless, some studies suggest that self-reports provide a fairly accurate indication of screening behaviors (Gordon et al, 1993).

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References

1. Abotchie PN, Shokar NK. Cervical cancer screening among college Students in Ghana: knowledge and health beliefs. *Int J Gynecol Cancer*. 2009; 19(3): 412-6.
2. Allahverdipour H, Emami A. Perceptions of cervical cancer threat, benefits, and barriers of Papanicolaou smear screening programs for women in Iran. *Women Health*. 2008; 47(3): 23-37.
3. Amarin ZO, Badria LF, Obeidat BR. Attitudes and beliefs about cervical smear testing in ever-married Jordanian women. *Eastern Mediterranean Health J*. 2008; 14(2): 389-97.
4. Austin LT, Ahmad F, McNally MJ, Stewart DE. Breast and cervical cancer screening in Hispanic women: A literature review using the Health Belief Model. *Women Health Issues*. 2002; 12(3): 122-8.
5. Avci IA. Factors associated with breast self-examination practices and beliefs in female workers at a Muslim community. *Eur J Oncol Nurs*. 2008; 12: 127-133.
6. Barata PC, Mai V, Howlett R, Gagliardi AR, Stewart DE. Discussions about self- obtained samples for HPV testing as an alternative for cervical cancer prevention. *J Psychosom Obstet Gynaecol*. 2008; 29(4): 251-257.
7. Brotto LA, ChouAY, Singh T, et al. Reproductive health practices among Indian, Indo-Canadian, Canadian East Asian, and Euro-Canadian Women: the role of acculturation. *J Obstet Gynaecol Can*. 2008; 30: 229-38.
8. Byrd TL, Chavez R, Wilson KM. Barriers and facilitators of cervical cancer screening among Hispanic women. *Ethn Dis*. 2007; 17: 129-134.
9. Chesun A, Harncharoen K, Taechaboonsermsak P, Siri S. Factors related with cervical cancer screening test among Thai muslim women in Satun province. *Asia J Public Health*. 2012; 3(3): 79-85.
10. Forouzanfar MH, Foreman KJ, Delossantos AM, et al. Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. *Lan-*

- cet. 2011; 378: 1461-84.
11. Glanz K, Rimer BK, Viswanath K. *Health behavior and health education: theory, research, and practice*. 4th edition, John Wiley & Sons, Inc, 2008.
 12. Gordon NP, Hiatt RA, Lampert DI. Concordance of self reported data and medical record audit for six cancer screening procedures. *J Natl Cancer Inst*. 1993; 85(7): 566-70.
 13. Guvenç G, Akyuz A, Acikel CH. Health Belief Model Scale for Cervical Cancer and Pap Smear Test: psychometric testing. *J Adv Nurs*. 2010; 67(2): 428-437.
 14. Hajjalizadeh K, Ahadi H, Jomehri F, Rahgozar M. Health beliefs and screening behavior of cervical cancer among the women of Bandar Abbas. *Life Sci J*. 2013; 10(1): 545-551.
 15. Keshavarz Z, Simbar M, Ramezankhani A. Factors for performing breast and cervical cancer screening by Iranian female workers: A qualitative model study. *Asian Pacific J Cancer Prev*. 2011; 12: 1517-22.
 16. Lawshe CH. A quantitative approach to content validity. *Pers Psychol*. 1975; 28(4): 563-575.
 17. Lee EE, Tripp-Reimer T, Miller AM, et al. Korean American Women's beliefs about breast and cervical cancer. *Oncol Nursing Forum*. 2007; 34: 713-20.
 18. Lee EE, Fogg L, Menon U. Knowledge and beliefs related to cervical cancer and screening among Korean American women. *West J Nurs Res*. 2008; 30(8): 960-974.
 19. Lee-Lin F, Mstat PM, Menon U, et al. Cervical Cancer Beliefs and Pap Test Screening Practices Among Chinese American Immigrants. *Oncology Nurs Forum*. 2007; 34(6): 1203-9.
 20. Leyva M, Byrd T, Tarwater P. Attitudes towards cervical cancer screening: A study of beliefs among women in Mexico. *Calif J Health Promot*. 2006; 4(2): 13-24.
 21. McFarland DM. Cervical cancer and Pap smear screening in Botswana: knowledge and perceptions. *Int Nurs Rev*. 2003; 50: 167-175.
 22. McFarland DM. Beliefs about the causes of cervical cancer in Botswana: implications for nursing. *Int Nurs Rev*. 2009; 56: 426-32.
 23. McFarland DM. Associations of demographic variables and the Health Belief Model constructs with Pap smear screening among urban women in Botswana. *Int J Women Health*. 2013; 5: 709-716.
 24. McMullin JM, De Alba I, Chávez LR, Hubbell FA. Influence of beliefs about cervical cancer etiology on Pap smear use among Latina immigrants. *Ethn Health*. 2005; 10(1): 3-18.
 25. Mosavel M, Simon C, Oakar C, et al. Cervical cancer attitudes and beliefs-a Cape Town community responds on World Cancer Day. *J Cancer Edu*. 2009; 24: 114-9.
 26. Noroozi A, Tahmasebi R. Factors Influencing Breast Cancer Screening Behavior among Iranian Women. *Asian Pacific J Cancer Prev*. 2011; 12: 1239-1244.
 27. Paskett ED, Tatum C, Rushing J, et al. Racial differences in knowledge, attitudes, and cancer screening practices among a triracial rural population. *Cancer*. 2004; 101: 2650-9.
 28. Pirzadeh A, Amidi Mazaheri M. The Effect of Education on Women's Practice Based on the Health Belief Model About Pap Smear Test. *Int J Prev Med*. 2012; 3(8): 585-90.
 29. Reis N, Bebis H, Kose S, Sis A, Engin R, Yavan T. Knowledge, behavior, and beliefs for cervical cancer and screening in Turkey. *Asian Pacific J cancer Prev*. 2012; 13: 1463-1470.
 30. Rezaie-Chamani S, Mohammad-Alizadeh-Charandabi S, Kamalifard M. Knowledge, attitudes and practice about Pap smear among women referring to a public hospital. *J Fam Reprod Health*. 2012; 6(4): 177-82.
 31. Rosenstock IM, Strecher VJ, Becker MH. Health Belief Model and preventive health behavior. *Health Educ Mono*. 1988; 2: 354-86.
 32. Safaei A, Khanlari M, Momtahan M, et al. Prevalence of high-risk human papillomavirus types 16 and 18 in healthy women with cytologically negative pap smear in Iran. *Indian J Pathol Microbiol*. 2010; 53: 681-5.
 33. World Health Organization. *Cervical Cancer Screening in Developing Countries. A report of WHO Consultation*. World Health Organization, Geneva, 2005.
 34. Young EQ, Davis MS. *Women's Health: A Primary Care Clinical Guide*. 3rd ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.

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Periodontal health status and Oral health behavior among the 5th year dental students of Medical faculty University of Nis

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Abstract

Introduction: Oral hygiene is considered as an important factor for maintaining oral health and general health. Inadequate implementation of oral hygiene care cause destruction of the supporting tissue of teeth, frequent occurrence of caries and its complications.

Aim: The aim of study was to evaluate oral health, periodontal status and hygiene habits of the 5th year students of Medical Faculty University of Nis.

Methods: Questionnaire was filled in by 43 students (20 men and 23 women). The oral cavity status and periodontal status was estimated by clinical examination conducted by one dentist.

Results: The subjects ranged from 21-28 years of age and overall mean age was 23.81 ± 1.59 years. The number of filled teeth were 7.14 ± 4.07 ; while the number of decayed teeth were 1.44 ± 1.72 . Plaque index according to Sillness and Loe was $Pi = 1.12 \pm 0.32$; supragingival Calculus index was $CI = 0.95 \pm 0.58$; subgingival calculus index was $CI = 0.08 \pm 0.28$. Gingival index showed mild gingival inflammation in all participants, while CPITN community periodontal index of treatment needs showed that basic periodontal therapy was necessary to be done. The majority of participants (69.77%) were brushing their teeth three times a day, but only 2.33% of participants were brushing their teeth once a day. The most frequent washing technique was combined (81.40% of participants). Single toothbrush is used for less than 3 months by majority of subjects (55.81%), while usage of additional instruments

of oral hygiene once a day is reported by 83.72% of participant. Usage of mouth rinse solution is reported by 48.84% of participants. More than half of participants (51.16%) consumed sweets every day. Current smokers were 34.88% while former smokers were 14.29% of participants. Researchers also noted that 23.26% were suffering from recurrent aphthous ulceration, 32.56% were suffering from viral infections, 18.60% were suffering from chronic disease and 41.46% had some bad habits like *finger nail biting*, grinding and clenching teeth. Various changes on tongue were found: Lingua plicata 18.60%, Lingua geographica 9.30%, Papillitis 9.30% and coated tongue 16.28%. Candidosis were found with prevalence of 2.33%. Angular lesions in the form of Cheilitis angularis were detected with prevalence of 6.98%.

Conclusions: Based on conducted questionnaire and analysis of obtained results it could be concluded that the oral health status of 5th year dental students of Medical Faculty University of Nis was satisfying. It is necessary to carry out additional procedures in terms of check-ups. The oral health education programs should be intensified to promote oral healthcare.

Key words: periodontal status, oral health, dental students

Introduction

Oral health is an integral component of general health. It can be defined as "a standard of health of the oral and related tissues which enables an individual to eat, speak, and socialize without

active disease, discomfort or embarrassment and which contributes to general well-being”(1). Oral health is important for physical and psychological well-being (2). There is evidence that oral health depends upon biological, social and environmental factors, mental and physical health (3-5). Research in the past few years has revealed the causal link between oral diseases and systemic diseases.

Oral health knowledge is considered to be an essential prerequisite for health-related practices (6), and studies have shown that there is an association between increased knowledge and better oral health (7, 8). Those who have assimilated the knowledge and feel a sense of personal control over their oral health are more likely to adopt self-care practices (9).

Oral health has also been found to profoundly influence the quality of life. Dental caries and periodontal disease are the highly prevalent diseases in many populations. Different studies reported variations in prevalence of caries and periodontal disease among different countries and among different sub-groups of the same society (10, 11). They are highly irreversible once they occur and also have complex etiology. Although primary preventive techniques exist, they do not confer total protection.

Oral health affects people physically and psychologically and influences how they grow, enjoy life, look, speak, chew, taste food and socialize, as well as their feelings of social well-being (12).

Students also represent part of this critical population. Experimental consumption of alcohol and cigarettes (13) combined with poor oral habits during this period of growing up results in greater incidence of caries and periodontal diseases (14).

It is important for students to create healthy foundation for long-term preserving of oral health by incorporating adequate attitudes and habits. Dental students, thanks to the improvements and perfection of their own behavior and attitudes towards oral health during their education (15-17) can certainly contribute to the population education.

A good quality of life is possible if students maintain their oral health and become free of oral disease. The level of oral health knowledge and practices of dental students is unknown and worthy of investigation. The Serbian students' oral health and hygiene still have been not sufficiently studied.

Aim

The aim of the study was to evaluate oral health, periodontal status and hygiene habits among the 5th year students of Medical Faculty of University of Nis.

Methods

The research was carried out on 43 dental students (fifth year of study). The study was conducted according to the protocol- Attachment 1. Questionnaire was filled in by 43 students (20 men and 23 women).

The survey procedures were designed to protect students' privacy and to allow anonymous participation. The oral cavity status and periodontal status was estimated by clinical examination conducted by one dentist with the use of a dental chair, with artificial lighting by means of a basic diagnostic set: a dental probe, a dental mirror and a WHO (World Health Organization) periodontal probe. Dental caries was diagnosed by visual examination, using a probe and a dental mirror utilizing the criteria recommended by the WHO.

Continuous (measurable) data were expressed as mean value \pm standard deviation (mean \pm sd). Discontinuous (attribute) data were presented as frequency and percentage.

Results

Out of 43 participants, 23 (53.49%) were female (Table 1).

Table 1. Gender structure of participants

Gender	Number of patients
Female	23 (53.49%)
Male	20 (46.51%)
Total	43 (100%)

The subjects ranged from 21 - 28 years of age and overall mean age was 23.81 ± 1.59 years.

The oral status in participants was showed in Table 2. The number of filled teeth were 7.14 ± 4.07 ; while the number of decayed teeth were 1.44 ± 1.72 .

Periodontal health status in participants was showed in Table 3. Oral Hygiene Indices Simplified (OHI-S) of Greene and Vermillion (1964) were

approximately the same: Plaque index according to Sillness and Loe (1964) $Pi=1.12\pm0.32$; supra-gingival Calculus index $CI=0.95\pm0.58$; subgingival calculus index $SCI=0.08\pm0.28$. Plaque index showed that dental plaque was covered more than one third, but less than two third of the tooth surface (Table 3).

Table 2. Oral status in participants (mean \pm sd)

Number of extracted teeth	1.35 \pm 1.51
Number of fixed bridges	0.19 \pm 0.59
Decayed teeth	1.44 \pm 1.72
Filled teeth	7.14 \pm 4.07
I class	3.93 \pm 2.47
II class	2.47 \pm 2.33
III class	0.42 \pm 1.05
IV class	0.00 \pm 0
V class	0.28 \pm 0.88
VI class	0.02 \pm 0.15

Table 3. Periodontal status in participants (mean \pm sd)

Pi	1.12 \pm 0.32
BI	1.00 \pm 0.31
Gi	1.00 \pm 0.31
Ci	0.95 \pm 0.58
SCI	0.08 \pm 0.28
PDI	4.07 \pm 0.26
CPITN	2.02 \pm 0.41

Gingival health evaluation was conducted by using gingival index according to Sillness and Loe (1964). Gingival index showed mild gingival inflammation in all participants, while CPITN community periodontal index of treatment needs showed that basic periodontal therapy was necessary to be done (Table 3).

Table 4. Results of maintaining oral hygiene and bad habits

Using of toothbrush	43		100.00%
Using of additional instruments of oral hygiene once a day (dental floss, interdental brushes)	36		83.72%
Using of mouth rinse solution	21		48.84%
Frequency of teeth brushing (1x, 2x, 3x)	1 (2.33%)	12 (27.91%)	30 (69.77%)
Brushing movements (\uparrow , \leftrightarrow , mixed)	5 (11.63%)	3 (6.98%)	35 (81.40%)
Changing of toothbrush (3m, 6m, 1 year)	24 (55.81%)	16 (37.21%)	3 (6.98%)
Consumption of sweets (everyday, sometimes)	22 (51.16%)		21 (48.84%)
Active smokers	15		34.88%
Former smokers	4		14.29%
Drugs using	3		7.14%
Chronic disease	8		18.60%

All of 43 participants (100%) were using toothbrush and toothpaste for oral hygiene, daily. The majority of participants (69.77%) were brushing their teeth three times a day, but only 2.33% of participants were brushing their teeth once a day. The most frequent washing technique was combined (81.40% of participants). Single toothbrush is used for less than 3 months by majority of subjects (55.81%), while usage of additional instruments (dental floss and interdental brushes) of oral hygiene once a day is reported by 83.72% of participant and usage of mouth rinse solution is reported by 48.84% of participants (Table 4).

More than half of participants (51.16%) consumed sweets every day. Current smokers were 15 participants (34.88%). Former smokers were 4 participants (14.29%). The percent of the participants who were suffering from chronic disease were 18.60% (Table 4).

Table 5. Health status of oral mucosa in participants

Recurrent aphthous ulceration	10	23.26%
Viral infection	14	32.56%
Bad habits (fingernail biting, chewing pens, grinding and clenching teeth)	17	41.46%
Lingua plicata	8	18.60%
Lingua geographica	4	9.30%
Papillitis	4	9.30%
Coated tongue	7	16.28%
Lingua glabra	0	0.00%
Cheilitis angularis	3	6.98%
Candidosis	1	2.33%

According to anamnesis, it was observed that 23.26% of participants were suffering from recurrent aphthous ulceration, 32.56% of participants were suffering from viral infections. Researchers also noted some bad habits like *finger nail biting*, chewing pens, grinding and clenching teeth in 41.46% of participants.

Various changes on tongue were found in participants: Lingua plicata -18.60%, Lingua geographica -9.30%, Papillitis 9.30% and coated tongue -16.28%. Candidosis were found in participant with prevalence of 2.33%. Angular lesions in the form of Cheilitis angularis were detected in participants with prevalence of 6.98% (Table 5).

Discussion

This study revealed that oral hygiene status of students of 5th year of Medical faculty, University of Nish were satisfying, according to results of oral hygiene indices which were low. Evidence had showed that strong knowledge of oral health demonstrates better oral care practice (18).

It is advised by the American Dental Association that the teeth should be brushed at least twice a day (19) and tooth floss should be used at least once a day (20). In this study, of all the students, observed to perform oral care, the rate of the ones stating to perform it three times a day was 69.77%. The rate was observed to be higher than that of Kirtiloglu et al. (21) (68%) obtained in a study carried out on non-dental university students in Turkey, but in Rimondini et al. (22) study, the rate was higher (92.1%) than in this study. The rate for daily flossing (83.72%) was higher than those reported in other studies from Canada (23) (22.3% in 1992), the USA (24) (31.6% in 1989), and Singapore (25) (35.0%).

Different studies (26,27) estimated the links between oral health and oral hygiene habits. In this study, plaque index was determined as mean value \pm standard deviation (1.12 ± 0.32) and it was approximately the same like in Akar et al. (28) study where plaque index was 1.01 (± 0.40). No relationship was observed between the plaque index value and the methods and frequencies of oral health care. Only 34.88% of students were current smokers and 14.29% were former smokers, which confirmed the fact that students are familiar

with the importance of bad influence of cigarette smoke on their health.

Oral health is important component of general well being and it greatly affects quality of life of an individual (29). It is important for adolescents to create healthy foundation for long-term preserving of oral health by incorporating adequate attitudes and habits. Dental students, thanks to the improvements and perfection of their own behavior and attitudes towards oral health during their education (30- 32) can certainly contribute to the population education. This is especially important in case of their colleagues from other faculties who often lack the proper awareness about oral health and its importance. Dental students should be a role-model for their colleagues and patients, teaching them the importance of oral hygiene habits and attitudes based on self protection principles (frequent tooth brushing, reduced consumption of refined carbohydrates, fluoride usage) and regular utilization of dental services (33).

Conclusion

Based on conducted questionnaire and analysis of obtained results it could be concluded that the oral health status of the 5th year dental students of Medical Faculty University of Nis was satisfying. It is necessary to carry out additional procedures in terms of check-ups, basic periodontal therapy and remotivation. The oral health education programs should be intensified to promote oral healthcare a lifelong practice.

References

1. Skeie M, Skaret E, Espelid I, Misvær N. Do public health nurses in Norway promote information on oral health? *BMC Oral Health* 2011; 11: 23.
2. Bopp ML. The Surgeon General's Report on Oral Health Dental Hygiene: You can Depend on Us. *J Dent Hygiene* 2001; 75(IV): 263.
3. Dolan T, Gooch B, Bourgue L. Associations of self-reported dental health and general health measures in the Rand Health Insurance Experiment. *Community Dent Oral Epidemiol* 1991; 19: 1-8.

4. Disney JA, Graves RC, Stamm JW, et al. The university of North Carolina caries risk assessment study: further developments in caries risk prediction. *Community Dent Oral Epidemiol.* 1992; 20: 64-75.
5. Osterberg T, Lundgren M, Emilson CG. Utilization of dental services in relation to socioeconomic and health factors in the middle aged and elderly Swedish population. *Acta Odontol Scand* 1998; 56(1): 41-7.
6. Rimondini L, Zolfanelli B, Bernardi F, Bez C Self-preventive oral behavior in an Italian university student population *J Clin Periodontol* 2001; 28: 207-211.
7. Hamilton ME, Coulby WM Oral health knowledge and habits of senior elementary school students *J Publ Health Dent* 1991; 51: 212-218.
8. Ľstrřm AN, Masalu JR. Oral health behavior patterns among Tanzanian university students: a repeat cross-sectional survey *BMC Oral Health* 2001; 1: 1-12.
9. Saito A, Kikuchi M, Ueshima F, Matsuoto S, Hayakawa H, et al. Assessment of oral self-care in patients with periodontitis: a pilot study in a dental school clinic in Japan. *BMC Oral Health* 2009; 9: 27.
10. Global Oral Health Data Bank. Geneva: World Health Organization; 2001.8. Marthaler TM, O'Mullane DM, Vrbic V. The prevalence of dental caries in Europe 1990 – 1995. *Caries Res* 1996; 30: 237 – 255.
11. Health and health behavior among young people. Currie C, Hurrelmann K, Settertobulte W, editors. WHO; 2000.
12. Sheiham A. Oral Health, General Health and Quality of life. *Bull World Health Org* 2005; September: 83(9): 644. Epub 2005 September 30.
13. Petersen PE, Jiang H, Peng B, Tai BJ, Bian Z. Oral and general health behaviours among Chinese urban adolescents. *Community Dent Oral Epidemiol.* 2008; 36(1): 76–84.
14. Al-Hussaini R, Al-Kandari M, Hamadi T, Al-Mutawa A, Honkala S, Memon A. Dental health knowledge, attitudes and behaviour among students at the Kuwait University Health Science Centre. *Med Princ Pract.* 2003; 12(4): 260-5.
15. Leao A, Sheiham A. Relation between clinical dental status and subjective impacts on daily living. *J Dent Res.* 1995; 74(7): 1408-13.
16. Rong WS, Wang WJ, Yip HK. Attitudes of dental and medical students in their first and final years of undergraduate study to oral health behaviour. *Eur J Dent Educ.* 2006; 10(3): 178-84.
17. Dagli RJ, Tadakamadla S, Dhanni C, Duraiswamy P, Kulkarni S. Self reported dental health attitude and behavior of dental students in India. *J Oral Sci.* 2008; 50(3): 267-72.
18. Smyth E, Caamano F, Fernández-Riveiro P. Oral health knowledge, attitudes and practice in 12-year-old schoolchildren. *Med Oral Patol Oral Cir Bucal,* 2007; 12(8): E614-E620.
19. American Dental Association. Basic brushing. Chicago: American Dental Association, Division of Communications; 1996.
20. American Dental Association. Basic flossing. Chicago: American Dental Association, Division of Communications; 1984.
21. Kirtiloğlu T, Yavuz US. An assessment of oral self-care in the student population of a Turkish university. *Public Health.* 2006 Oct; 120(10): 953-7.
22. Rimondini L, Zolfanelli B, Bernardi F, Bez C. Self-preventive oral behavior in an Italian university student population. *J Clin Periodontol.* 2001 Mar; 28(3): 207-11.
23. Payne BJ, Locker D. Relationship between dental and general health behaviors in a Canadian population. *J Public Health Dent.* 1996 Summer; 56(4): 198-204.
24. Ronis DL, Lang WP, Farghaly MM, Passow E. Tooth brushing, flossing, and preventive dental visits by Detroit-area residents in relation to demographic and socioeconomic factors. *J Public Health Dent.* 1993 Summer; 53(3): 138-45.
25. Soh G. Racial differences in perception of oral health and oral health behaviours in Singapore. *Int Dent J.* 1992 Aug; 42(4): 234- 40.
26. Aleksejūniene J, Eriksen HM, Holst D. Variation in caries treatment experience in 35-44-year-old Lithuanians. *Community Dent Oral Epidemiol.* 2000; 28: 365-64.
27. Aleksejuniene J, Holst D, Grytten JI, Eriksen HM. Causal patterns of dental health in populations. An empirical approach. *Caries Res* 2002; 36(4): 233–40.
28. Akar GC, Uluer H, Ozmutaf NM, Ozgur Z, Gokce B. An Assessment of Oral Health Status and Dental Plaque of Non-Dental School Students in Turkey. *Acta Stomatol Croat.* 2010; 44(1): 26-33.
29. Inglehart MR, Bagramian RA, NP - editors. Oral health – related quality of life. Chicago: Quintessence Publishing; 2002.

30. Leao A, Sheiham A. Relation between clinical dental status and subjective impacts on daily living. *J Dent Res.* 1995; 74(7): 1408-13.
31. Rong WS, Wang WJ, Yip HK. Attitudes of dental and medical students in their first and final years of undergraduate study to oral health behaviour. *Eur J Dent Educ.* 2006; 10(3): 178-84.
32. Dagli RJ, Tadakamadla S, Dhanni C, Duraiswamy P, Kulkarni S. Self reported dental health attitude and behavior of dental students in India. *J Oral Sci.* 2008; 50(3): 267-72.
33. Al Omari QD, Hamasha AA. Gender-specific oral health attitudes and behavior among dental students in Jordan. *J Contemp Dent Pract.* 2005; 6(1): 107-14.

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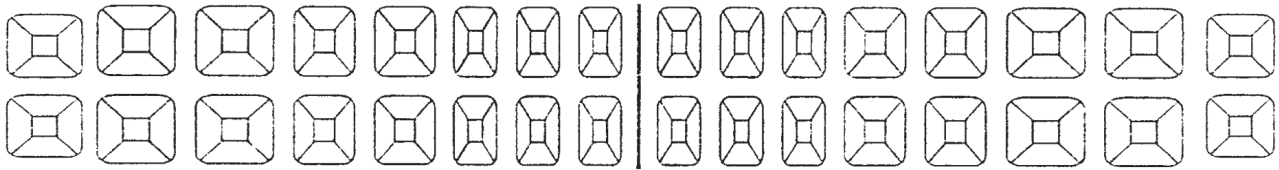
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Attached 1

Gender Male Female Age _____



Number of extracted teeth _____

Number of fixed bridges _____

Filled teeth _____

I kl _____, II kl _____, III kl _____, IV kl _____, V kl _____

Number of fixed bridges _____

Periodontal Status

PI _____

BI _____

CPITN _____

CI _____

Gi _____

SCI _____

PDI _____

Questionary

- | | | | |
|---|---------------------|------------|------------|
| 1. Using toothbrush? | + | - | |
| 2. Using of mouth rinse solution? | + | - | |
| 3. Using of additional instruments of oral hygiene once a day (dental floss, interdental brushes) | + | - | |
| 4. How many times per day You brushing teeth? | 1x | 2x | 3x |
| 5. Brushing movements? | ↑ ↔ | combinated | |
| 6. Changing of toothbrush | 3m | 6m | 1year more |
| 7. Sweet consumption | every day sometimes | | |
| 8. Active smoker | + | - | |
| 9. Former smoker | + | - | |
| 10. Using Medicaments | + | - | |
| 11. Which one? | | | |
| 12. Chronic disease | + | - | |
| 13. Which one? | | | |
| 14. Afte | + | - | |
| 15. Viral infections | + | - | |
| 16. Bad habits (fingernail biting, chewing pens etc) | + | - | |
| 17. Lingua plicata | + | - | |
| 18. Lingua geographica | + | - | |
| Papillitis | + | - | |
| Coated lingua | + | - | |
| Cheilitis angularis | + | - | |
| Candidosis | + | - | |
| 19. Additional _____ | | | |

Drug susceptibility of *E. coli* strains isolated from patients with UTI by disc diffusion agar method in Salmas city of Iran

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Abstract

Background and objectives: UTIs, are the most common bacterial infections in childhood while common in adults and women are more vulnerable to UTI development than men. Since the delay in diagnosis and suitable diagnosis can bring about irreversible outcomes such as renal chronic failure, it is necessary to treat UTI after its diagnosis.

As bacteria sensitivity to antibiotics vary over time and from place to place and suitable antibiotics is necessary to the treatment of UTI, the present study was carried out to identify the most effective antibiotic against bacteria producing UTI in Salmas.

Methods: this study was done on 573 patients referring to one of private laboratories in Salmas city, of whom 396 and 177 were women and men, respectively. The urine samples taken from the patients were cultivated in the EMB and Blood Agar environments. By means of biochemical tests, the UTI-inducing bacteria were identified and antibiogram was done only on *E. coli* isolates. Of positive cultures, (the cultures with over 10⁵ colonies) half of McFarland was provided and antibiogrammed in the culture environment of Mueller-Hinton agar. The diameter of auras of non-growth was measured with specific ruler and the results were divided into sensitive, semi-sensitive and resistant groups based on CLSI standard table.

Results: Of the total 573 samples, 103 were positive (68 women and 35 men) of which 70 samples (68%) were related to *E. coli*. therefore, the most likely cause of UTI was determined to be *E. coli* other isolated bacteria were: *Staphylococcus saprophyticus*, 13 samples (12.6%), *Enterobacter* (6.8%), *proteus* 5 samples (4.8%), and *Klebsiella pneumoniae* 4 samples (3.9%), *streptococcus* and *pseudomonas* 2 samples (1.19%).

Conclusion: *E. coli* is the most common pathogen of urine infection but its drug sensitivity is different in different regions. In Salmas city, the most effective antibiotics are nitrofurantoin, ceftriaxone, amikacin, nalidixic acid, respectively, against *E. coli* which has the greatest resistance to ampicillin, and co-trimoxazole.

Key words: *E. coli*, UTI, drug sensitivity, Salmas

Introduction

Although most bacterial diseases have been disappeared by preventive actions such as vaccination, UTI has remained as the most common bacterial infection among children and adults and a big health problem all over the world (1). The rate of incidence of UTI is greater in females than in males due to the fact that the urine tract is shorter in females which increases the access of bacteria to bladder and that the females' urine tract opens near the source of bacteria (vagina) (2).

The most common cause of UTI (80%) is the presence of *E. coli* strains in the colon but other bacteria such as *Klebsiella*, *proteus*, *pseudomonas*, *Enterobacter*, *Staphylococcus saprophyticus*, and protozoans may result in UTI (1-9, 11, 13, 14). UTI is of great importance in the breast fed and children because it is unknown and without any sign (2, 3, 6, 15). Therefore, lack of diagnosis and duly treatment can bring about chronic renal failure, tissue damage, scar and disorder of renal performance. The rapid treatment of UTIs by suitable drugs before the result of culture and antibiogram is determined plays an important role in prevention from producing scars in kidneys. Since the drug sensitivity and resistance UTI-inducing bacteria are different in different places to antibiotics, the present study was carried out to identify

the most effective antibiotics against UTI- inducing bacteria in Salmas so that suitable prescription of antibiotics reduces then undue consumption of other antibiotics.

Material & methods

The present study was done on 573 patients suspicious to UTI who referred to private laboratories in Salmas in 2012. The clean catch mid stream specimens taken from patients were cultivated in environments of Blood Agar and EMB and after 48 h of incubation, the positive cultures were specified (>105 CFU/ml). After biochemical tests such as indole, methyl red, citrate, catalase test, coagulase, were done and TSI culture environment was used, the UTI- inducing bacteria were identified at the extent of genus. As *E.coli* was supposed to be the most common pathogen, the antibiotic sensitivity test was done on *E.coli* specimens.

As Agar diffusion disc method is one of the popular method confirmed by CLSI, it can be used to determine the drug sensitivity of microorganism if valid antibiotic discs are applied (17). The present study was carried out through Iranian discs (padtan Teb) in Kirby-Bauer method on *E.coli* specimens. To do so, *E.coli* containing cultures were used to provide bacterial suspension according to McFarland No 0.5 tube. Using sterile swap, we cultivated some of the obtained suspension on Mueller-Hinton agar plate. Then, with sterile pence, Iran-made antibiotic discs (Padtan Teb) containing & discs of nitrofurantoin, nalidixic acid, amikacin, gentamicin, gentamicin, ceftriaxone, ampicillin, co-trimoxazole were place on the plate and zones was measured with special ruler and the results were divided into sensitive, intermediate, and resistant groups based on CLSI for each antibiotic. *E.coli* ATCC 25922 was used as quality control.

Results

Of the 573 patients referring to laboratory, 396 (69/11%) and 177 (30/89%) were female and male, respectively. Of the 573 samples of culture, 103 were positive (cultures containing 105 CFU/ml or more) of which 68 and 35 were females and males, respectively. The contamination rate was 1/94 for female to males (approximately 2 times) (Table 1).

Table 1. Total number of patients according to sex and their contamination

percent	N of infected	percent	N	Sex
66	68	69.11	369	female
34	35	30.89	177	male
100	103	100	573	sum

The most common pathogen isolated from patients samples was *E.coli* which was allocated to of 103 positive samples. (68%). The remaining 32% belonged to bacteria of *Staphylococcus saprophyticus*, *Enterobacter spp*, *Proteus spp*, *Klebsiella spp*, *Streptococcus spp* and *Pseudomonas spp* the number and percentage of which are shown in table 2.

Table 2. The frequency of isolated bacteria from positive cultures

Bacteria	Frequency	
	N	percent
<i>E. coli</i>	70	68%
<i>Staphylococcus saprophyticus</i>	13	12.62%
<i>Enterobacter spp</i>	7	6.80%
<i>Proteus spp</i>	5	4.85%
<i>Klebsiella spp</i>	4	3.88%
<i>Streptococcus sp</i>	2	1.94%
<i>Pseudomonas spp</i>	2	1.94%
Sum	103	100%

As the youngest and oldest contaminated subject were 2-65 years old, the patients were classified in 7 age groups of 1-10, 11-20, 21- 30, 31-40, 41-50, 51-60, and 61-70, the frequency of contaminated of each group is shown in table 3 in terms of sex.

As seen, the greatest number of contaminated subject was in 1-10 age group at 63, with 40 females and 23 males. The least number of was at 11-20 age group at 3, all of whom were female. The age group of 51-60 stood at the second place in terms of contamination at the number of 12, 8 and 4 of whom were female and male, respectively. As seen in table 3, the number of contaminations is higher among females than male in all groups.

As mentioned before, regarding *E.coli* to be the most common pathogen of UTI, the antibiotic sensitivity test was done only on *E.coli* specimens.

The antibiotics used were nitrofurantoin (300 µg), nalidixic acid (30 µg), amikacin (30 µg), gentamicin (10 µg), ciprofloxacin (5 µg), ceftriaxone (30 µg), ampicillin (10 µg) and co-trimoxazole

Table 3. The frequency of contaminated subjects in age groups separated by sex. (NR : not reported)

Percent	Percent	Male	Female	sex Age groups
22.33	38.83	23	40	1-10
0	2.91	NR	3	11-20
1.94	3.88	2	4	21-30
1.94	4.85	2	5	31-40
2.91	3.88	3	4	41-50
3.88	7.77	4	8	51-60
1	3.88	1	4	6170
34	66	35	68	Sum

(1.25 µg/23.75 µg) and the results of antibiogram were as the following. Of the 70 positive cultures of *E.coli*, 61 were sensitive to nitrofurantoin. The number of resistant strains were 2 and that of intermediate was 7. The least effective antibiotic was co-trimoxazole for which 18, 9 and 43 were reported to be sensitive, intermediate and resistant, respectively. The results of antibiogram are shown in table 4.

Table 4. The results of antibiogram of 70 *E.coli* categories (the numbers are in percentage). S: Sensitive I: Intermediate R: Resistant

Drug	S	I	R
Nitrofurantoin	87))61	10))7	3))2
Ceftriaxone	84))59	6))4	10))7
Amikacin	53))37	26))18	21))15
Nalidixic acid	49))34	10))7	41))29
Gentamycin	45))32	19))6	46))32
Ciprofloxacin	38))27	16))11	46))32
Ampicillin	30))21	17))12	53))37
Co-trimoxazole	26))18	13))9	61))43

Regarding table 4, the drugs of Nitrofurantoin, Ceftriaxone, Amikacin, and Nalidixic acid are the most effective against *E.coli*, respectively. More than half of *E.coli* cases showed no resistance to Ampicillin, and co-trimoxazole.

Discussion

UTIs are a serious health problem which millions of people suffer from yearly(1, 2, 10, 25). In the U.S.A, 3.5 billion dollars is spent for the treatment of UTI annually(10).

UTIs are the second common infection in body which are more common in females, in that the-

ir incidence is 3-5% and 1% in women and boys, respectively(16, 19). UTIs are seen in all age ranges but they are of great importance in the breast-fed and children because it is symptom-free and delayed treatment can bring about chronic renal failure, tissue damage, scar, and disorder in kidney operation(2, 3, 6, 15). The rapid treatment of UTIs with suitable medication before the result of antibiogram plays unimportant role in preventing from the mentioned symptoms.

It has been proved that *E.coli* is the most common bacterium producing UTIs (1-8, 13-20, 23-32). In the present study on 573 patients referring to a private laboratory in Salmas, this issue was confirmed for *E.coli* to be the most common pathogen of UTI (68%).

In Fesharaki Nia et al.(19) study, *E.coli* was involved in 75% of UTI in children.

In Rolf Beetz et al. (20) study in Germany, *E.coli* was known to be the most common pathogen at 63%, in consistency with ours. they expressed that resistance to Ampicillin has increased in a variety of places remarkably during the last 20 years. In Fatemeh Fallah et al.(16) study, *E.coli* is reported to be the most common pathogen isolated from UTI at 75%. In our study, the second most common pathogen is *Staphylococcus saprophyticus* the same as that in Saraj et al.(21) study in Ahvaz. In our study, the newborn and children under 10 years old consisted the greatest number of the subject inflicted with UTI (61.16%). The rate of infection with UTI is different for children in the studies. For example, in Fesharaki Nia et al.(19) study it was 73.8% while in Sorkhi et al.(22), Ghadamli et al.(23), Ghazi Moghadam et al.(24), it was 81%, 86.5% and 58%, respectively.

Despite the different rates of infliction, *E.coli* has been reported to be the most common pathogen.

The drug resistance to microorganisms producing UTI is increasing and the bacteria sensitivity to antibiotics is changing; therefore, this study aimed at determining the most effective antibiotic against UTI in Salmas to get a way to reduce taking antibiotics. For example, in V, Kumamoto et al.(25) study in Japan (2000), the most effective medications were co-trimoxazole, and ampicillin while in our study these were the least effective ones. Fatemeh Fallah reported(16) the resistance to co-trimoxazole as 55.6% which is consistent with our study. Fesharaki Nia et al.(19) reported the sensitivity of *E.coli* to ceftriaxone and co-trimoxazole at 71.4% and 69%. Reygaert Wanda in the USA reported(11) drug resistance of *E.coli* to Nitrofurantoin, and Ceftriaxone negligible at 6% while the greatest resistance was to Ampicillin. (78%). The resistance to Ciprofloxacin was reported to be 41%, consistent with our study.

In Younis et al.(26) Study, the maximum resistance is related to ampicillin & co-trimoxazole comparing the results of studies carried out in Iran and other parts of the world, one can conclude that the efficacy of each drug differs from place to place, showing that investigation of drug sensitivity of bacteria must be performed regularly so that the most effective medication is specified to prevent treatment failure. Akbari-Nakhjavani et al.(27) study confirms this claim. These researchers studied the effect of Nalidixic acid, ofloxacin, Norfloxacin and Ciprofloxacin on the *E. Coli* isolated from hospitalized patients in several hospitals.

In this research, Nitrofurantoin, and Ceftriaxone were reported to be the most effective drugs and *E.coli* showed the least resistance to these two drugs. In Rahem Khoshbakht et al. (28) Study, *E.coli* was the most common pathogen of UTI. In their study, Nitrofurantoin and Ciprofloxacin were the most effective drug and Ampicillin and co-trimoxazole the least effective drugs, as confirmed by our study. The *E.coli* sensitivity to Nitrofurantoin was 90.78%. In another study by Dr. Sedighi et al.(29) in Hamedan, Nitrofurantoin was determined to be the most effective drug against *E.coli*.

In K.D. Deshpande et al. (17) Study in India, *E.coli* was recognized to be the most common bacterium of UTI at 59.2% but their antibiogram

result showed the *E.coli* sensitivity to Ceftriaxone at 36.4%, in contrast with 84% in our study. Instead, the *E.coli* sensitivity to Nitrofurantoin has been reported to be 84%.

Due to sensitivity of *E.coli* to Nitrofurantoin, the low consumption of this drug and its resistance to ampicillin are attributed to cellular wall (presence of impermeable external membrane), existence of 10 Betalactamase enzyme in *E.coli* strains or the wide consumption of this drug.

In Allen. R et al.(30) study in England, the resistance to Ampicillin was 53% in consistence with our study. Although the effect of antibiotics is different in vitro and in vivo conditions, our study showed that over 80% of UTIs in Salmas can be treated with administration of Nitrofurantoin and Ceftriaxone. Also, treatment with co-trimoxazole and ampicillin may fail in 70% of cases. Sensitivity to ampicillin and Nalidixic acid was acceptable while it is suggested that the tests to investigate the medication sensitivity are performed regularly as the sensitivity and resistance of UTI-inducing agents to antibiotics vary since the greatest amount of UTI is seen in under-eleven-year age range, it is worth mentioning that children may not express their concern at this age. Therefore, the parents are advised to refer to medical labs once a year to test their children for the amount of UTI. The parents' inattention may bring irreversible outcomes.

Conclusion

It is undoubted that *E.coli* is the major pathogen of UTIs. The studies have shown that medication sensitivity of this bacterium differs from a city to another city. The physicians of Salmas are recommended to introduce and refer their patients for urine culture and antibiogram to labs before administering antibiotics to their patients so that antibiotics are not taken unduly. They must base their prescription on *E.coli* and prescribe the most effective drugs consisting of Nitrofurantoin, Ceftriaxone, and Nalidixic acid. The resistance of *E.coli* to Ampicillin and co-trimoxazole was seen to be high although there is no significance difference in terms of study place.

References

1. Bodaghi E. About Urinary Tract Infection. *Iranian Journal of Pediatric Society*, 2010; 2(1): 1-3.
2. Dielubanza JE, Schaeffer JA. Urinary Tract Infections in Women. *Medical Clinics of North America*, 2011; 97(1): 27-41.
3. Finnell SM, Carroll AE, Downs SM. Technical report - diagnosis and management of an initial UTI in febrile infants and young children. *Pediatrics*, 2011; 128(3): 749-770.
4. Funfstuck R, Ott U, Naber GK. The interaction of urinary tract infection and renal insufficiency. *International Journal of Antimicrobial Agents*, 2006; 28S: S72-S77.
5. Indu S, Deepjyoti P. Prevalence of community acquired urinary tract infections in silchar medical college, Assam, India and its antimicrobial susceptibility profile. *Indian Journal of Medical Sciences*, 2012; 66(11): 273-279.
6. Yashwant K, Shivani S, Anshu Sh, Kavaratty Raju Mani. Antibigram and characterization of resistance markers among *Escherichia coli* Isolates from urinary tract infections. *J Infect Dev Ctries*, 2013; 7(7): 513-519.
7. Heffner AV, Gorelick HM. Pediatric Urinary Tract Infection. *Clinical Pediatric Emergency Medicine*, 2008; 9: 233-237.
8. Matthews SJ, Lancaster WJ. Urinary Tract Infections in the Elderly Population. *The American Journal of Geriatric Pharmacotherapy*, 2011; 9(5): 286-309.
9. Nateghian AR, Robinson LJ, Mohandessi S, Hooman N. Resistance pattern of breakthrough urinary tract infections in children on antibiotic prophylaxis. *Journal of Infection and Public Health*, 2009; 2: 147-152.
10. Mittal R, Aggarwal S, Sharma S, Chhibber S, Harjai K. Urinary tract infections caused by *Pseudomonas aeruginosa*: A minireview. *Journal of Infection and Public Health* 2009; 2: 101-111.
11. Wanda R, Ilir J. Green tea as an effective antimicrobial for urinary tract infections caused by *Escherichia coli*. *Frontiers in Microbiology* 2013; 4(article 162): 1-4.
12. Renuart JA, Goldfarb MD, Mokomane M, Tawana OE, Narasimhamurthy M, et al. Microbiology of Urinary Tract Infections in Gaborone, Botswana. *PLOS ONE*, 2013; 8(3): 1-6.
13. Inês L, Teresa R, António R, Adelaide A. Frequency and antimicrobial resistance patterns of bacteria implicated in community urinary tract infections: a ten-year surveillance study(2000–2009). *BMC Infectious Diseases*, 2013; 13(9): 1-14.
14. Arjunan M, Al-Salamah AA, Amuthan M. Prevalence and antibiotics susceptibility of uropathogens in patients from a rural environment, Tamilnadu. *American Journal of Infectious Diseases*, 2010; 6: 29–33.
15. Sadari H, Owlia P, Jalali Nadoushan MR, Zaeri F, Zandieh E. A 3-Year Study Of Demographic Characteristics Of Patients With Urinary Tract Infection, Microbial Etiology, And Susceptibility Of Isolated Bacteria To Antibiotics In Shaheed Mostafa Khomeini Hospital. *Iranian Journal of Pathology*, 2006; 1(3): 99-104.
16. Fallah F, Behzadnia H, Moradi A, Eslami G, Sharifian M, Rafiee S, et al. Antimicrobial resistance pattern in urinary tract infections in children on continuous ambulatory peritoneal dialysis. *Iranian Journal of Clinical Infectious Diseases* 2008; 3(3): 155-159.
17. Deshpande KD, Pichare AP, Suryawanshi NM, Davane MS. Antibigram of gram negative uropathogens in hospitalized patients. *International Journal of Recent Trends in Science And Technology*, 2011; 1(2): 56-60.
18. Ronald AR, Nicolle LE, Stamm E, Krieger J, Warren J, Schaeffer A, et al. Urinary tract infection in adults: research priorities and strategies. *International Journal of Antimicrobial Agents*, 2001; 17: 343–348.
19. Fesharakinia A, Malekaneh M, Hooshyar H, Aval M, Gandomy-Sany F. The survey of bacterial etiology and their resistance to antibiotics of urinary tract infections in children of Birjand city. *Journal of Birjand University of Medical Sciences*. 2012; 19(2): 208-215.
20. Beetz R, Westenfelder M. Antimicrobial therapy of urinary tract infections in children. *International Journal of Antimicrobial Agents*, 2011; 38S: 42-50.
21. Saraj M, Mowla K, Ghorbani A, Etemadi A, Cheraghy M, Mahmoodlo A, et al. Identification of Out-patient Urinary Pathogens and Antibiotic Susceptibility Pattern in Ahwaz, Iran 2002-2003. *Yafteh*. 2005; 6(4): 41-47.
22. Sorkhi H, Jabbarian Amiri A, Askarian A. *Escherichia Coli* and Drug Sensitivity in Children with Urinary Tract Infection. 3. 2005; 14(54): 23-28.
23. Ghadamli P, Mokhlesi P. Survey of bacterial and antibiotic susceptibility of urinary tract infections in infants and children. *Teb va Tazkiyeh*. 1998; 28: 8-14.

24. Ghazi Moghadam B, Ghabsami A, Vakili M. Drug resistance in bacterial isolates from urinary tract infections in Gorgan. *The Iranian Journal Urology*. 2002; 9(35): 29-34.
25. Kumamoto V, Tsukamoto T, Matsukawa M. comparative studies on activities of antimicrobial Organisms isolated from patients with urinary infections. *Jpn J Antibiot*, 2002; 55: 598-655.
26. Younis N, Al-Nader M, Jbar I, Mardeni R. Uropathogens and their antibiotic susceptibility among children with urinary tract infection treated at Prince Hashem Bin Al-Hussein hospital. *JRMS*. 2010; 17(2): 41-5.
27. Akbari Nakhjavani F, Mirsalehian A, Hamidian M, Kazemi B, Mirafshar M, Jabal Ameli F, et al. Antimicrobial susceptibility testing of *Escherichia coli* strains isolated from urinary tract infections to fluoroquinolones and detection of *gyrA* mutations in resistant strains. *DARU*, 2007; 15(2): 94-99.
28. Khoshbakht R, Salimi A, Aski HS, Keshavarzi H. Antibiotic Susceptibility of Bacteria Isolated from Urinary Tract Infections in Karaj, Iran. *Jundishapur J Microbiol*, 2013; 6(1): 86-90.
29. Sedighi I, Solgi A, Alikhani MY, Emad Momtaz H, Mihani F. Comparison of Two Different Disk Diffusion Agar Tests in Determination of Antibiotic Susceptibility for E-Coli Isolated from Urinary Tract Infection in Pediatrics. *Scientific journal of Hamedan university of medical sciences & health services*, 2010; 17(1): 17-20.
30. Watson RA. Pediatric Urinary Tract Infection. *EAU Update Series*, 2004; 2: 94-100.
31. Saifi M, Pourshafie MR, EshraghianMR, Dallal MMS. Anti-Microbial Resistance of Enterococci Isolated from Urinary Tract Infections in Iran. *Iranian Biomedical Journal*, 2008; 12(3): 185-190.
32. Dubrovsky AS, Foster JB, Jednak R, Mok E, McGillivray D. Visibility of the urethral meatus and risk of urinary tract infections in uncircumcised boys. *CMAJ*, 2012; 1-8.

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Prevalence of obesity and relationship with body mass index and symptoms of asthma in adolescents

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Abstract

To investigate the relationship between Body Mass Index (BMI) and asthma symptoms in adolescents between 13 and 14 years, to estimate the prevalence of obesity in this age group. This is a cross-sectional study with a quantitative approach which was rated the Body Mass Index (BMI) and applied the Questionnaire International Study of asthma and Allergies in Childhood (ISAAC) phase III (asthma module) to determine the prevalence of asthma and related symptoms, as well as its severity in 85 teenagers. According to the assessment of asthma in relation to BMI, it was found that there were significant findings, as well as in males and females. However, the association between BMI and asthma symptoms, there was a significant association to present as disturbed sleep and impaired speech.

Conclusions: In this sample the prevalence of obesity was low, this fact may have contributed to the nonsignificant findings between asthma and BMI.

Key words: Obesity; Body Mass Index; Asthma.

Introduction

Asthma is a chronic inflammatory disease having as main characteristic the airway hyperresponsiveness associated with variable airflow limitation that may be reversible either spontaneously or with treatment [1]. It is one of the most common childhood diseases, chronic respiratory disease constituting the most commune among children and adolescents. According to the Department of

the Unified Health System (DATASUL) asthma in 2005 was responsible for 18.7% of hospitalizations for problems respiratórios [2].

Predisposing factors for the onset of asthma symptoms are numerous, among them stand out respiratory infections, exposure to environmental allergens, family history of asthma, breastfeeding and drug use. Respiratory infections of viral origin are regarded as the most important factor in the onset of symptoms in children under five years. Among the most important environmental pollutants are exposure to passive smoke and carbon dioxide [3].

From the 90's various research has been pointing an association between increased body mass index (BMI) and the prevalence of asthma. This association was seen initially in children and adults in more recently. Longitudinal studies indicate a relationship between the rise in obesity and the incidence of asthma [1].

Obesity has been recognized as a health problem that can trigger other diseases and have a chronic character [4]. In Brazil, its prevalence varies according to the region of the country. In studies Abrantes et al. [5] observed a prevalence of obesity in children aged 8.2 to 11.9%, and teens of 6.6 and 8.4% in the Northeast and Southeast, respectively. Other studies conducted in the cities of São Paulo (SP) and Salvador (BA) found a prevalence of obesity of 10.5 schoolchildren in public schools and 15.8% in students from private schools [6].

With the increasing prevalence of obesity and asthma several surveys began investigating the relationship between these two diseases by age.

Obesity presents associated with various comorbidities (diabetes mellitus, cardiovascular disease, dyslipidemia, among others) and asthma by having shortness of breath and chest pain hinders the activities of everyday life and eventually results in sedentarism [6].

Asthma and obesity are conditions that pose public health problems, which some studies suggest obesity as a risk factor for asthma and vice versa. How to find the existence of this relationship is still under discussion, we realized the need and importance of studying a possible association of these two diseases, because only by knowing the causes and repercussions of both cause in people's lives is that actions of health promotion can be drawn, benefiting not only the individual but the whole community.

The present study aims to identify the prevalence and symptoms of asthma and to investigate the relationship between Body Mass Index (BMI) and asthma symptoms in adolescents between 13 and 14 years, to estimate the prevalence of obesity in this age group.

Methods

This study is a cross-sectional quantitative held in two public schools in the city of Cajazeiras - PB developed in May April and May 2012. It was initially made contact with teens to explain the objectives and procedures of the research and deliver the terms of consent (IC) for parents and / or guardians to sign. In another day it was performed the anthropometric measurements and it was applied the questionnaire on asthma in a private room at the school by two trained researchers. Only adolescents who gave informed consent signed by the responsible role in the research. To determine the prevalence of asthma and related symptoms it was applied the ISAAC phase III (asthma module).

We interviewed 85 adolescents 13-14 years, 54, 2% were female and 45.8% male. The 85 teenagers who participated in the study were divided into four groups: 4.8% undernourished, eutrophic 69, 4%, 17.6% overweight and 8.2% obese.

The study included adolescents of both genders, aged between 13 and 14 years and excluded adolescents who had respiratory diseases. Anthropometric measurements were used a digital scale

(brand: G-Tech/Glass 200; manufacturer: Tech) to evaluate the weight capacity of 180 kg and sensitivity of 100g, a stadiometer aluminum (brand: Sanny) to measure the height. BMI (kg/m²) was calculated and compared to the values used by NCHS, and nutritional status according to the recommendations of the World Health Organization (WHO), in which individuals with a BMI below the fifth percentile were classified as malnourished; eutrophic with BMI at or above the fifth percentile and below 85, overweight with a BMI at or above the 85th percentile and below 95, and obese with a BMI at or above the 95th percentile. To determine the prevalence of asthma and related symptoms, as well as its severity was used the ISAAC phase III (asthma module) [8]. This research follows the Resolution 196/96 regulating the human research in Brazil and was approved by the Ethics Committee of the Faculdade Santa Maria, under the Protocol 04638112.7.0000.5180.

The data were recorded in the database of the computer program SPSS (Statistical Package for Social Sciences) for Windows, version 15.0, and analyzed using descriptive and inferential statistics. For descriptive procedures were presented gross and relative measures (frequencies and percentages), measures of central tendency (mean and median) and variability (standard deviation and range). The statistical inference procedures, in turn, were performed by calculating the odds ratio (odds ratio), which estimates the risk of certain characteristic occurs through another (in this case, asthma based on BMI) and by means of Chi-square test, which identifies associations between variables. Finally, for the interpretation of the information, we adopted a confidence interval of 95% and a significance level of 5% ($p < 0.05$).

Results

To calculate the odds ratio (odds ratio) of presenting features and symptoms of asthma based on BMI, participants were divided into two groups: those with more than 50 percentile (higher standard group) and those with percentile or less 50 (group criteria below). Participants who were normal weight had less chance, odds ratio (OR) of less than 1, having been diagnosed with asthma have wheezing after exercise presented, have filed nocturnal

Table 1. Evaluation of wheezing / asthma based on BMI

Variables	Esp.	Percentile>50		Percentile ≤ 50		OR	IC 95%	
		F	%	f	%		Min.	Max.
Wheezing sometimes	Yes	11	12.9	7	8.2	1.71	0.59	4.97
	No	32	37.6	35	41.2			
Wheezing in the last 12 months	Yes	5	5.9	4	4.7	1.25	0.31	5.01
	No	38	44.7	38	44.7			
Some crisis	Yes	4	4.8	4	4.8	0.94	0.22	4.07
	No	39	46.4	37	44.0			
Disturbed sleep	Yes	6	7.1	3	3.5	2.10	0.49	9.05
	No	37	43.5	39	45.9			
Impaired speech	Yes	3	3.5	1	1.2	3.07	0.30	30.81
	No	40	47.1	41	48.2			
Asthamever	Yes	4	4.7	6	7.1	0.61	0.16	2.35
	No	39	45.9	36	42.4			
Wheezing after exercise	Yes	6	7.1	9	10.6	0.59	0.19	1.84
	No	37	43.5	33	38.8			
Nocturnal cough	Yes	12	14.1	13	15.3	0.86	0.33	2.19
	No	31	36.5	29	34.1			

Legend: Esp.: Specification, OR: odds ratio, CI: confidence interval.

Table 2. Evaluation of wheezing / asthma based on BMI in males and females

Variables		Percentile>50		Percentile ≤ 50		OR	IC 95%	
		Yes (%)	No (%)	Yes (%)	No (%)		Min.	Max.
Wheezingsometimes	Male	7.7	48.7	2.6	41.0	2.52	0.23	26.72
	Female	17.4	28.3	13.0	41.3	1.94	0.54	6.95
Wheezing in the last 12 months	Male	5.1	51.3	2.6	41.0	1.60	0.13	19.27
	Female	6.5	39.1	6.5	47.8	1.22	0.21	6.80
Some crisis	Male	5.1	51.3	2.6	41.0	1.60	0.13	19.27
	Female	4.4	42.2	6.7	46.7	0.73	0.11	4.89
Disturbedsleep	Male	7.7	48.7	0.0	43.6	-	-	-
	Female	6.5	39.1	6.5	47.8	1.22	0.21	6.80
Impaired speech	Male	2.6	53.8	0.0	43.6	-	-	-
	Female	4.3	41.3	2.2	52.2	2.52	0.21	30.01
Asthamever	Male	7.7	48.7	10.3	33.3	0.51	0.09	2.68
	Female	2.2	43.5	4.3	50.0	0.57	0.04	6.82
Wheezingafterexercise	Male	10.3	46.2	7.7	35.9	1.03	0.19	5.41
	Female	4.3	41.3	13.0	41.3	0.33	0.06	1.86
Nocturnal cough	Male	10.3	46.2	7.7	35.9	1.03	0.19	5.41
	Female	17.4	28.3	21.7	32.6	0.92	0.28	3.03

Legend: Esp.: Specification, OR: odds ratio, CI: confidence interval.

cough and had to have made some crisis. However, since their confidence intervals were maximum greater than 1, these results can not be considered significant statistical point of view. These same findings were observed in other variables, so that a BMI lower or higher than the median of the 50th percentile is not a risk factor for presenting all the

characteristics and symptoms investigated. Descriptive and inferential data are detailed in Table 1.

In order to check these symptoms by taking as basis the gender of the participants also have calculated the chances of developing such symptoms as a function of BMI percentile. These previous results which were not observed significant chan-

Table 3. Association between BMI and asthma symptoms and characteristics

Variable	Esp.	Malnourished $x < 5$		Eutrophic $5 \leq x < 85$		Overweight $85 \leq x < 95$		Obese $x > 95$		p
		f	%	f	%	f	%	f	%	
Wheezing sometimes	Yes	0	0.0	12	14.1	3	3.5	3	3.5	0.37
	No	4	4.7	47	55.3	12	14.1	4	4.7	
Wheezing in the last 12 months	Yes	0	0.0	5	5.9	3	3.5	1	1.2	0.52
	No	4	4.7	54	63.5	12	14.1	6	7.1	
Some crisis	Yes	0	0.0	5	6.0	2	2.4	1	1.2	0.82
	No	4	4.8	53	61.3	13	15.5	6	7.1	
Disturbed sleep	Yes	0	0.0	4	4.7	2	2.4	3*	3.5	0.02*
	No	4	4.7	55	64.7	13	15.3	4	4.7	
Impaired speech	Yes	0	0.0	1	1.2	1	1.2	2*	2.4	0.01*
	No	4	4.7	58	68.2	14	16.5	5	5.9	
Asthma ever	Yes	1	1.2	7	8.2	1	1.2	1	1.2	0.77
	No	3	3.5	52	61.2	14	16.5	6	7.1	
Wheezing after exercise	Yes	1	1.2	10	11.8	1	1.2	3	3.5	0.21
	No	3	3.5	49	57.6	14	16.5	4	4.7	
Nocturnal cough	Yes	0	0.0	20	23.5	3	3.5	2	2.4	0.41
	No	4	4.7	39	45.9	12	14.1	5	5.9	

Legend: Esp: specification; Desnut.: Malnourished; Eutrof: eutrophic.; *: Significant ($p < 0.05$).

ces between variables in participants males and females (Table 2).

Association between asthma symptoms and BMI

Nutritional status, in each corresponding group, was also assessed in terms of asthma symptoms. It was found that wheezing present, is sometimes in the past 12 months or after exercise, as well as having presented the crisis, having been diagnosed with asthma and provide nighttime cough are not associated with nutritional status statistical criteria, since with $p > 0.05$. However, there was a significant association to present as disturbed sleep ($p < 0.02$) and impaired speech ($p < 0.01$). That is, participants that have these characteristics are associated with the upper 95 percentile, or obesity. However, it emphasizes the importance of replication of such information with larger sample, since most of the subjects in this study belonged to the group of normal weight, having low effective sample the other groups. These data are detailed in Table 3.

Discussion

The relationship between BMI and asthma has tornadobastante evident through clinical and expe-

perimental studies. There are several methods proposed to explain the relationship between obesity and asthma, but there is no conclusive answer. According to the results of the Household Budget Survey (HBS) from 2008 to 2009 conducted by IBGE in partnership with the Ministry of Health the weight of Brazilians has increased in recent years. The proportion of boys and young men 10-19 years old overweight increased from 3.7% (1974-75) to 21.7% (2008-09) and among girls and young women the growth of overweight was 7.6% to 19.4%. weight gain in adolescents 10 to 19 years was continued for the last 34 years, being more visible in males as their index rose from 3.7% to 21, 7%. Among the young statistics from 7.6% to 19% between 1974-75 and 2008-09. Since obesity has become less intense, but with an upward trend, from 0.4% to 5.9% among boys and young men, and from 0.7% to 4.0% in the genre feminine [9]. In this survey the prevalence of obesity was very low (8.2%), however, overweight had the highest percentage (17.6%).

In the last two decades there has been a significant increase in rates of obesity, which has coincided with a high prevalence of asthma in all world [4]. The association between asthma and obesity is common among children and adolescents. Some studies indicate that the gain or loss of weight may

be responsible for triggering and the severity of asma [9].

Asthma and obesity are diseases that have a high prevalence etiologies, clinical phenotypes and different gravities, having a strong environmental, genetic and inflammatory. In recent decades epidemiological studies have theorized that there is a relationship between the two diseases, since there was an increase in prevalence of both in the same period [11]. According Shore [12] asthma obesity is strongly influenced since this increases the prevalence, incidence and possibly the severity of asthma.

According Story [13] the association between asthma and obesity can arise due to common etiologies such as inflammation of the airways, the mechanical effect of obesity on lung volume changes in hyperresponsiveness of the airway, as well as changes in the practice of physical and diet. To Shore [12] the biological basis of this relationship still includes the action of adipokines, such as tumor necrosis factor-alpha, leptin and adiponectin. The leptin level is increased in asthmatic children compared to healthy subjects [14].

Adipose tissue is an endocrine organ responsible for releasing a multitude of factors, including adipokines that are linked to immunity and inflammatory response and show an increase in their levels in cases of obesity, characterized by a state of mild chronic inflammation [15].

With obesity is a greater production of adipokines that promote repercussions in various bodily functions such as the immune system in the control of food intake, energy balance, among others. Adipokines may exert antagonistic actions in the inflammatory process, may cause an imbalance between pro-and anti-inflammatory responses by inducing inflammatory or hypersensitivity [16].

In studies Cassolet al. [17] found a positive association between a BMI below the 95th percentile and the prevalence of wheezing ever (OR = 0.83, 95% CI 0.61 to 0.99, $p < 0.05$), and wheezing with exercise (OR = 0.74, 95% CI: 0.55-0.99, $p < 0.05$), compared to a BMI at or above the 95th percentile. However, in studies of Cunha et al.[18], there were no statistically significant differences between the students in any of the ISAAC questions, in which the age of 13 was selected because of evidence of remission of asthma symptoms in puberty demonstrated in some studies.

Casagrande et al. [19] claim, in his research, that the total number of school children who had wheezing at least once in their lifetime was 55.2% ($n = 1,829$), while 31.2% ($n = 1,033$) responded positively to the question of wheezing in the last 12 months, considered asthmatic. According to the study of Breda et al. [2] the prevalence of severity of asthma symptoms nighttime waking was 2.1%; wheezing episodes in the last 12 months, one to three seizures was 8.1%; with four or more seizures was 3.3% and 3.7% limitation of speech.

In studies Fatuch and Rosario Filho [20] women with BMI > 30 have a 1.8 times greater risk of having asthma than non-obese women, a finding that does not occur in men. According to Pellegrino et al. [21], different from childhood to adult asthma is more prevalent in women, which is in accordance with that observed in the same study in which 72.5% of the patients were women.

According to studies by Dutra et al. [22] noted the relationship between BMI and the incidence of asthma, since this correlation is more aimed at women. Furthermore, we observed higher levels of leptin in obese women compared to obese men. In the present study it was found that there was a significant relationship between the variables and the adolescent male and female.

Cunha et al.[18] found significant results in the investigation of disturbed sleep for one or more nights and difficulty speaking due to wheezing reported fact only 1% of the responses to both. In studies Lima et al.[23] 8.5% of students reported having sleep disturbance due to wheezing and 3.9% had difficulty speaking due to wheezing in the last year. Participants in this study were overweight or obese does not. However, in this study we observed a significant association to present as disturbed sleep and impaired speech, and participants who had these characteristics are associated with obesity group with percentile higher than 95, while the other variables are not associated nutritional status to statistical criteria. Saraiva et al. [1] explain that obesity increases the risk of gastro-oesophageal reflux and sleep disorder, in turn, can cause or worsen asthma.

Conclusion

There was no association of asthma symptoms with BMI nor a statistically significant difference

in the relationship between obesity and asthma for all inquiries by the ISAAC phase III. There was significant disruptive sleep and impaired speech due to wheezing.

References

1. Saraiva SA, Xisto DG, Dias CM, Silva JRL, Rocco PRM. Entendendo os mecanismos relacionados a obesidade e asma. *Pulmão (Rio J)*. 2007; 16: 39-43.
2. Breda D, Freitas PF, Pizzichini E, Agostinho FR, Pizzichini MMM. Prevalência de sintomas de asma e fatores de risco associados em adolescentes escolares de 13 e 14 anos dos municípios de Tubarão e Capivari de Baixo, Santa Catarina, Brasil. *Cad Sau Publ*. 2009; 25: 2497-2506.
3. Sarinho ESC, Sarinho S, Ferreira OS, Brito WP, Filho ASA, Cartaxo CGB. Fatores de risco para asma infantil em Fernando de Noronha: Estudo do tipo caso-controle. *J Pediatr*. 2005; 71: 270-272.
4. Basso DF, Corso AC, Kupek TE. Associação entre obesidade e asma. *Rev Ciênc Méd*. 2007; 16: 221-231.
5. Abrantes MM, Lamounier JA, Colosimo EA. Prevalência de sobrepeso e obesidade em crianças e adolescentes das regiões sudeste e nordeste. *J Pediatr*. 2002; 78: 335-340.
6. Camilo DF, Ribeiro JD, Toro ADC, Baracat ECE, Filho AAB. Obesidade e asma: associação ou coincidência? *JPediatr*. 2010; 86: 6-14.
7. National Center For Health Statistics (NCHS). Centers For Disease Control And Prevention. Atlanta, GA: Department of Health and Human Services at: www.cdc.gov/growthcharts. Accessed: 08/02/2009.
8. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J*. 1995; 8: 483-91.
9. Instituto Brasileiro de Geografia e Estatística. POF 2008-2009: desnutrição cai e peso das crianças brasileiras ultrapassa padrão internacional. www.ibge.gov.br/home/presidencia/noticias/noticia_visualiza.php?id_noticia=1699&id_pagina=1. Accessed: 10/07/2012.
10. Rodrigues JC, Takahashi A, Olmos FMA, Souza JB, BussamraMHF, CardieriJMA. Efeito do índice de massa corpórea na gravidade da asma e na reatividade brônquica induzida pelo exercício em crianças asmáticas com sobrepeso e obesas. *Rev Paul Pediatr*. 2007; 25: 207-13.
11. Camilo DF, Ribeiro JD, Toro ADC, Baracat ECE, Barros Filho AA. Obesity and asthma: association or coincidence? *J Pediatr*. 2010; 86: 6-14.
12. Shore SA. Obesity and asthma: lessons from animal models. *J Appl Physiol*. 2007; 102: 516-528.
13. Story RE. Asthma and obesity in children. *Curr Opin-Pediatr*. 2007; 19: 680-684.
14. Fatuch MO, Rosário Filho NA. Relação entre obesidade e asma. *J Pediatr*. 2005; 28: 84-88.
15. Trayhurn P, Wang B, Wood I.S. Hypoxia in adipose tissue: a basis for the dysregulation of tissue function in obesity? *Br J Nutr*. 2008; 100: 227-235.
16. Prado WL, Lofrano MC, Oyama LM, Dâmas AR. Obesidade e adipocinas inflamatórias: implicações práticas para a prescrição de exercício. *Rev Bras Med Esporte*. 2009; 15: 378-383.
17. Cassol VE, Rizzato TM, Teche SP, Basso DF, Hirakata VN, Maldonado M, Colpo E, et al. Prevalência e gravidade da asma em adolescentes e sua relação com índice de massa corporal. *J Pediatr*. 2005; 81: 305-309.
18. Cunha MR, Vasconcelos CCS, Barbosa AR, Xavier TT. Sintomas asmáticos em escolares de 8 e 13 anos. *Ver Saúde*. 2006; 2: 12-20.
19. Casagrande RRD, Pastorino AC, Souza RGL, Leone C, Solé D, Jacob CMA. Prevalência de asma e fatores de risco em escolares da cidade de São Paulo. *Rev Saú Públ*. 2008; 42: 517-23.
20. Fatuch MOC, Rosário Filho NA. Relação entre obesidade e asma. *Rev Bras Alerg. Imunopatol*. 2005; 28: 84-88.
21. Pelegrino NRG, Gaganello MM, Sanchez FF, Pado-vani CR, Godoy I. Relação entre o índice de massa corporal e a gravidade da asma em adultos. *Jorn Bras Pneumol*. 2007; 33: 641-646.
22. Dutra MC, Arnoni CP, Sousa CA, Lago ERJ, Fronza FCAO, Pagani LG, et al. Relação entre obesidade e asma: uma revisão atualizada. *Rev Bras Obes Nutr e Emagr*. 2009; 3: 424-431.
23. Lima WL, Lima EVNCL, Costa MRSR, Santos AM, Silva AAM, Costa ES. Asma e fatores associados em adolescentes de 13 e 14 anos em São Luís, Maranhão, Brasil. *Cad. Sau. Publ*. 2012; 28: 1046-1056.

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Predicting junk food consumption by extending the theory of planned behavior: the role of descriptive norms

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Abstract

Background and objective: Unhealthy food choice especially in younger people could lead to diverse chorionic disease and morbidity in the adulthood. The aim of this study was to determine the efficacy of theory planned behavior (TPB), extended by descriptive norm, to predict intention and consumption of junk foods in a group of Iranians adolescents.

Methods: 271 boys high schools (between 15-18 years) students randomly selected and participated in the study. Hierarchical multiple regression analysis were performed to test the predictive power of the classic TPB and extended TPB by descriptive norm.

Results: The results showed the TPB predecessors explained the 22.5% of variance in intention to consume junk food and after adding the descriptive norm; variance increased 12/5 % and arrived to 35%. Descriptive norm ($\beta=.38$, $p<.01$) and attitude ($\beta=.29$, $p<.01$) was the strongest predictor of intention in the extended model. Also the TPB and extended model explained the 9% and 14% of variance in behavior respectively. Attitude ($\beta=.27$, $p<.01$) and PBC ($\beta=.18$, $p<.01$) was significant predictor of behavior.

Conclusion: Intervention designed to reduce unhealthy nutritional behavior for adolescents, should specific attention pay to the adolescent's perception of important people nutrition behavior, their attitude to use this foods and perceived control for refrain junk foods consumption.

Key words: Junk food consumption, theory of planned behavior, high schools boys, descriptive norms

Introduction

Obesity has become one of the most important health issue throughout the world (1,2) and a growing public health problem among children, adolescent and adult (3,4). Obesity is associated with cardiovascular disease, hypertension and dyslipidemia (5). finding from the first national non communicable disease (NCD) risk factor surveillance in Iran showed that prevalence of overweight and obesity altogether was 42.8% (6). this finding suggests that Iranians people are of the high risk of chronic disease such as cardiovascular disease (CVD) and diabetes in the near future. In other hand based on world health organization (WHO) estimates, by the year 2020, chronic disease will be account for nearly $\frac{3}{4}$ of all death in the developing country (7). NCD's such as cancers, CVD and diabetes is increasing remarkably in the eastern Mediterranean region and it is expected that currently 47% of the region Borden of disease due to the NCD, will augment to 60% by arriving 2020 year (8).

One of the most health related concern is the occurrence of nutrition transition, which has led to outbreak of nutritional origin malady and obesity among Iranians people (9). obesity and overweight is mainly due to positive energy balance in which energy input is higher than energy output. Consumption of high calorie content food among adolescence is one the energy balance related behavior (10). Results of a national study among 6-18 years old students in Iran indicate unhealthy dietary habit including consumption of junk food (fatty, salty and sweet snack) (11).

Junk food definition is: energy dense foods with high sugar/fat/salt content and low nutrition value in

terms of protein, fiber, vitamin and mineral content (12). The changeable risk factors such as unhealthy diet are the main causes of the NCD (7). The progressive prevalence of adolescents overweight and obesity is mainly attributed to unhealthy dietary behavior including the increase in eating fast foods, soft drinks and energy dense foods and also decrease in physical activity (13,14). Dietary habit that causing inadequate nutrient intake result in developing chronic disease such as diabetes, coronary heart disease and hypertension (15). Consumption of foods high in salt, fat, sugar and calorie content by children lead to development of obesity, hypertension, and dyslipidemia and glucose tolerance (16).

Promoting healthy eating practice in children and adolescent can help abate the growing rate of obesity. Because result of a national study among Iranians adolescent showed high prevalence of junk food consumption (11), it seems necessary to explore the factors influence the intention and behavior of junk food consumption in order to designing effective intervention aimed at changing their dietary behavior and prevent unfavorable consequence of this behavior on health. But such intervention are may be to more effective while target theory-based important determinant (17) and reviews of literature on health behavior change interventions, showed that theory based intervention have large effect compared to those lacking a theoretical basis (18). Utilization of a relevant theoretical framework provides structure to recognize the potential factor that influencing junk food consumption. Supported by this fact junk food consumption especially by adolescents is an obvious target for behavior intervention. To our knowledge, but unfortunately, there have been few theoretical studies focused on understanding or intervening to reduce unhealthy food consumption and therefore the factors that predict junk food intake remain to be unrecognized considerably.

In the present study we used the theory of planned behavior (TPB) as the theoretical framework to identify key factor influencing junk food consumption. The TPB (19) is successfully used to study health related behavior (20-23) also in dietary behavior and food domain TPB was extensively used (24-28) including junk foods (29).

Although there is some evidence show that the TPB can predict healthy dietary behaviors (30) but it has been shown these variance is lower than

other health related behaviors (31). This issue be possible due to complex nature of food choice behaviors, therefore there is a need for incorporate other component that maybe affect the eating behavior. The predictive power of TPB has been proved in numerous study and meta-analysis (32, 33). For example Armitage and Conner (2001) (32) analyzed 185 TPB-based studies and report that TPB accounted for 39% and 27% of variance in intention and behavior respectively.

In general, the TPB is regarded to be an appropriate model for developing health related change intervention (34). The TPB (19) posits that behavioral intention is the immediate precursor and most proximal determinant of the behavior and strong intention means more likely to perform behavior. The intention also assumed to be a function of Attitude, subjective norms and Perceived behavioral control.

Attitudes reflect an overall favorable or unfavorable evaluation about performing a behavior. The subjective norm is the perceived opinion of important people in their life that would want them to perform or not perform of the behavior and finally perceived behavior control (PBC) are the individuals perception of the degree of control that they have up on behavior and has both direct and indirect (thorough intention) influence on behavior.

Armitage and Conner in their meta-analysis (32) found that the strongest predictor of intention was attitude, PBC and subjective norms, respectively. But according to Ajzen (1991) assumption, the effect of the TPB components might differ across population, behavioral domain and situations and variable relative significance relies on behavior and population and it is not always constant. One of the weaknesses of TPB is the failure of subjective norms to predict intention (19, 35). To decline this problem some authors suggested that it may be useful to made a distinct between subjective (injunctive) and descriptive norms (32, 36). Injunctive norms is viewed alike to subjective norms and they involve the perception of important other approval or disapproval of relevant behavior but descriptive norms is related to perception of what important other actually do.

To reduce low predictability of subjective (injunctive) norms Ajzen 2002 suggested that it can be useful to include items designed to entrap des-

criptive norms simultaneously to measure of subjective norms. Although in later version of TPB Ajzen and Fishbein (37) proposed that it is preferable to combine this two construct in the model, but some studies result don't support this incorporation and indicated that this two variable are separate from each other (38,39) and even sometimes the predictability power of descriptive norms is higher than subjective norms (40).

As mentioned above, Armitage and Conner reported that subjective norms were the weakest predictor of intention. In this relation they proposed that the number of items that employed to measure subjective norms can moderate the correlation between subjective norms and intention. For example while single item used to capture these construct, the correlation will be weaker than multiple items. Another probable reason for the weak predictability of subjective norms is the small width definition of these construct for encompass all aspect of social impression (40,41) and therefore other social norms should be included in the model (40-43). Ajzen (2002) (44) proposed that because important peoples always are perceived to accept favorite and don't accept unfavorable behaviors subjective norms often found to have low variability. Based on Cialdini and et al. 1990 (39) social influence could come from various sources and therefore they offer it may be helpful to differentiate between injunctive and descriptive norms and including both in the model. Also Ajzen (1991) stated that model is open to further elaboration if new important component identified. A series of variables have been shown to be appropriate extensions to the TPB. One of these variables that explained additional variance in intention and enhanced predictive utility of TPB is descriptive norm (45).

Result of a meta-analysis that conduct by Rivas and Sheran (46) showed that descriptive norm enhanced the variance explained in intention 5% after the TPB constructs had been take in account. Also result of some studies showed that descriptive norms could predict the intention independently of subjective norms (47). Although important other such father, mother or family may expect the children to have healthy food choice, but if they for example had unhealthy food habit, according to observational learning (48) their act can influence the eating behavior of children. Therefore children

observation of influential people manner may have more powerful effect on their behaviors than their demand or desires. In other hand Iranian households mainly consist of extended family in which family member have close relationship with each other and consequently it is expected that the trait, attitude and behavior of member influence the attitude and behavior of other member. To our knowledge very few studies to date have examined junk food consumption in the framework of theory of planned behavior among Iranian boys high school and no studies have applied the TPB extended by descriptive norms to junk food consumption neither in Iran nor in world. The aim of the current study therefore is 1: to examine that to what extent the TPB is capable to predict both junk food consumption intention and junk food consumption behavior, 2: to determine whether descriptive norms could increase significantly the explained variance of junk food consumption intention after controlling for the impact of TPB component.

Subjects and method

The current study employed a cross-sectional design and was part of a larger study examining the efficacy of a TPB based intervention on reducing junk food consumption in high school students in Bandarabass, Iran. Ethical approve and study protocol for this study was granted by the Tehran University of Medical Science, school of public health medical ethic committee and review board. After obtaining relevant ethical approve, the agreement of local educational authorities in Bandarabbass was obtained and presentation letter sent to relevant high schools. Data were collected from students from 10 boy's high schools in Bandarabbass city that randomly selected among all boys high school in this town. Of each school one class randomly selected to participate in the study, therefore finally 10 classes from 10 schools take part in the study. Every class population was between 25-30 students. Enrollment in the project occurred during the 2011-2012 educational year and the respondent received a small gift for their participation in the study. Initially 290 male high school students were selected to participation and a letter of study introduction and invitation was sent to selected students' parents in which confi-

dentiality and volunteer participation mentioned. Parents could keep their children's from participating in the study by signing the specific space in the invitation form (they should sign the form and declare the agreement or disagreement for their child participation). Finally 271 student (M age=16, SD=1.03, range= 15-18) signed informed consent and returned the relevant questionnaire (19 student don't fill the questionnaire because of intendancy or parents disagreement, therefore participation rate was 93.4%). Researchers checked out the information in every questionnaire immediately after delivery by students and want them to fill out the empty answers; therefore missed data was very little. Criteria for entrance in the study were not on a specific dieting (prescribed by a physician or dietician) at the time of study. The principal investigator was present during instrument completion to answer any question if needed.

Measures

The questionnaire included direct self-report measure of TPB, constructed in line with Ajzen (2002)(44) recommendation and Jillian et al guideline (49). The TPB instrument reviewed by 5 faculty members expert in health education and scale development. After proffer modification, instrument pilot tested with 10 students, which based on their comments, resulted in small change in some of questions for better understanding and clarification of instruction. Also junk food consumption was assessed based on a valid FFQ (50) and expertise panel viewpoint. After some trivial change for better understanding of FFQ questionnaire, the instrument pilot tested among 50 adolescent (correlation among baseline and 1 month follow up was 0.7). respondent were asked to demonstrate on how many days and times during the past week they consumed each of 26 items of more popular junk foods in Iran. Then for calculate total junk food consumption sum of all item scores counted as junk food consumption numbers during one week. Before answering questions about intention, beliefs and junk food consumption, students were presented within the questionnaire, the definition and sample of junk food (such as chips, puffs, candy, biscuit, cookies ...). Intention was assessed by three items. I intend to eat junk food during the next week (extremely

likely=7, extremely unlikely=1), I am sure I will eat junk food in the next week (very certain=7, very uncertain=1), for the next week I plan to eat junk food (strongly agree=7, strongly disagree=1). Cronbachs α was 0.73. Attitude toward junk food consumption were measured with the mean of 5 semantic items, each measured on a 7 point differential scale: for me eating junk food in the next week would be: very good=7 very bad=1, very beneficial=7 very harmful=1, very pleasant=7 very unpleasant=1, very enjoyable=7 very unenjoyably=1, very useful=7 very worthless=1. Cronbachs α for this scale was 0.83. the subjective norms was assessed by the mean of three items on a 7 point scale: most people who are important to me think that: I should eat junk food =7/ I should not eat junk food=1. it is expected of me that I eat junk food in the next week: strongly agree=7/strongly disagree=1. people in my life whose opinions I value would approve=7/ disapprove=1 of my eating junk food in the next week. Cronbach's α for this scale was 0.7. Descriptive norms were measured by 3 items: most people who are important for me eat junk food in the next week, completely true=7/completely false=1. The people in my life whose opinions I value eat=7/ don't eat=1 junk food in the next week. Those who are close to me eat junk food in the next week: extremely true=7/extremely false=1. Cronbachs α for this scale was 0.77. perceived behavioral control was measured by 4 items: for me not to eat junk food in the next is easy=7/difficult=1. If I wanted to, I could avoid eating junk food in the next week, definitely true=7/definitely false=1. it is mostly up to me whether or not I eat junk food in the next week, strongly agree=7/strongly disagree=1. How much control do you believe you have over eating junk food in the next week, complete control=7/ no control=1.. Cronbachs α for this scale was 0.75. TPB construct were measured by summation of each relevant item scores divided by the number of relevant items.

Data analysis and Results

Data were analyzed using SPSS version 19 with an alpha level of 0.05. Descriptive statistics include means, standard deviations and frequencies were calculated for all variable. To explore association between determinant variable, Pearson

correlations were performed for all variable. The bivariate correlation matrix along with the means and standard deviation were presented in the table 2. The amount of missing data was extremely small because questionnaires immediately after delivery by student rechecked by researcher for unfilled questions and promptly want them to response at that place. Simple descriptive statistics were used to analyze the demographic data. Chi-square test of independence was conduct to evaluate the differences between group that don't participate in the study and participant. There were no significance differences in demographic variables between two groups, therefore in this paper only the participant analyses are reported. A hierarchical linear regression analysis was performed to predict intention to junk food consumption. The independent variables were entered in two blocks: 1: attitude, subjective norm and perceived behavioral control and 2: the descriptive norm as the additional predictor was added to regression analysis. Another hierarchical regression analysis was conduct to predict junk food consumption. Intention and PBC were entered as independent variable in step one and attitude, subjective norm and descriptive norm was added in step two. The survey assessed demographic variables including age, class standing, parent's educational level and employment status. Simple descriptive statistics were used to analyze the demographic data. The final sample was comprised of 271 male high school students between 15-18 years old with the average of 16.36 and standard deviation of 1.1. Class standing was distributed with 28.4%, 29.2%, 21.8% and 20.7% in the first, second, third and fourth grade level respectively. Most of students father was employed in nongovernmental section (43.2%) and 39.9% was employed in governmental section. Major of student's mothers was housekeeper (86.3%) and dominant (31% of father and 28.4% of mother) educational level of parents was high school (table 1 show the demographic characteristic of samples).

The mean of respondent junk food consumption was 28.9 per week (nearly 4 times per day). The score of intention to consume junk food was 4.49 ± 1.57 , suggesting that adolescents had positive intention to consume junk food. Mean and standard deviation for other TPB variable are presented in table 2. Table 1. Demographic charac-

teristic of sample

Characteristic	N	%
Age range		
15	77	28.4
16	75	27.7
17	63	23.2
18	56	20.7
Class standing		
1th	77	28.4
2th	79	29.2
3th	59	21.8
4th	56	20.7
Father education		
Primary	52	19.2
Secondary	59	21.8
High school	84	31
Academic	76	28
Mother education		
Primary	74	27.3
Secondary	63	23.2
High school	77	28.4
Academic	57	21
Father job		
Governmental employment	108	39.9
Nongovernmental employment	117	43.2
Un employment	46	17
Mother job		
House keeper	234	86.3
Employment	37	13.7

Bivariate correlation between the variable showed that junk food consumption was more correlate with the attitude($r=0.29$), PBC($r=-0.23$) and intention($r=0.21$) respectively and descriptive norm($r=0.5$), attitude($r=0.45$), subjective norm($r=0.29$) and PBC($r=-0.13$) were significant correlate of intention respectively. PBC was negative and significant correlate of both behavior and intention (PBC questions were measured such that higher scores indicate a lower level of control and therefore difficulty to refrain from junk food consumption), so the intention and consumption of junk food increased with lower level of control to refrain these foods.

A hierarchical multiple linear regression in two steps was conduct to determine the importance of TPB variables in addition to descriptive norm for predict of intention to junk food consumption (see table 3).the Result from step 1(attitude, subjective norm and PBC as independent variables) showed that the TPB variables described the %22.5 of vari-

Table 2. The bivariate correlation, mean and standard deviation of study variables

Variables	Mean	SD	1	2	3	4	5	6
1. Junk food consume	28.9	17.94	-	.216**	-.233**	.293	.056	.085
2. Intention	4.49	1.57	-	-	-.133*	.455**	.299**	.5**
3. PBC	5.65	1.05	-	-	-	-.132*	-.024	-.034
4. Attitude	3.63	1.36	-	-	-	-	.442**	.343**
5. Subjective norm	4.07	1.51	-	-	-	-	-	.305**
6. Descriptive	3.82	1.49	-	-	-	-	-	-

*correlation is significant at the .05 level

**correlation is significant at the.01 level

Note : A high mean value for intention, subjective norm and attitude indicate that this variable in favor of junk food consumption for PBC a high mean indicate the lower perceived control for avoid junk food consumption .

Table 3. Summary of hierarchical regression (R^2 , F and β) analysis for predicting intention to consume junk food

Step	Predictor	β step1	R^2	F	β step2	R^2	F
1.	.225 Attitude Subjective norm PBC	25.84** .39** .124* -.078					
2.	.351 Attitude Subjective norm PBC Descriptive norm	35.97**	.29** .05 .384**		-.08		

* $p < .05$

** $p < .01$

β = standardized regression coefficient

Table 4. Summary of hierarchical regression (R^2 , F and β) for predicting junk food consumption

Step	predictor	β step1	R^2	F	β step2	R^2	F
1.	.089 Intention PBC	13.11** .189** -.208**					
2.	.139 Intention .118 PBC Attitude Subjective norm Descriptive norm	8.552**			-.185** .27** -.08 -.04		

* $p < .05$

** $p < .01$

ance in intention ($R^2=0.225$, $F(3, 267) = 25.84$, $P < 0.01$) and attitude ($\beta=0.39$, $p < 0.01$) was the strongest predictor of intention also subjective norm was the significant predictor of intention ($\beta=0.12$, $p < 0.05$). PBC were not related to the intention ($\beta=0.07$, $p > 0.05$). In second step while descriptive norm (as extended variable) were added to the regression, model could predicted the %35.1 of variance on intention to consume junk food ($R^2=0.351$, $F(4, 266) = 35.97$, $P < 0.01$). Descriptive norm ac-

counted for a %12.6 increase in explained variance in intention and exert the strongest relationship with intention ($\beta=0.38$, $p < 0.01$). Also attitude remained significant predictor of intention ($\beta=0.29$, $p < 0.01$) although importance of attitude was decreased. But subjective norm ($\beta=0.05$, $p > 0.05$) and PBC ($\beta=-0.08$, $p > 0.05$) become non-significant predictor in this step. To test the predictive validity of TPB variables in relation to junk food consumption another hierarchical multiple regressions was performed

(see table 4). In step 1, intention and PBC entered to the regression as independent variables. Result showed that both PBC ($\beta=0.2$, $p<0.01$) and intention ($\beta=0.18$, $p<0.01$) were significant predictor of junk food consumption. Model explained the %8.9 variance on behavior ($R^2=0.089$, $F(2, 268)=13.11$, $P<0.01$). PBC showed slightly further β coefficient and exert the strongest predictor of behavior. In step 2 all TPB variables include, attitude, subjective norm and descriptive norm added to the equation and %13.9 of variance predicted by the model ($R^2=0.139$, $F(5, 265)=8.552$, $P<0.01$). therefore adding these variable increase %5 of variance in behavior. Attitude ($\beta=0.27$, $p<0.01$) and PBC ($\beta=0.18$, $p<0.01$) were independent predictor of behavior While intention, subjective norm and descriptive norm ($p>0.05$) were not.

Discussion

The researches in relation to junk food consumption by using TPB has been limited and to our knowledge the current study is the first to determine role of descriptive norm in the context of TPB among adolescent for predicting junk food consumption and intention. The aims of this study was to increase the current knowledge about the role of TPB variables and descriptive norms in explain junk food consumption intention and behavior and provided support for the construct of attitude, subjective norm and descriptive norm for predicting intention. The high average of junk food consumption in adolescents at this study demonstrate the importance of understanding the influential factor in choosing this food and following designing the effective strategies for decrease use of this unhealthy food. Results of Armitage and Conner(2001)(32) meta-analysis of the theory of planned behavior showed that TPB component could explain 39% of variance in intention, nonetheless analyze regression of classic TPB in our study explained only %22.5 of variance on intention, that was lower than figure reported by them. Nonetheless the extended model could predict about 35% of variance on intention that was considerable increment and upcoming to the Armitage and Conner figure report. They also find that subjective norm was the weakest predictor of intention and hence proposed to work on additional

norms (such as descriptive norm) and says that it may increase the ability of the normative belief to predict intention. But finding of our investigation in relation with the ability of descriptive norm for predicting intention to eat junk food is considerable and surprising. Report of a meta-analysis of 14 TPB studies in 5801 samples that performed by Ravis and Sheeran (46) for determine the role of descriptive norm as an additional predictor in the TPB, showed that this construct after controlling for other TPB variables, increased 5% of explained variance on intention. Multiple linear regression analysis in the current study displayed that after entrance of descriptive norm to the equation, it could to increase %12.6 of explained variance on intention to consume junk food and become the strongest predictor of intention. Also based on Cohen guideline (51) correlation between intention and descriptive norm was large($r=0.5$). This finding is higher than Ravis and Sherran report and therefore can increase our insight into the determinant factor of unhealthy behavior generally and junk foods consume specifically. Additionally while subjective norm was a significant predictor of intention in step 1(classic TPB) nonetheless after entering the descriptive norm in step2, subjective norm become a no significant predictor. The effect of TPB variables on behavior and intention could differ thorough different behavior and situation (19), Therefore for example when subjective norm or attitude have more exerting power, they maybe more determinant than PBC. Also our findings are in line with two other finding of Ravis and Sherran. First they hypothesized that in younger sample the influence of descriptive norm is stronger compared to older samples and their hypothesis was based on social influence and developmental cycle at life span of human. Second; based on salience and enjoyment hypothesis, they suppose that the correlation between descriptive norm and intention may be stronger in risky behavior for health in comparison with healthy behaviors. Since our samples and behavior field was adolescents and unhealthy eating, respectively, the role of descriptive norm in explain high proportion of intention in the present study are in line with Ravis and Sherran report and support their finding. In the first model of our study for predicting intention, attitude had the greatest β coefficient (in line

with Armitage and Conner meta-analysis report) and then subjective norm also was a predictor of intention, while PBC were not. Two findings at this step were considerable, first the role of subjective norm as second significant predictor of intention and second the inability of PBC for predicting intention. While several studies (i.e. Armitage and Conner meta-analysis) found the significant PBC - intention relation and weak or no significant subjective norm-intention relation, this study revealed that in the junk food domain and adolescent samples, subjective norm has a material role for predicting intention and PBC didn't significant predictor. The result of Katherine and colleagues (52) study for predicting consumption food low in saturated fats, showed that attitude and subjective norm but not PBC predicted the intention. O'Conner and White finding also revealed that attitude and subjective norm, but not PBC, were significant determinant of non-users willingness to accept a free trial of functional foods and vitamin supplement. The results of our study demonstrate the important role of descriptive norm in predicting intention to eat unhealthy foods. The role of descriptive norm in adolescent junk food consumption was neglected too much extent in researches, nonetheless this role is surveyed in some of other food domain. Distinction between social norm (subjective norm) and descriptive norm in food domain displayed in earlier studies (21, 47) and present study provided support for this hypothesis. However remarkable number of studies based on TPB, failed to find significant relationship between subjective norm and intention (19,27,53) the present investigation showed the importance of subjective norm and descriptive norm in prediction of intention to consume junk food in adolescent. Therefore both subjective norm and descriptive norm influence the intention to consume junk food but the role of descriptive norm is more important because before adding the descriptive norm to the regression analysis subjective norm was the second predictor of intention and after entering the descriptive norm to the equation only descriptive norm remained significant and further subjective norm were not predictor of intention. Jacobsen and et.al (54) showed that descriptive norm in adolescent are likely more influential than subjective norm because they yet don't

developed the self regularly skills fully and if this skills not good developed it cause the role of descriptive norm is more important until subjective norm. The influence of subjective norm and specifically descriptive norm in adolescent junk food consumption could also such explained that Literatures review indicate that adolescence period is of the most times that social norm influence the behavior of human (55) and adolescence is of the foremost age period that expectation and behavior of household, parents, siblings, peers and friends affect the perceptions and behaviors of individual thorough observation and imitation (48). If they felt that important other confirm junk food consumption, didn't negative evaluation in this relation or while they consume junk food, it is expectable that adolescent also consume this foods. In comparison with adults, adolescent likely more influenced by family, peer and reference group and more dependent in their decisions for choice foods. Therefore it is expectable that social norm or descriptive norms construct have greater role in this age group. Our finding in relation to power of PBC to predict intention are contradict with some of other TPB studies (19,32,56,57) and PBC couldn't predict intention to consume junk food but PBC emerged as the most significant predictor of behavior at classic TPB and second significant predictor in the extended model. this means that perceived control to junk food consumption has no role in intention formation but directly influence the behavior. The stronger role of PBC that intention means that the junk food consumption is less intentional process and more affected by PBC than intention therefore another important actor such as habit (58) maybe impress the behavior. while parent always give the spending money to their children and junk food is abundant and available in the stores and super markets and Cafeterias in school, they have easy access to this food and because of junk food always are cheaper than other healthy foods, adolescent regularly buy and eat this foods and therefore it maybe form a habit and become routine behavior. Consequently intention in such behavior domain is less detrimental for behavior and following PBC intention relationship weekend and PBC directly affected the behavior. Predictability power of TPB, between various studies is different(56). The explained vari-

ance in behavior in the current study is lower than most of other report (e.g. Armitage & Conner 2001) and traditional and extended TPB predicted 9% and 14% of variance on behavior respectively. This result indicated that since food choice behaviors have a Complex nature other influential factor should include in the model (such as habit). Another reason for low predictability power of model for behavior could be the wide range of junk foods that assessed in our study. It is clear that the whatever the surveyed behavior were more specific, the TPB. Power for predict behavior increase (59). Although intention in the first model predicted the behavior but in second step didn't. Sometimes translation of intention into behavior could be difficult such as situation or behavior in that, different barriers or control factor prevented the behavior implementation. Dietary behavior are often become habitual and in such case the intention – behavior relationship decreased and rational decisions didn't play important role in predict behavior (60, 61). nonetheless our finding is in line with De Bruijn (20) and colleagues, their finding revealed that both PBC and intention predict the saturated fat consumption and PBC was a stranger predictor than intention furthermore intention and PBC altogether explained only 8% of variance in fat intake. In the present study we explore the role of TPB variable and the additive effect of descriptive norm to explain intention toward junk food consumption and our finding showed that descriptive norm significantly increased the explained variance on intention. But some limitation of our study need is needed to be mentioned. First the cross-sectional native of our study, that all study variables were measured simultaneously, therefore causal effects inference could vitiate. Second the self-report measures, which can be regarded as an investigation limitation and finally we didn't ask about portion size of different junk food in questions because diversity of this food in size and type could be confusing and hence we only assessed the frequency of this foods. nevertheless this study is one of the scarce researches attended the role of descriptive norm in explanation of behavior of intention and to our knowledge this is the only study that included the descriptive norm in the TPB frame work for describe the intention and behavior of adolescent toward junk food. Therefore if

we want to planning for reduce consume of unhealthy foods especially among adolescents we need to attend the attitude, social norms and PBC for effectiveness of our program. Furthermore more investigation in the future is needed to recognize the other factors that influence this behavior.

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References

1. Hejazi N, Mazlom Z. *Socioeconomic Status, Youth's Eating Patterns and Meals Consumed away from Home. Pakistan Journal of Biological Science*, 2009; 12(9): 730- 733.
2. *World Health Organization: Obesity: Preventing and Managing the Global Epidemic: Report of a WHO consultation on Obesity. Geneva 1997.*
3. Van den Hork K, Van Dommelen P, Van Buuren S, Verkerk PH, Hirasing RA. *Prevalence of Overweight in the Netherlands in 2003 compared to 1980 and 1997. Archives of disease in childhood*, 2007; 92: 992-995.
4. Schokker DF, Visscher TL, Nooyens AC, Van Baak MA, Seidell JC. *Prevalence of overweight and Obesity in the Netherlands. Obesity review*, 2007; 8: 101-108.
5. Freedman DS, Dietz WH, Srinivasan SR, Berenson GS. *The relation of overweight to cardiovascular risk factors among children and adolescents: The Bogalusa Heart Study. Pediatrics* 1999; 103: 1175-1182.
6. Kelishadi R, Alikhani S, Delavari A, Alaedini F, Safaie A, Hojatzadeh E. *Obesity and associated lifestyle behaviours in Iran: Finding from the first National Non-communicable Disease Risk factor Surveillance Survey. Public Health Nutrition*: 2007; 11(3): 246-251.
7. *World health organization (WHO). Obesity: Preventing and Managing the Global Epidemic, 1st ed. Report of a WHO Consutation on Obesity, Geneva, 3-5 June 1997. WHO/NUT/NCD/98.1. Geneva: WHO, 1998.*
8. *The World Health Report 2002. Reducing risk, promoting healthy life. Geneva, World Health Organization, 2002: 57-61: 162.*

9. Bidad K, Anari S, Tavasoli S. Dietary Intakes of Adolescent Girl in Relation to Weight Status. *Iranian Publ Health*, 2008; 37(1): 114-8.
10. WHO. WHO/FAO. WHO Technical Report Series 916. Diet, nutrition and the prevention of chronic diseases. Geneva: WHO, 2003.
11. Kelishadi R, Ardalan G, Gheiratmand R, Gouya M, Razaghi E, Delavari A, et al. Association of physical activity and dietary behaviors in relation to the body mass index in a national sample of Iranian children and adolescents: CASPIAN Study. *Bull World Health Organ*, 2007; 85(1): 19-26.
12. Kaushik JS, Narang M, Parakh A. Fast Food Consumption in Children. *Indian Pediatrics*, 2011; 48, 97-101.
13. Austin SB, Melly SJ, Sanchez BN, Patel A, Buka S, Gortmaker SL. Clustering of fast-food restaurant around schools: A novel application of spatial statistics to the study of food environments. *Am. J. Public Health*, 2005; 95: 1575-1581.
14. Kant AK, Graubard BI. Eating out in America, 1987-2000: Trends and nutritional correlates. *Pre. Med*, 2004; 38: 243-249.
15. Steffen L, Kroenke CH, Yu X, Pereira MA, Slaterry ML, et al. Associations of plant food, dairy product and meat intakes with 15 y incidence of elevated blood pressure in young black and white adults: The coronary artery risk development in young adults (CARDIA) study. *Am. J. Clin. Nutr.*, 2005; 82: 1169-1177.
16. Indian food worse than western junk. Available from: timesofindia.indiatimes.com/article_show/1755418.cms. Accessed July 14, 2010.
17. Boger RP, Brug J, Van Assema P, Dagnelie PC. Explaining fruit and vegetable consumption: The Theory of Planned Behaviour and misconception of personal intake levels. *Appetite*, 2004; 42(2): 157-166.
18. Goldstein MG, Whitlock EP, DePue J. Planning Committee of the Addressing Multiple Behavioral Risk Factors in Primary Care Project. Multiple behavioral risk factor interventions in primary care. Summary of research evidence. *Am J Prev Med*. 2004; 27: 61-79.
19. Ajzen I. The Theory of Planned Behavior. *Organizational Behavior and Human Decision Processes*, 1991; 50(2): 179-211.
20. De Bruijn GJ, Kroeze W, Oenema A, Brug J. Saturated Fat Consumption and The Theory of Planned Behaviour: Exploring Additive and Interactive Effects Of Habit Strength. *Appetite*, 2008; 51: 318-323.
21. Berg C, Jonsson I, Conner M. Understanding choice of milk and bread for breakfast among Swedish children aged 11-15 years: an application of the theory of planned behavior. *Appetite* 2000; 34: 5-19.
22. Bissonnette MM, Contento IR. Adolescents perspectives and food choice behaviors in terms of the environmental impacts of food production practices: application of a psychosocial model. *J Nutr Ed* 2001; 33: 72-82.
23. Lien N, Lytle LA, Komro KA. Applying theory of planned behavior to fruit and vegetable consumption of young adolescents. *Am J Health Promot* 2002; 16(4): 189-197.
24. Dennison CM, Shepherd R. Adolescent food choice: an application of the theory of planned behavior. *J Hum Nutr Diet* 1995; 8: 9-23.
25. Povey R, Conner M, Sparks P, James R, Shepherd R. Application of the theory of planned behavior to two dietary behaviors: roles of perceived control and self-efficacy. *Br J Health Psychol*. 2000; 5: 121-139.
26. Tak NI, TeVelde SJ, Oenema A, Van Der Horst K, Timperio A, Crawford D, Brug J. The Association Between Home Environmental Variables And Soft Drink Consumption Among Adolescents. *Exploration of Mediation By Individual Cognitions And Habit Strength*. *Appetite*, 2011; 56: 503-510.
27. Conner M, Norman P, Bell R. The Theory Of Planned Behavior And Healthy Eating. *Health Psychol*. 2002; 21: 194-201.
28. Blanchard CM, Fisher J, Sparling PB, et al. Understanding adherence to 5 servings of fruits and vegetables per day: a Theory of Planned Behavior perspective. *J Nutr Educ Behav*. 2009; 41: 3-10.
29. Karimi-Shahanjarini A, Rashidian A, Majdzade R, Omidvar N, Ghazi Tabatabai M, Shojaezadeh D. Parental Control Junk-Food Consumption: A Mediating and Moderating Effect Analysis I. *Journal of Applied Social Psychology*. 2012; 42(5): 1241-1265.
30. Nejad LM, Wertheim EH, Greenwood KM. Predicting dieting behavior by using, modifying, and extending the theory of planned behavior. *Journal of Applied Social Psychology*, 2004; 34: 2099-2131.
31. Bogers RP, Brug J, Van Assema P, Dagnelie PC. Explaining fruit and vegetable consumption. The theory of planned behavior and misconception of personal intake levels. *Appetite*, 2004; 42: 157-166.
32. Armitage CJ, Conner M. Efficacy of the Theory of Planned Behavior: a meta-analytic review. *Br J Soc Psychol*. 2001; 40: 471-499.

33. Conner M, Sparks P. The theory of planned behavior and health behaviours. In *Predicting Health Behaviour*; Conner M, Norman P (eds). Open University Press: Buckingham; 1996; 121-162.
34. Hardeman W, Johnston M, Johnston DW, Bonetti D, Wareham NJ, Kinmonth AL. Application of the Theory of Planned Behaviour in behavior change interventions: A systematic review. *Psychology and Health*, 2002; 17(2): 123-158.
35. Trafimow D, Finlay K. The importance of subjective norms for a minority of people. *Personality and Social Psychology Bulletin*, 1996; 22: 820-828.
36. Sheeran P, Orbell S. Augmenting the theory of planned behavior: Roles for anticipated regret and descriptive norm. *Journal of Applied Social Psychology*. 1999; 29: 2127-2142.
37. Ajzen I, Fishbein M. The influence of attitudes on behavior. In D. Albarracin, B. T. Johnson, & M. P. Zanna (Eds.), *The handbook of attitudes* (173-221). Mahwah, NJ, USA: Lawrence Erlbaum, 2005.
38. Conner M, McMillan B. Interaction effects in the theory of planned behavior: Studying cannabis use. *British Journal of Social Psychology*, 1999; 38: 195-222.
39. Cialdini RB, Reno RR, Kallgren CA. A focus theory of normative conduct: Recycling the concept of norms to reduce littering in public places. *Journal of Personality and Social Psychology*, 1990; 58: 1015-1026.
40. Rivas A, Sheeran P, Armitage CJ. Augmenting the theory of planned behavior with the prototype/willingness model: Predictive validity of actor versus abstainer prototypes for adolescents health-protective and health-risk intentions. *British Journal of Health Psychology*, 2006; 11: 483-500.
41. Terry DJ, Hogg MA, White KM. The theory of planned behavior: self-identity, social identity and group norms. *Br. J. Soc. Psychol.* 1999; 38: 225-244.
42. Heath Y, Gifford R. Extending the theory of planned behavior: Predicting the use of public transportation. *Journal of Applied Social Psychology*, 2002; 32: 1559-1816.
43. Norman P, Clark T, Walker G. The theory of planned behavior; descriptive norm, and the moderating role of group identification. *Journal of Applied Social Psychology*, 2005; 35: 1008-1029.
44. Ajzen I. Constructing a TPB Questionnaire: Conceptual and Methodological Considerations, <http://www.people.umass.edu/ajzen/pdf/tpb.measurement.pdf>, 2002.
45. O'Keefe DJ. *Persuasion: Theory and Research*, 2nd ed. Sage Publications, Thousand Oaks, CA, 2002.
46. Rivas A, Sheeran P. Descriptive norms as an additional predictor in the theory of planned behavior: a meta-analysis. *Curr. Psychol.* 2004; 22(3): 218-233.
47. Louis W, Davies S, Smith J, Terry D. Pizza and pop and the student identity: The role of referent group norms in healthy and unhealthy eating. *Journal of Social Psychology*, 2007; 147(1): 57-74.
48. Bandura A. *Social learning theory*. Englewood, Cliffs, NJ: Prentice-Hall, 1977.
49. Francis JJ, Eccles MP, Johnston M, Walker A, Grimshaw J, et al. *Constructing Questionnaires Based on The Theory of Planned Behaviour: A Manual for Health Services Researchers*. Centre for Health Services Research University of Newcastle. Available at: http://pages.bangor.ac.uk/~pes004/exercise_psych/downloads/tpb_manual.pdf, 2004.
50. Mirmiran P, Azadbakht L, Azizi F. Dietary behavior of Tehranian adolescent does not accord with their nutritional knowledge. *Public Health Nutr*, 2007; 10(9): 897-901.
51. Cohen J. A power primer. *Psychological Bulletin*, 1992; 112: 155-159.
52. White KM, Terry DJ, Troup C, Remple LA, Norman P. Predicting The Consumption of Food Low in Saturated Fats Among People Diagnosed with Type 2 Diabetes and Cardiovascular Disease. *The Role of Planning in the Theory of Planned Behavior*. *Appetite*, 2010; 55: 348-354.
53. Mahson D, Cowan C, McCarthy M. The role of attitudes, subjective norms, perceived control and habit in the consumption of ready meals and takeaway in Great Britain. *Food Quality and Preference*, 2006; 17(6): 474-481.
54. Jacobsen RP, Mortensen CR, Cialdini RB. Bodies obliged and unbound. Differentiated response tendencies for injunctive and descriptive social norms. *Journal of Personality and Social Psychology*, 2011; 100: 433-448.
55. Pasupathi M. Age differences in response to conformity pressure for emotional and nonemotional material. *Psychology and Aging*, 1999; 14: 170-174.
56. Godin G, Kok G. The Theory of Planned Behavior: a review of its applications to health-related behaviors. *Am J Health Promot.* 1996; 11: 87-98.
57. Backman DR, Haddad EH, Lee JW, Johnston PK, Hodgkin GE. Psychosocial predictors of healthful

dietary behavior in adolescents. J NutrEducBehav. 2002; 34: 184-193.

58. *Saba A, Di Natale R. A study on the mediating role of intention in the impact of habit and attitude on meat consumption. Food Quality and Preferences, 1999; 10: 69-77.*
59. *Baranowski T, Cullen K, Baranowski J. Psychosocial correlates of dietary intake: advancing dietary intervention. Annu Rev Nutr. 1999; 19: 17-40.*
60. *Verplanken B, Aarts H. Habit, attitude, and planned behavior: Is habit an empty construct or an interesting case of goal-directed automaticity? European Review of Social Psychology, 1999; 10: 101-134.*
61. *Aarts H, Paulussen T, Schaalma H. Physical exercise habit: on the conceptualization and formation of habitual health behavior. Health Educational Research, 1997; 12(3): 274-362.*

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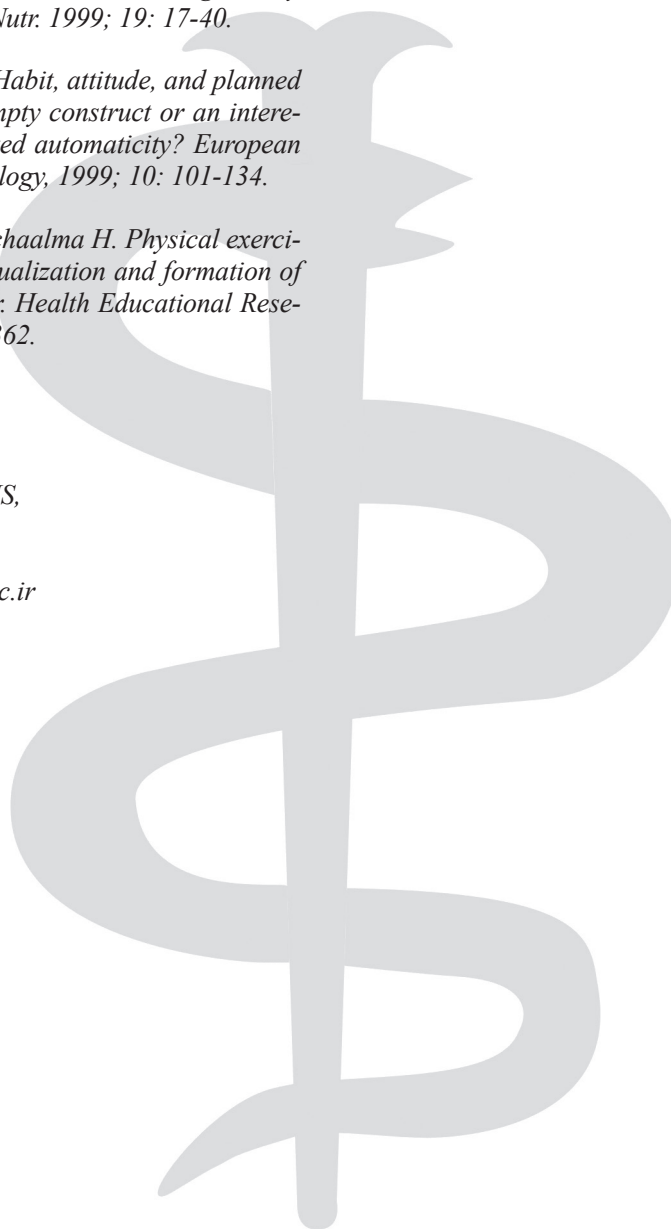
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Medication storage among university students in Saudi Arabia

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Abstract

Objective: Leftover medicines mostly result in wastage of country resources as well as reduction of the quality of life of the general public. This study aims to measure university students' knowledge and practice regarding medicines' storage at home.

Methods: A cross sectional research design using convenience sampling technique was adopted in this study. A pre-validated questionnaire was distributed to university students in the western region of Saudi Arabia from March 2013 to June 2013. All data was analyzed using SPSS version 16.0 and any P-value of less than 0.05 was considered significant.

Results: A total of 1446 valid response were successfully collected. Majority of respondents 75% have stored medicines at home. Only 47% of them follow the storage instructions for medicines. Pain killers were the highest category of the stored medicines 73% followed by cold/flu/antihistamines 68% and antibiotics 40%. Slightly more than half of the respondents (53%) regularly check the expiry date of the stored medicines. The majority of respondents store their medicines in the refrigerator 52% followed by bedroom 24% and kitchen 21%. One-third of respondents 36% stated that their stored medicines at home are within children reach.

Conclusion: It is concluded that university students practice inappropriate medication storage and management at home. It is recommended to include topics related to good medications practice in the curriculum of all areas of specialization at the university level and enhance efforts to increase public awareness of proper storage and use of medications at home.

Key words: medications, storage, students, Saudi Arabia

Introduction

High rate of medications sharing and self medication was observed in many developed and developing countries¹⁻⁴. Frequent sharing of medications among families could place them to risks and diverse consequences^{5,6}. A cross sectional study in Australia among 204 families found that whenever the number of medications increased at home, there are an increase in severity of illness, increase hoarding of medicines and increased therapeutic duplications⁷.

High rate of self medication and sharing of medications among families could result from frequent medications storage at home. Thus, improper and unnecessary storage of medications at home could negatively affect on the community health. A high proportion of medicines are required to be stored in a dry and cool place at room temperature 15°-25°C⁸. Storing medications in humid place or exposing them to direct sunlight could affect on the stability and quality of these medications⁹. Thus, storing medications especially tablets and capsules in the toilet or window ledges could degrade these medicines and reduce their efficacy. On the other hand, other medications require special storage conditions like refrigerator. Miss placing refrigerated or room temperature medications, could significantly affect on the quality and efficacy of these medications. Therefore, there is no standard place to store all medications. Each medicine requires its own storing conditions. Thus, reading the medicine leaflet and following the storage instructions is very important¹⁰. Place of medications' storage should be away from children reach. Storing medications in places within the reach of children might expose those children to hazards and might cost them their lives. A study in the US found that more than 70000 children are

admitted annually to the emergency room due to medications overdose. Where 95% of children of less than 5 years old were admitted to the emergency department due to unsupervised medications over dose¹¹.

In addition to the need of the proper storage conditions for medications, it is of the same importance to know type and length of medications storage. Certain medications such as creams, drops and suspensions might need to be disposed after the end of the treatment or can be stored for a week as a maximum. Expired, crumbly and obviously discolored medications should be disposed immediately⁹. Keeping these medications for long time could definitely reduce their efficacy and most properly reduce patient's quality life.

In this study, university students were targeted since it is believed that university students are the most educated category at home. Thus, knowing their practices about medications storage could give us a great idea about the current practice towards medications storage at home, as well as informing us about the possible interventions that might be needed to target those households. Jeddah, Makkah, and Taif were selected for the study. Even though these three cities are only 170 Km away from each other, there are three different climates in these cities. Jeddah is very humid and hot city where the temperature ranges between 35°- 45°C most of the year. Makkah is also a very hot city but with dry weather. Temperature ranges between 35°- 45°C most of the year. Taif is a dry and less hot compared to Makkah and Jeddah. Temperature ranges between 30°- 35°C most of the year. Thus it is important to know the practices of medications storage in these three different cities in the western region of Saudi Arabia. Therefore, this study aimed to measure the current practices of medications storage among university students in the western region of Saudi Arabia.

Methodology

A cross-sectional study design was carried out in three universities in the Western region of Saudi Arabia. These universities are Taif University in Taif, Um Al-Qura University in Makkah and King Abdul Aziz University in Jeddah. About 1700 questionnaires were conveniently distributed to

the students in the public areas of the each campus from March 2013 to June 2013.

The questionnaire was developed after broad literature review. Face and content validation was done by experts from the Clinical Pharmacy Department at Taif University. Questionnaire was divided into four sections. First section was about respondents' demographics such as age, gender, educational level, living area and number of family members. Section two was about general knowledge and certain practices about medications storage as well as types of medications stored at home. Third section covered the duration of medications storage at home and respondents awareness and practices towards medications expiry date. Last section was about the place of medications storage at home and respondents' awareness regarding the need of different places of medications storage for different types of medications.

Respondents of this study should meet the following three criteria: (1) they should be students in Taif University, or Um Al-Qura University or King Abdul Aziz University, (2) able to read and write in Arabic, and (3) agreed to give a verbal informed consent. Respondents who did not meet these criteria were excluded from this study.

Data collectors met with the students in public areas in each campus like restaurants, bookshops and libraries. First, data collectors introduced themselves to the students and briefed them about the study. Then, they informed them that all data will be kept confidential and their participation in the study will be voluntarily. Students were given the questionnaire upon their approval to give verbal informed consent to participate in this study. Answering the questionnaire did not take more than 10 minutes for completion.

Data obtained from this survey were coded, entered and then analyzed using the Statistical Package for Social Sciences (SPSS) Version 16. Frequencies and percentages were used to describe the results whereas Chi-square and Fisher Exact tests were used to determine the association between the general public demographic profiles and their knowledge and practices towards medication storage. *P*-value < 0.05 was considered significant.

Results

A total of 1446 valid responses were successfully obtained during a period of 4 months of data collection (June 2013 – October 2013). Males represented about 93% of the total responses. Makkah respondents were about 40% followed by Taif respondents 30% and finally Jeddah respondents 26%. Majority of respondents were rural residents 83% with family size 5-10 members 63%. Full respondents' details are presented in Table 1.

Table 2 demonstrates respondents' knowledge regarding medication storage at home. About 75% of respondents stated that they have stored medicines at home. 53% of them don't have first aid kit at home. Whereas about 50% of them have more than 5 medicines stored at home. Slightly less than half (48%) don't know the names of stored medicines at home. Only 51% of our respondents read the leaflet provided with the medication package while only 47% of them follow the instructions of

medication storage. Varied responses were noticed from Makkah and rural residents. Higher proportions of rural respondents have first aid kit at home, have less than 5 medicines stored at home and don't know the names of stored medicines at home. In addition, higher proportions of Makkah residents have less than 5 medicines stored at home and know the names of stored medicines at home.

Table 3 shows types of medicines stored at home. A bit less than three-quarters of respondents, 73%, store pain killers at home. Whereas flu/cold medications represented the second highest stored medicines at home, 69%. In addition, about 40% of respondents store antibiotics at home. Cardiovascular medications were the least stored medicines at home which presented only 6% of the responses. Higher proportions of urban residents store pain killers; flu/cold medicines while a higher proportion of rural residents stored digestive medicines and do not store antibiotics at home. Furthermore, higher proportions of Taif

Table 1. General Characteristics of the Respondents

Demographic characteristics		Frequency	Percentage
Gender	Male	1348	93.2
	Female	98	6.8
Age	≤20	175	12.1
	20-25	1214	83.3
	>25	57	3.9
Nationality	Saudi	1386	96.0
	None Saudi	58	4.0
Education Level	1 st year	285	19.7
	2 nd year	266	18.4
	3 rd year	383	26.4
	4 th year	272	18.8
	5 th year	158	10.9
	6 th year	78	5.4
Marital Status	Single	1298	90.0
	Married	119	8.3
	Widowed/Divorced	25	1.7
City Name	Makkah	587	40.5
	Jeddah	378	26.3
	Taif	480	33.2
Residence Location	Rural	1186	83.0
	Urban	242	17.0
Family Members	< 5 members	335	23.3
	5-10 members	917	63.8
	>10 members	185	12.9
Chronic	Yes	515	35.5
	No	917	63.5

Table 2. Knowledge Regarding Medication Storage at Home

Section	Responses (n) (%)		City	Age	Education level	Residence location	No. Family Members
	Yes	No					
Do you have medicines stored at home	1085 (75.4)	354 (24.6)	0.020	0.368	0.064	<0.001	0.034
Do you have first aid kit at home?	678 (47.2)	757 (52.8)	0.062	0.129	0.054	0.004	0.529
Roughly, how many stored drugs do you have at home?							
Don't have	261 (18.1)	-					
< 5	476 (33.0)	-					
5-10	391 (27.1)	-	<0.001	0.133	0.001	<0.001	<0.001
10-15	125 (8.7)	-					
>15	188 (13.0)	-					
Do you know the name of stored medicines at home?	734 (51.2)	701 (48.2)	0.021*	<0.001	0.161*	0.001*	0.837*
Is it important to know the name and use of the medicines that you are using?	1015 (91.5)	122 (8.5)	0.001	0.087	<0.001	<0.001	<0.001
Do you store the medicines with their original package?	1335 (92.2)	103 (7.8)	0.058	0.543	0.069	<0.001	0.086
Do you keep the leaflet provided with medicines?	1281 (82.1)	257 (17.9)	0.136	0.746	0.661	0.175	0.394
Do you read the leaflet provided with medicines?	734 (51.1)	701 (48.9)	0.439	0.963	0.719	0.391	0.645
Do you follow the instructions of medicines storage?	681 (47.5)	753 (52.5)	0.710	0.987	0.528	0.567	0.777

* Fisher Exact Test

residents do not store antibiotics and digestive medicines at home.

Table 4 shows types of medicines dosage forms stored at home. Tablets and capsules were stored by 83% of respondents. Syrups and creams represented the second and third highest dosage forms of medicines stored at home 61% 50%, respectively. Ampoules were the least dosage form of medicines stored at home, 13%. Higher proportions of urban residents store tablet/capsule and cream dosage forms. In addition, higher proportions of Jeddah residents store syrup and cream dosage forms.

Table 5 demonstrates respondents' awareness about the expiry date of medicines. About 78% of respondents were aware about the presence of expiry date for medicines. Only 53% of them check the expiry date of the stored medicines and about one-third of them check the expiry date on a monthly basis. Surprisingly, about 16% of the respondents were willing to use expired medicines.

Table 6 shows the duration of medicines stored at home. 29% of respondents agreed that they store their medicines until their expiry date or until the end of treatment recommended by the physician or

Table 3. Types of Medication Stored at Home

Section	Responses (n) (%)		City	Age	Education level	Residence location	No. Family Members
	Yes	No					
Pain Killers	1051 (73.0)	388 (27.0)	0.004	0.113	0.046	<0.001	0.293
Cold/Flu/Antihistamines	986 (68.6)	452 (31.5)	0.029*	0.070	0.652*	0.002*	0.213*
Asthma and respiratory	274 (19.0)	1165 (81.0)	0.618*	0.461	0.540*	0.065*	0.941*
Stomach and Digestive	318 (22.1)	1121 (77.9)	<0.001	0.862	0.006	<0.001	0.077
Antibiotics	570 (39.6)	868 (60.4)	<0.001	0.059	0.333	<0.001	<0.001
Vitamins	343 (23.9)	1095 (76.1)	<0.001	0.360	0.503	<0.001	0.003
Cardiovascular	90 (6.3)	1349 (93.7)	0.709	0.015	0.020	0.447	0.221
Hypertension	230 (16.0)	1209 (84.0)	0.177	0.839	0.075	0.149	0.848
Diabetes	411 (28.6)	1026 (71.4)	0.575	0.064	0.025	0.868	0.001
Others	121 (8.4)	1318 (91.6)	0.040*	0.437*	0.397*	0.420*	0.447*

* Fisher Exact Test

Table 4. Dosage Form of Medication Stored at Home

Section	Responses (n) (%)		City	Age	Education level	Residence location	No. Family Members
	Yes	No					
Tablets and Capsules	1191 (82.9)	247 (17.2)	0.136	0.063	<0.001*	0.004*	0.004*
Syrups	879 (61.2)	558 (38.8)	0.001*	0.534	0.854*	<0.001*	0.010*
Creams	714 (49.7)	724 (50.3)	<0.001	0.307	0.173	<0.001	<0.001
Ampoules	191 (13.3)	1246 (86.7)	0.058*	0.899	0.187*	0.071*	0.295*
Drops	450 (31.3)	988 (68.7)	<0.001	0.112	0.907	<0.001	0.014
Others	67 (4.7)	1371 (95.3)	0.163*	0.015	0.262*	0.204*	0.464*

* Fisher Exact Test

pharmacist. Used suspensions were not stored by one-quarter of our respondents whereas medicines were stored until their future need was presented by 14% of respondents. Decision to store or through medicines depended mainly on their future need was presented by 63% of respondents while 17% of respondents store all medicines regardless of their future need or expiry date. Higher proportions of female respondents, rural residents, and families with more than 10 members in size, store medicines until the end of treatment recommended by physi-

cian or pharmacist. In addition, higher proportions of 4th year students, family members of more than 10 members, and Taif residents never store used fluids. Furthermore, higher proportions of male respondents, 4th year students, urban residents, families with 5-10 members in size and Jeddah residents, decide to store or throw the leftover suspensions based on their future need.

Table 7 represents place of medications storage at home. More than two-thirds of respondents were aware that medicines require special place

Table 5. Awareness about Expiry Dates of Medications Stored at Home

Section	Responses (n) (%)		City	Age	Education level	Residence location	No. Family Members
	Yes	No					
Do you know that there is an expiry date for medicine?	1126 (78.1)	316 (21.9)	0.594	0.547	0.100	0.045	0.037
Do you regularly check the expiry date of the stored medicines?	761 (52.8)	680 (47.2)	0.112	0.071	0.084	0.567	0.339
If your answer in the previous question is yes, how many times do you check the expire date?							
Once a month	316 (33.9)		<0.001*	0.975	0.119	0.001*	<0.001*
Once every 2 months	239 (25.7)						
Once every 6 months	104 (11.2)						
Once a year	30 (3.2)						
Others	242 (26.0)						
Is it possible for you to use expired medicines?	227 (15.8)	1212 (84.2)	0.073	0.919	0.079	0.057	<0.001
Do you check the expire date of the medicines before buying them?	606 (42.1)	833 (57.9)	0.103*	0.379*	0.471*	0.710*	0.199*

* Fisher Exact Test

Table 6. Duration of Medications Storage at Home

Section	Yes	City	Age	Education level	Residence location	No. Family Members
For how long do you keep medicines stored at home?						
Until I consume all of it regardless of its expiry date	407 (23.8)	<0.001*	0.095*	0.057*	0.001*	0.001*
Until I notice a change in the medicine color	152 (10.6)					
Until its expiry date	418 (29.1)					
Until the end of the treatment according to the physician or pharmacist recommendation	426 (29.6)					
Others	35 (2.5)					
For how long do you keep the liquid medicines after finishing the treatment and using part of it?						
I don't store them	361 (25.1)	0.002*	0.064	0.003	0.022*	<0.001*
Three days or less	252 (17.5)					
Up to one week	224 (15.6)					
Up to one month	84 (5.8)					
Until I need them	202 (14.0)					
There is no specific time	171 (11.9)					
Until its expiry date	146 (10.1)					
Your decision to through or store the medicine depends on:						
Its price	172 (12.0)	0.008	0.207	<0.001*	0.003	0.006
Its future needs	897 (62.7)					
I keep all medicines	254 (17.7)					
Others	108 (7.5)					

* Fisher Exact Test

for storage. Half of them have special medications cabinet at home. About 36% of respondents confirmed that children can reach the place of medications storage. And almost 43% of respondents store their medications in the refrigerator. In addition, suspension medicines are stored in the refrigerator by 52% of respondents. Higher proportions of rural and Jeddah residents were aware that medicines require special conditions for storage. In addition, higher percentages of male and urban residents are informed by pharmacists about the place of medicine storage. Furthermore, greater proportions of females store their medicines in the kitchen whereas Makkah residents store their medicines in the refrigerator. Finally, higher proportions of males, Makkah and Jeddah residents store suspension medicines in the refrigerator.

Discussion

Treatment process starts from diagnoses of the illness to the prescription of the right medications at the right doses and ends with the proper administration and patient adherence to the prescribed regimen. If the patient was correctly diagnosed and prescribed the right medicines with the right quantity, but stored them in improper place, this means that he will consume ineffective medicines that either will not cure him or will increase the severity of his illness. Thus, medications storage is a critical stage that completes the treatment process. Proper medications storage, means keeping these medicines active, efficient and safe. While improper storage of those medications means less active, inefficient, and unsafe medicines that might harm patients and their family members especially

Table 7. Place of Medications Storage at Home

Section	Responses (n) (%)		City	Age	Education level	Residence location	No. Family Members
	Yes	No					
Do you know that medicines need special environment for storage?	979 (68.2)	456 (31.8)	0.029	0.078	0.625	0.014	0.029
Do you have at home special cabinet for medicines?	711 (49.6)	723 (50.4)	0.313	0.020	0.472	0.004	0.015
Does the pharmacist inform you about the place of storing medicines?	412 (28.7)	1022 (71.3)	0.369	0.248	0.025	0.007	0.044
At home, do you separate family members medications from each other when you store them	675 (47.1)	758 (52.9)	0.239	0.880	0.321	0.523	0.156
Can children at home reach the stored medicines?	518 (36.2)	914 (63.9)	0.010*	0.359	0.914*	0.740*	0.068*
Where do you normally store the medicines at home?							
Bathroom	82 (5.7)		<0.001*	0.782	0.123	0.347*	0.081*
Bedroom	340 (23.7)						
Kitchen cabinet	299 (20.9)						
Refrigerator	620 (43.2)						
Others	93 (6.5)						
Where do you keep suspensions after mixing them with water?							
Bathroom	73 (5.1)		<0.001*	0.668	<0.001	0.039*	<0.001
Bedroom	266 (18.6)						
Kitchen cabinet	269 (18.8)						
Refrigerator	748 (52.3)						
Others	74 (5.2)						

* Fisher Exact Test

children if placed accessible to children. Discussing medications storage need to cover four main points. First point is the place of storage, whereas the second point is the conditions of this place like temperature, humidity, exposure to direct sunlight, and accessibility by children. Third point to be discussed is the type of the stored medicines and finally duration of storage. These points are discussed in the next few paragraphs.

A total of 1446 respondents successfully responded to this survey. Females represented 6.8% of the total respondents. This low number of female respondents is due to the Saudi culture of separating males and females and not allowing males to directly contact with females. At universities, female campuses are totally separated from male campuses where males are not allowed to get in to female campuses. Since our data collectors were males, we could not get more responses from female respondents. Families in Saudi Arabia are of large size. More than three quarters of our respondents are of more than 5 family members. About one-third of our respondents have family members with chronic diseases.

In this study, 75% of respondents stated that they store medicines at home whereas only 47% of them have first aid kit. These findings are less than that reported for Basrah city in Iraq where 94% of the studied households stored medicines at home¹². In our study, 49% of respondents stored more than 5 medicines at home. This figure is far from what was found in Basrah, Iraq. It was found that 94% of their households store a mean of 14.26 medicines at home¹². Having large number of medicines stored at home would lead to the increase of the severity of illness, increase of the therapeutic duplication⁷ and might lead to high rate of self medication which was found in many studies^{1, 4, 6, 13}.

Reading medicine's leaflet and following storage instructions are very helpful. Fifty one percent of respondents read the medication leaflet and only 47% follow the storage instructions. Not following storage instructions might affect on the stability and efficacy of the medicine that could expose patients and their family members to unpleasant consequences.

Pain killers accounted for 73% of the stored medicines at home. This was followed by cold/flu/antihistamines 68%, antibiotics 40% and vita-

mins 24%. Several studies explored the types of medicines stored at home in different countries. In USA, a study was conducted in 24 homes found that 42% of the stored medicines were pain killers, 39% for cold/allergy, 23% for stomach and digestive system, 20% vitamins and only 6% antibiotics¹⁴. Another study in Iraq found 26.5% of the stored medicines were antibiotics, 19.6% analgesics, 6.9% vitamins and 9% antihistamines¹². In Pakistan, pain killers represented 88% of the stored medicines, this was followed by antipyretics 65%, antihistamines 44% and antibiotics 35%¹. Storing antibiotics in large quantities would lead to high rate of self medication with antibiotics that increase antibiotic resistance¹⁵.

Expiry date of medicines means that medicines should be disposed and not be used by patients beyond that date. In our study, only 53% of respondents check the expiry date of the stored medicines regularly while 16% of respondents are willing to take expiry medicines. Not checking the expiry date of medicines would result in accumulating and consuming expired medicines by patients. Our findings are similar to those reported elsewhere worldwide¹⁴.

General public should be informed about the place and duration of medication storage especially if this medication requires specific place of storage like refrigerator or need to be disposed immediately after the end of the treatment. For example, in our study, 14% of respondents store suspension dosage form medicines for future need use and about 10% store them until their expiry date. Pharmacists who are the primary source of information about medicines played insufficient role in informing patients about the proper and safe ways of medications storage since only 29% of respondents said that pharmacists informed them about the proper ways of medications storage.

Medicines should be placed in a dry and cool place, away from direct exposure to sunlight and at sites inaccessible by children⁹. In this study, 43% of medicines are stored in the refrigerator, 21% in the kitchen, 24% in the bedroom, and 5.7% in the bathroom. Storing medicines in the bathroom expose them to high level of humidity and temperature which might lead to the degradation of the medicine and reduction of its efficacy⁹. A study in Nigeria found that 48% of their respondents

store their medicines in bags, 4% in the kitchen, 4% in the bathroom, 32% on the dining table and 26% on the top of refrigerator¹⁶. In US, 78% of respondents stated that they store their medicines in the bathroom, 6% in the bedroom, and 98% in the kitchen¹⁴. In Qatar, 5.1% of respondents store their medicines in the kitchen, 25% in the refrigerator, and 50% in the bedroom¹⁷. Certain medications such as suspensions should be stored in the refrigerator. In this study, only 52% of respondents store suspensions in the refrigerator. Higher proportions of Makkah and Jeddah residents store their medicines in the refrigerator. This could be due to the high temperature during the year in Jeddah and Makkah compared to Taif.

In addition, 36% of respondents stated that they store their medicines at home in a place accessible to children. Exposing children to medicines would render them to high risk. A study in Iraq found that only 42% of medicines were stored properly and most other places of storage were accessible to children¹². A study in Malta among students aged 14-16 years found that 24% of them had taken at least one medicine without adult supervision during the previous three months¹⁸. On the other hand, about 70000 children are admitted annually to the emergency department in the US due to medications overdose¹¹. In addition, 95% of children, less than 5 years of age, visited emergency department were due to unsupervised medication overdoses¹¹.

Conclusion

Large amounts of medications are stored in respondents' households. About half of the respondents follow the storage instructions and regularly check their medicines for expiry date. Large numbers of medicines were stored in the refrigerator which could affect on their stability and efficacy. There should be a public campaign led by Saudi Ministry of Health or Non Governmental Organizations to increase the awareness of the public regarding medications storage at home. In addition, it is recommended to include topics related to good medications practice in the curriculum of all areas of specialization at the university level.

Limitations

This study faced main challenge of getting good number of female respondents since researchers couldn't recruit female data collectors and regulations in the Kingdom of Saudi Arabia don't allow males to enter female students' campus.

References

1. Zafar SN, Syed R, Waqar S, Zubairi AJ, Waqar T, Shaikh M, et al. Self-medication amongst university students of Karachi: prevalence, knowledge and attitudes. *J Pak Med Assoc.* 2008; 58(4): 214-217.
2. Sharma V, Thakur S, Bhatt N, Guleria R, Singh R. Self Medication And Drug Use Patterns In A Town Of Himachal Pradesh: A Survey International Journal of Advances in Pharmaceutical Research 2012; 3(8): 1058-1062.
3. Hassali MA, Shafie AA, Al-Qazaz H, Tambyappa J, Palaian S, Hariraj V. Self-Medication Practices Among adult population attending community pharmacies in Malaysia: an exploratory study. *Int J Clin Pharm.* 2011; 33(5): 794-799.
4. Hussain A, A K. Self Medication among University Students of Islamabad, Pakistan. A Preliminary Study. *Southern Med Review.* 2008; 1(1): 14-16.
5. Goldsworthy RC, Schwartz NC, Mayhorn CB. Beyond abuse and exposure: framing the impact of prescription-medication sharing. *Am J Public Health.* 2008; 98(6): 1115-1121.
6. Ellis J, Mullan J. Prescription medication borrowing and sharing--risk factors and management. *Aust Fam Physician.* 2009; 38(10): 816-819.
7. Sorensen L, Stokes JA, Woodward M, Roberts MS. Medication management at home: medication-related risk factors associated with poor health outcomes. *Age and Ageing* 2005; 34: 626-632.
8. Crichton B. Keep in a cool place: exposure of medicines to high temperatures in general practice during a British heatwave. *Journal Of The Royal Society Of Medicine* 2004; 97(7): 328-329.
9. Scott V. Storing Medications Safely. *Rainbow Rehabilitation Centers* 2005.
10. Vinker S, Eliyahu V, Yaphe J. The effect of drug information leaflets on patient behavior. *Isr Med Assoc J.* 2007; 9(5): 383-386.

11. Budnitz DS, Salis S. Preventing medication overdoses in young children: an opportunity for harm elimination. *Pediatrics*. 2011; 127(6): 2011-0926.
12. Jassim A-M. In-home Drug Storage and Self-medication with Antimicrobial Drugs in Basrah, Iraq. *Oman Med J*. 2010; 25(2).
13. Arikpo GE, Eja ME, Enyi-Idoh KH, Akubuenyi F, Ngang U, et al. Patterns Of Antibiotic Drug Use In Southern Nigeria Communities. *World Journal of Applied Science and Technology*. 2011; 3(1): 86-92.
14. Asti L, Jones R, Jeffrey A. Bridge. Acetaminophen and Expired Medication Storage in Homes with Young Children. *Journal of Clinical Toxicology*. 2012; 2(5).
15. Grigoryan L, Haaijer-Ruskamp FM, Burgerhof JG, et al. Self-medication with antimicrobial drugs in Europe. *Emerg Infect Dis*. 2006; 12(3): 452-459.
16. Obitte NC, Chukwu A, Odimegwu DC, Nwoke VC. Survey of drug storage practice in homes, hospitals and patent medicine stores in Nsukka, Nigeria *Scientific Research and Essay*. 2009; 4(11): 1354-1359.
17. Kheir N, Hajj ME, Wilbur K, Kaissi, R. & Yousif, A. An exploratory study on medications in Qatar homes. *Drug Healthc Patient Saf*. 2011; 3: 99-106.
18. Darmanin Ellul R, Cordina M, Buhagiar A, Fenech AJ, Mifsud A. Health complaints and use of medicines among adolescents in Malta *Pharmacy Practice* 2008; 6(3): 165.

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Mini Review: A narrative review about Renal Function Predictive Equations

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Abstract

Glomerular filtration rate (GFR) is an excellent marker of kidney function but due to inherent limitations of cost and complex procedure, it is not possible to measure GFR feasibly in clinical practice. As a substitute to cumbersome GFR measurement procedure, estimated GFR is used in clinical practice. Since more than a century, various renal function predictive equations have been developed and used. The landmark for these renal function predictive equations is believed to be serum creatinine, although new equations are using biomarkers other than serum creatinine for better estimation of GFR and consequently accurate diagnosis and staging of chronic kidney disease.

Key words: Biomarkers, Creatinine, Glomerular filtration rate, Kidney, Predictive equations, Renal

Introduction

Kidney patients either have diverse clinical presentations ranging from renal (hematuria) to extra-renal symptoms (edema, hypertension) or they might be completely asymptomatic with kidney disease being accidentally discovered months or years after an abnormal urinalysis or regular scheduled examination [1]. Moreover, as kidney is primarily responsible for three main functions of secretion, excretion and production of hormones, either all these functions will be disturbed in kidney patients or some functions will be diminished. For instance, patient with nephrogenic diabetes insipidus will have diminished ability to concentrate urine but on the other hand the remaining functions of kidney will be completely normal [2]. Once kidney disease is diagnosed, the extent of kidney

damage and the rate of progression of disease are the next two important concerns for a clinician. For centuries a single measurement of plasma creatinine (metabolic product of creatine derived from skeletal muscles) has been used to determine GFR and diagnosis of renal disease. Since being freely filtered from glomerulus and not metabolized by kidney, creatinine fulfills the criteria for an ideal endogenous biomarker to some extent.

The major limitation associated with creatinine is its secretion and reabsorption by proximal tubules as well as influence of dietary intake, muscle mass and various demographic factors on its plasma level [4]. These limitations lead to intra-individual variations (upto 5.3%) in plasma creatinine level. Moreover, due to tubular secretion of creatinine, serum creatinine level tends to be normal even if GFR is markedly reduced as seen in acute kidney injury (AKI) and becomes evident when more or approximately 50% of renal function has been lost. More precisely, serum creatinine can only be used to calculate GFR in individuals who have stable renal function [5].

Due to inherent limitations of single measurement of serum creatinine, 24-hour urine creatinine clearance was introduced as an alternative. This procedure requires an individual to collect urine sample for 24-hours. Calculation of creatinine clearance is based on the fact that if tubular secretion of creatinine is ignored, then the amount of filtered creatinine in urine will be equal to the product of serum creatinine and GFR.

Although glomerular filtration rate (GFR) has proven to be an excellent index for kidney function but due to its' complex and cumbersome measurement, it is not feasible to measure GFR in

clinical practice. In order to provide best alternative for GFR, various renal biomarkers have been utilized in clinical practice [3]. The current review attempts to shed light on different biomarkers of kidney function, extent of kidney dysfunction as well as progression of renal disease. In addition to the limitations associated with serum creatinine in estimating GFR, 24 hour urine creatinine clearance shows intra-individual variation of 11% along with cumbersome timed urine collection and increase chances of failure in collecting entire specimen [4,6]

Introduction of Estimated Glomerular Filtration Rate (eGFR)

There is no standardized method available for measurement of GFR. Inulin, gold standard for measurement of GFR, is not routinely used in clinical practice as it needs continuous bolus administrations along with timed urine collection. In order to overcome this situation, several recommending bodies e.g. National Kidney Foundation Disease Outcomes Quality Initiative (K-DOQI), NICE guidelines, renal association guidelines currently recommends use of estimated GFR (eGFR) [7]. eGFR provides an estimation of blood flow (ml/min) through glomeruli. Although eGFR serves as the best and most convenient alternative of measured GFR (mGFR) but still eGFR alone cannot be used in various conditions e.g. pregnancy, children, obesity, malnourished and amputees. Currently eGFR is calculated via renal function predictive equations [8].

Introduction of Renal function predictive equation

Renal function predictive equations estimate GFR by relying upon serum creatinine, demographic variables that effect GFR and various correction factors simultaneously. The main purpose of development of such equations is to measure extent of kidney function clinically without undergoing expensive and time consuming procedures. Although widely used in clinical settings as well as research studies, these equations cannot be used for estimation of GFR in cases where there is rapid fluctuations of serum creatinine concentration such as severely ill, obese, patients suffering from Acute kidney injury (AKI) or patients on Renal re-

placement therapy (RRT). The first clinically use renal function predictive equation was introduced in middle of nineteen century.

Cockcroft and Gault equation

Back in 1976, Cockcroft and Gault derived a renal function predictive equation that determines creatinine clearance (Ccr) on the basis of serum creatinine (S.Cr), demographic variables and correction factors. The equation was derived from the data of hospitalized men with chronic kidney disease (CKD). Only few females were included in this cohort. Although the original CG equation was not adjusted for body surface area (BSA) but later a correction factor for BSA 1.73 m² was added to increase accuracy of results [9]. Despite of its various shortcomings, CG equation has gained adequate prominence in clinical practice especially for dose calculation of drugs as FDA still recommends calculation of creatinine clearance by CG equation.

$$Ccr = \frac{(140 - \text{age}) \times \text{lean body weight (kg)}}{S.Cr \text{ (mg/dl)} \times 72} \times (0.85 \text{ if female})$$

A number of research studies have shown that CG-equation tends to over-estimate creatinine clearance resulting in false positive results. Possible reason behind over-estimation might be use of non-standardized creatinine assay as CG-equation was developed much earlier before the introduction of standardized creatinine assay. The National Institute for Standards and Technology in United States has released standard reference material for calibration of serum creatinine via Isotope dilution mass spectrometry (IDMS). As the CG-equation was based on the fact that creatinine production increases with weight, the inclusion of weight in equation may over-estimate result as increase weight does not refer to increase muscle mass only, it also symbolizes obesity or increase fat mass.

Modification of Diet in Renal Disease (MDRD) equation

MDRD equation was derived from the data of a multi-center clinical trial that was originally conducted to evaluate the effect of control of dietary protein and blood pressure on the progression of renal disease. As a result of this study, four different formulas were derived to calculate GFR. The simplest proposed formula is as follow:

$$\text{GFR} = 186.3 \times [\text{S.Cr } (\mu\text{mol/L}) \times 0.0011312]^{-1.154} \times \text{age (years)}^{-0.203} \times (0.724 \text{ if female}) \times (1.21 \text{ if black})$$

The major advantage of MDRD equation over CG- equation is non-requisite of height and weight in formula and moreover it gives eGFR instead of creatinine clearance [10,11]. Unlike CG equation, standardize serum creatinine value can be used in MDRD equation to prevent inter laboratory variations in results. Moreover, this formula is not validated for individuals less than 18 years.

Common Inherent limitations of CG and MDRD equation

Both equations are considered less accurate among obese and individuals with normal or near to normal GFR. Moreover variability of results has been observed with these equations in different age groups, renal allograft recipients, pregnancy, children and different ethnicities particularly Asians [12].

CKD-EPI equation

Unlike CG and MDRD equation, CKD-EPI equation was developed from population having wide range of GFR i.e. population with and without kidney disease. Therefore, this equation provides most accurate results in clinical settings when GFR is normal or mildly reduced [13]. Number of studies has confirmed a lower prevalence of CKD and a better prediction of risk among study subjects with CKD-EPI equation as compared to both CG and MDRD equation. This accurate lower prevalence of CKD as estimated by CKD-EPI will result in proper utilization of resources as fewer individuals will be truly categorized to have CKD. CKD-EPI equation based on both serum creatinine and cystatin C respectively is available. Moreover, equation incorporating both serum creatinine and Cystatin C is also available [7].

$$\text{GFR} = 141 \times \min(\text{Scr}/k, 1)^{\alpha} \times \max(\text{Scr}/k, 1)^{-1.209} \times 0.993^{\text{age}} \times 1.018 (\text{fe}) \times 1.159 (\text{black})$$

For female: $k=0.7$, $\alpha=-0.329$

For male: $k=0.9$, $\alpha=-0.411$

Schwartz formula

In the middle of 1970s, Schwartz devised a formula to estimate GFR in children. The original formula was based on three main variables; height,

weight and an empirical constant (k), where the value of k varies depending on age; Infant (LBW less than 1 year) $k=0.33$, infant (term less than one year) $k=0.45$, child or adolescent girl: $k=0.55$, adolescent boy: 0.77 . The major limitation associated with this formula is approximate over-estimation of GFR by 20-40 % [14]. However, in 2009 the formula was updated by using standardized creatinine assay. The main limitation associated with Schwartz formula is the selection of appropriate value for the constant (k) as the value of k depends on the gold standard used for estimation of renal function i.e. inulin, cystatin C, creatinine clearance.

Overall Limitations of Renal Function Predictive equations

The inherent limitation associated with renal function predictive equations is the use of serum creatinine that is not a sensitive renal biomarker as it is affected by several renal and non-renal factors that are independent of both kidney function and kidney injury. Secondly, these equations tend to show variations in result among different populations. Such populations include obese, different ethnicities, any condition leading to unusual muscle mass, pregnancy and patients' with high GFR [11,12].

Cystatin C biomarker Predictive equation

Cystatin C is a low molecular protein that is produced by all nucleated cells of the body. Recently number of renal function predictive equations using cystatin C has been published and compared with serum creatinine estimating equations. Majority of the studies have found that both cystatin C concentration and cystatin C based equations to be superior than both serum creatinine and creatinine based predictive equations [15]. Certified standard assay for standardization of serum cystatin C are also available to avoid any variations in result. The main disadvantage associated with use of cystatin C or its equation is high cost. Moreover, level of cystatin C markedly increases with advance age, thyroid dysfunction and use of certain medications such as glucocorticoids [16]. Moreover, number of research studies have shown that level of cystatin C markedly fluctuates in different trimesters of pregnancy with highest level in third trimester [17,18].

Future of Renal Function Predictive equations

Overall it is not possible to conclude which estimating equation serves as the best estimator of GFR. It should be kept in mind that all estimating equations are mathematical derivations and no equation is ideal for entire population [19]. The purpose of these equations is to help clinicians in diagnosing and staging kidney diseases in clinical practice [7]. Keeping limitations of these equations in mind and using different equation in different setting might result in better performance of such equations.

Conclusion

The quest of an ideal biomarker for early identification of kidney dysfunction still continues. As compared to traditional biomarkers, fortunately novel biomarkers for detection and monitoring of renal dysfunction are under observation and analysis of their performance is being done on the basis of cost, sensitivity and specificity. Need of the hour is to identify such biomarker that can be conveniently use in clinical practice, give specific results for special population such as pregnancy, elderly and give best combination of cost and early identification of renal dysfunction.

Authors' contribution

A.S.A and Y.H.K have drafted the initial copy of manuscript. A.H.K and T. H.M have read and gave suggestions for further improvement. The final copy of manuscript was approved by A.S and F.J.

References

1. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Annals of internal medicine*, 2003; 139(2): 137-147.
2. Bichet DG. Nephrogenic diabetes insipidus. *Advances in chronic kidney disease*, 2006; 13(2): 96-104.
3. Rule AD, Larson TS, Bergstralh EJ, Slezak JM, Jacobsen SJ, Cosio FG. Using serum creatinine to estimate glomerular filtration rate: accuracy in good health and in chronic kidney disease. *Annals of internal medicine*, 2004; 141(12): 929-937.
4. Myers GL, Miller WG, Coresh J, Fleming J, Greenberg N, Greene T, et al. Recommendations for improving serum creatinine measurement: a report from the Laboratory Working Group of the National Kidney Disease Education Program. *Clinical Chemistry*, 2006; 52(1): 5-18.
5. Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function—measured and estimated glomerular filtration rate. *New England Journal of Medicine*, 2006; 354(23): 2473-2483.
6. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *American Journal of Kidney Diseases*, 2003; 41(1): 1-12.
7. Florkowski CM, Chew-Harris JS. Methods of estimating GFR—different equations including CKD-EPI. *The Clinical Biochemist Reviews*, 2011; 32(2): 75.
8. Chin PKL, Florkowski CM, Begg EJ. The performances of the Cockcroft-Gault, Modification of Diet in Renal Disease Study and Chronic Kidney Disease Epidemiology Collaboration equations in predicting gentamicin clearance. *Annals of Clinical Biochemistry: An international journal of biochemistry and laboratory medicine*, 2013; 50(6): 546-557.
9. Rostoker G, Andrivet P, Pham I, Griuncelli M, Adnot S. A modified Cockcroft-Gault formula taking into account the body surface area gives a more accurate estimation of the glomerular filtration rate. *Journal of nephrology*, 2006; 20(5): 576-585.
10. Kuan Y, Hossain M, Surman J, El Nahas AM, Haylor J. GFR prediction using the MDRD and Cockcroft and Gault equations in patients with end-stage renal disease. *Nephrology Dialysis Transplantation*, 2005; 20(11): 2394-2401.

11. Lin J, Knight EL, Hogan ML, Singh AK. A comparison of prediction equations for estimating glomerular filtration rate in adults without kidney disease. *Journal of the American Society of Nephrology*, 2003; 14(10): 2573-2580.
12. Froissart M, Rossert J, Jacquot C, Paillard M, Houillier P. Predictive performance of the modification of diet in renal disease and Cockcroft-Gault equations for estimating renal function. *Journal of the American Society of Nephrology*, 2005; 16(3): 763-773.
13. Stevens LA, Schmid CH, Greene T, Zhang YL, Beck GJ, Froissart M, et al. Comparative Performance of the CKD Epidemiology Collaboration (CKD-EPI) and the Modification of Diet in Renal Disease (MDRD) Study Equations for Estimating GFR Levels Above 60 mL/min/1.73 m². *American Journal of Kidney Diseases*, 2010; 56(3): 486-495.
14. Schwartz GJ, Haycock GB, Edelmann CM, Spitzer A. A simple estimate of glomerular filtration rate in children derived from body length and plasma creatinine. *Pediatrics*, 1976; 58(2): 259-263.
15. Peralta CA, Katz R, Sarnak MJ, Ix J, Fried LF, De Boer I, et al. Cystatin C identifies chronic kidney disease patients at higher risk for complications. *Journal of the American Society of Nephrology*, 2011; 22(1): 147-155.
16. Shlipak MG, Fyr CLW, Chertow GM, Harris TB, Kritchevsky SB, Tylavsky FA, et al. Cystatin C and mortality risk in the elderly: the health, aging, and body composition study. *Journal of the American Society of Nephrology*, 2006; 17(1): 254-261.
17. Akbari A, Lepage N, Keely E, Clark HD, Jaffey J, MacKinnon M, Filler G. Cystatin-C and beta trace protein as markers of renal function in pregnancy. *BJOG: An International Journal of Obstetrics & Gynaecology*, 2005; 112(5): 575-578.
18. Filler G, Bökenkamp A, Hofmann W, Le Bricon T, Martínez-Brú C, Grubb A. Cystatin C as a marker of GFR—history, indications, and future research. *Clinical biochemistry*, 2005; 38(1): 1-8.
19. Botev R, Mallié JP, Wetzels JF, Couchoud C, Schück O. The clinician and estimation of glomerular filtration rate by creatinine-based formulas: current limitations and quo vadis. *Clinical Journal of the American Society of Nephrology*, 2011; 6(4): 937-950.

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Prevalence of generalized anxiety disorder in adolescents and youth in Lahore urban community Pakistan

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Abstract

Objectives: The study is aimed at determining the prevalence of generalized anxiety disorder in adolescents and youth. It will help us to design preventive strategies in our target population and to promote mental health.

Methodology: A cross sectional study was conducted to identify various symptoms associated with generalized anxiety disorder in adolescents and youth. The sample size calculated was 498 and rounded off to 500. Non probability purposive sampling approach was used to recruit study subjects. Prior consent was obtained from all selected study subjects. P value less than 0.05 was considered significant.

Results: In the study total 500 subjects were included from both public and private educational institutions in Lahore. The gender distribution of generalized anxiety disorder was 7% male and 9% female among adolescents and 12% males and 14% females among youth.

According to the study, the major factors causing GAD were long examination (76%), fear of failure (79%), increased work load (82%), long study hours (64%). The comparison of symptoms of generalized anxiety disorder in adolescents and youth showed statistical significant generalized anxiety disorder GAD in youth with more than 4 persistent symptoms according to ICD 10 criteria. P value was less than 0.05.

Conclusions: Generalized Anxiety Disorder was found more in youth and females. The research showed that factors such as increased work load, and long study hours etc could contribute to generalize anxiety disorder.

Key words: Generalized Anxiety Disorder, Adolescents, Youth.

Introduction

Amongst the various anxiety disorders, 'generalized anxiety' is a traditionally recognized clinical phenomenon¹. However, generalized anxiety disorder (GAD) is a relatively new category for the significant mental disorders. Generalized anxiety disorder (or GAD) is characterized by excessive, exaggerated worrying and tension about everyday life events without an evident provoking factor. The worry is mostly unrealistic or out of proportion for the circumstances.²

The adolescents and youth are defined by the United Nations, as persons between the ages of 10 to 19 years and between 15 and 24 years, respectively.³ The study deals with the prevalence, diagnosis (as per ICD- 10 criteria) and implications of this disorder in the said section of the population at present. GAD is the second most frequent disorder in primary care after depression, hence, signifying the importance of understanding the disease.⁴ And thus, this also highlights the need for designing an effective preventive and diagnostic plan for this disorder in addition to investigating treatment options for those who are already suffering from it. In addition to this, probable factors contributing to GAD in youth and adolescents will also be explored. Anxiety disorders are composed of different groups of psychological difficulties with wide-ranging intensities and clinical presentations. A fundamental component shared by all anxiety disorders is intense fear and unnecessary worry.⁵ Adolescence and youth mark the stages of gradual transition from childhood to adulthood, which are two overlapping but distinct phases of physical changes marking puberty and physical maturation.⁶ Radical alterations in hormonal and somatic conditions in addition to considerable changes in behavior and the structural and functi-

onal organization of the brain.⁷ Many psychological functions such as social brain, emotional processing and executive control go through striking changes. In adolescence nonlinearly increased onset of various psychiatric disorders, for example anxiety, posttraumatic stress disorder (PTSD), bipolar disorder (BP) etc are observed compared to periods of childhood and adulthood.⁸⁻¹⁰ Studies on the gender differences for the anxiety disorder showed considerable difference in anxiety disorder rates for men and women. Boys are less likely to show symptoms of anxiety when compared to girls.¹¹ On the contrary, some studies reveal same rates of anxiety in boys and girls or are suggestive that anxiety level cannot be explained merely on the basis of biological sex.¹² Conversely, studies found that gender role orientation and pubertal development are deemed to be more important than biological sex.¹³ Quite recently, instead of being considered as an independent diagnosis, generalized anxiety disorder might be better presumed as a prodrome of major depression or other comorbid disorders.¹⁴ As far as the pathophysiology and clinical features of the disorder are concerned, the sleep problems and measures of anxiety severity were positively associated.¹⁵ Previous research has revealed that individuals with GAD commonly endorse symptoms of autonomic arousal.¹⁶ On the basis of structural equation modeling, researchers have reconciled these incongruous observations thereby indicating that raised autonomic arousal is associated with GAD.¹⁷ Many studies including ours suggest that the present educational course may have certain inadvertent detrimental effects on mental health of adolescents and youth, with a greater frequency of anxiety, stress and depression observed in certain age groups.¹⁸⁻²⁰

The study is aimed at determining the prevalence of generalized anxiety disorder in adolescents and youth. It will help us to design preventive strategies in our target population and to promote mental health. This age group of the population forms a significant part of the world's community and the social and mental needs of this section of the population need to be addressed. Thus, the study will help highlight the prevalence, and risk factors of generalized anxiety disorder in youth and adolescents. And given the escalating psychosocial burden associated with psychiatric disorders,

the identification of youth at highest risk for the illness will have a huge impact on public health.

Materials and methods

A cross sectional study was conducted to identify various symptoms associated with generalized anxiety disorder in adolescents and youth with particular reference to various determinants contributing to this disorder. Study population comprising of 500 students in public and private institutions who were divided into two groups according to age. One group included adolescents 10 to 19 years of age. The other group comprised of youth 20 to 29 years of age. They were willing to participate and fill the questionnaire and checklist. All information obtained was kept confidential. The generalized anxiety disorder GAD was diagnosed according to ICD 10 criteria. The sample size calculations were performed by using epi-info 2000 software. The sample size calculations were done at 95% confidence interval, 80% power of test, 7% prevalence of generalized anxiety disorder and the sample size was estimated as 498 and rounded off to 500. Non probability purposive sampling approach was used to recruit study subjects. Prior consent was obtained from all selected study subjects. The variables were said to be present if they occurred for 6 months or greater duration and they were listed as below:

Palpitations or pounding heart, sweating, trembling, dry mouth, difficulty in breathing, feeling of choking, chest pain, nausea or abdominal distress, feeling dizzy, feeling that objects are unreal and depersonalization, fear of losing control, fear of dying, hot flushes or cold chills, numbness or tingling sensation, muscle pains, restlessness, mental tension, sensation of lump in throat, exaggerated response to minor surprises, difficulty in concentrating, persistent irritability, difficulty in getting to sleep.

Any coexisting illness was also mentioned in the checklist. The study subjects suffering from thyroid diseases, tuberculosis, hepatitis and endocrine disorders were excluded from the study. Also not included were the people with organic mental disorder or psychoactive substance-related disorder. Frequency distributions, percentages were calculated. Comparison was performed and chi square test, odds ratio, 95% CI were calculated. P value less than 0.05 was considered significant.

Results

In the study total 500 subjects were included from both public and private educational institutions in Lahore for this study. 300 were adolescents i.e., group1 (10-19 years) and further 100 males and 200 were females. 200 were youth i.e., group2 (20-29 years) and further 100 were males and 100 were females.

The gender distribution of generalized anxiety disorder was 7% male and 9% female among adolescent group and 12% males and 14% females among youth group were diagnosed GAD according to ICD 10 criteria.

According to the study, the major factors causing GAD in students were long examination (76%), fear of failure present in (79%), work load more prominent in 82%, long study hours responsible in 64% of students. Among the other factors contributing to generalized anxiety disorder as indicated by their frequency and percentages were competition for getting position in class (44%), high academic achievements (45%), poor health status (18%), parental interference in career decision making (16%), worry about financial status (6%), emotional factors like break ups and conflicts in relationships (9%), while 49% of the su-

bjects think that participation in extracurricular activities plays a role in relieving anxiety.

The distribution of number of symptoms of generalized anxiety disorder in adolescents and youth are mentioned. (table 1,2)

The comparison of symptoms of generalized anxiety disorder in adolescents and youth showed statistical significant generalized anxiety disorder GAD in youth with more than 4 persistent symptoms according to ICD 10 criteria. P value less than 0.05. (table 3)

Discussion

Generalized anxiety is a recognized clinical phenomenon, however the generalized anxiety disorder (GAD) is a new category for the description of a unique mental disorder.²¹ Anxiety disorders are composed of psychological difficulties with wide-ranging intensities and a fundamental component is intense fear and unnecessary worry.²²

GAD has been found to have much more influence on health-related quality of life and role functioning when compared to other mental disorders in adolescents and youth.²³ People with GAD have been suggested to have relatively greater healthcare utilization and costs. GAD diagnosed patients also

Table 1. Distribution of number of persistent symptoms of GAD in Adolescents

No. of persistent symptoms	Adolescents (n=300)	Percentage
1	160	53%
2	50	16%
3	66	22%
>4	24	8%

Table 2. Distribution of number of persistent symptoms of GAD in Youth

No. of persistent symptoms	Youth (n=200)	Percentage
1	76	38%
2	64	32%
3	32	16%
>4	28	14%

Table 3. Comparison of number of persistent symptoms of GAD in Adolescents and youth

No. of Symptoms	Group1	Group2	Chi square	Odds ratio	95% CI	P value
1	160	76	11.32	1.86	1.27-2.73	0.0007
2	50	64	16.03	0.43	0.27-0.66	0.00006
3	66	32	2.74	1.48	0.91-2.43	0.09
>4	24	28	4.64	0.53	0.29-0.99	0.03

have a higher risk for suicide or suicide attempts.²⁴ Physical, behavioral, cognitive, and/or psychologic symptoms have also found to be associated with GAD. In addition co-morbidities were linked with higher absenteeism from work.²⁵

GAD has been linked with an early age of onset by many researchers with core periods for initial commencement in later adolescence with supplementary first incidence in early youth.²⁶ In the adolescent age group, various genetic, hormonal and environmental factors such as stress, conflict, communication gap with parents, disagreements may be attributed to the causation of this disorder in the said age group.²⁸ Adolescents with anxiety disorders went through relatively more negative life circumstances than those without the disorder.²⁹ Among adolescents, prevalence rates were found to be between 3.6% to 7.3%.³⁰

Various recent stressful life events maybe involved in the onset of emotional disorders such as GAD. Our research depicts higher frequency of the disorder among youth when compared to adolescents. To understand various probable causes which may lead to higher levels of Generalized Anxiety Disorder in youth in our setting, we must understand that the transition from adolescence to adulthood and the element of raised pressures and responsibilities associated with this particular age group.³¹ Other factors may include challenges in interpersonal relationships, conflicts in friendships or break in relationships, socioeconomic burden, pressure to choose the career of parents choice, pressure to meet the expectations by self and the family, stigma attached to discussing psychiatric disturbances, cultural and religious factors.³²

Women are twice as likely men to suffer from GAD.³³ In research performed in the Netherlands (Bijl et al, 1998) female predominance was observed while an epidemiological survey in South Africa depicted much higher rates in men (Bhagwanjee et al. 1998).³⁴⁻⁵ Our research reveals results concordant with aforementioned studies and shows higher levels in both age groups of adolescent (9%) and young (14%) females when compared to adolescent (7%) and young (12%) males. However, cultural specificity must be kept in mind while considering these gender differences. Data on the development of anxiety disorders in various investigations advocates the potential role

of genetic and environmental factors along with the significance of female reproductive hormones and related cycles in women.³⁶ Meanwhile, gender differences in the absorption, bioavailability, and distribution of psychotropic drugs were also observed and can help in streamlining potential medical therapy for females with anxiety disorders.³⁷ GAD afflicted females chiefly those who have one or more co-morbid disorders have greater likelihood of pursuing professional management for their disorder and hence this maybe a reason for the higher prevalence of GAD in females.

Many studies including ours suggest that the present educational course may have certain inadvertent detrimental effects on students' mental health, with a greater frequency of anxiety, stress and depression observed in students related to competitive examinations.³⁸ A number of factors have been put forward regarding the deterioration in students' mental health and these include academic pressure, workload, and financial concerns.³⁹ It is imperative to realize that psychological distress among students may affect their academic performance negatively, lead to academic dishonesty, and contribute to substance abuse.⁴⁰

High achievements has been found to be significant in contributing to anxiety disorders.⁴¹ Our study too revealed that 45% of students in our study sample felt the same. Self-reported stressors for students as identified included examinations, competition (quoted by 44% students in our study), amount of information to learn, time constraints, money (worry regarding financial status was reported by only 6% of students in our study), family concerns (a factor deemed important by 16% of subjects in our study) and these are congruous with the factors that we pointed in our study.⁴² Among different factors contributing to exam anxiety, extensive course load was reported as an important factor by 90.8% of the students according to researchers and colleagues while our study showed that 82% of the subjects had this belief which is less than what was observed by researcher and colleagues.⁴³ Thus, the prevalence of generalized anxiety disorder in particular among adolescents and youth is an area where hardly any research has been done. Our research henceforth, opens a new avenue for studies considering the significance in the education sector reforms for adolescents and youth.

The current research had been conducted on generalized anxiety disorder to explore its risk factors and to devise a prevention plan. In order to address the issue, a multidimensional prevention programme should be launched with the dynamic participation of all the stakeholders involved including the Government, physicians, patients and the society, in general. It is essential that the spotlight on treatment of adolescents and youth be shifted to an approach based on prevention and early intervention considering that many common mental disorders in adults first surface in the early ages and reduce the stigma associated with various psychosocial disorders to encourage people to seek professional help.⁴⁴ Successful assessment of mental health problems in patients should be based on practitioner's awareness about patient's beliefs regarding physical and mental health. Keeping in mind the western-eastern socio-cultural differences may help in planning effective management.

Strengths of the current study included representative use of standardized data collection protocols and achieving the objectives of our study besides identifying various probable factors which may contribute to higher rates of anxiety disorders in adolescents and youth. We were able to ascertain the demographic differences and found GAD more in the youth (age 20-29 years) as compared to adolescents (age 10-19 years) and also among females. Our research also explored various factors which could give rise to these findings. Research studies in specific segments of the population focus on greater details, and increase practicability of gauging participants in a clinical setting.

However, we also encountered some study limitations such as recall bias of the behavioral risk factors as we followed international guidelines in our study and used questionnaire and checklists based on ICD-10. Moreover, there is concurrent difficulty in diagnosis due to coexisting disorders and overlapping symptoms with various other disorders like endocrine, metabolic and chronic illnesses and that were excluded on history and past records.

This research was performed to lay the basic groundwork for ensuing further studies that can be used to recognize GAD in adolescents and youth to effectively deal with the mental health care needs of this chief section of the population.

The gender and age distribution in GAD in adolescents and youth showed significant variations and so must be considered for studies to follow.

Conclusion

Generalized Anxiety Disorder was found more in females, ages between 20-29 years of age as compared to male adolescents and youth.

The research showed that factors such as increased work load, long study hours, competition in examinations, fear of failure, burden of previous academic achievements, parental interference in career decisions could contribute to generalized anxiety disorder among students.

References

1. Rapee, R. *Generalized anxiety disorder: a review of clinical features and theoretical concepts*. *Clinical Psychological Review* 1991; 11: 419-440.
2. Üstün TB, Sartorius N, eds. *Mental Illness in General Health Care: An International Study*. Chichester, UK: John Wiley & Sons Ltd; 1995; 221-238.
3. Rapee RM, Barlow DH. *Generalized anxiety disorders, panic disorders, and phobias*. In: Sutker PB, Adams HE, editors. *Comprehensive handbook of psychopathology*. 3rd ed Kluwer Academic/Plenum Publishers; New York: 2001; 131-154
4. Ernst M, Pine DS, Hardin M. *Triadic model of the neurobiology of motivated behavior in adolescence*. *Psychol Med*. 2006 Mar; 36(3): 299-312.
5. Spear LP. *The adolescent brain and age-related behavioral manifestations*. *Neurosci Biobehav Rev*. 2000 Jun; 24(4): 417-63.
6. Pinyerd B, Zipf WB. *Puberty-timing is everything*. *J Pediatr Nurs*. 2005 Apr; 20(2): 75-82.
7. Romeo RD. *Adolescence: a central event in shaping stress reactivity*. *Dev Psychobiol*. 2010 Apr; 52(3): 244-53.
8. Casey BJ, Getz S, Galvan A. *The adolescent brain*. *Dev Rev*. 2008; 28(1): 62-77.
9. Burnett S, Sebastian C, Cohen Kadosh K, Blakemore S. *The social brain in adolescence: evidence from functional magnetic resonance imaging and behavioural studies*. *J Neurosci Biobehav Rev*. 2011 Aug; 35(8): 1654-64.

10. White AM. Understanding adolescent brain development and its implications for the clinician. *Adolesc Med State Art Rev*. 2009 Apr; 20(1): 73-90.
11. Uhlhaas PJ, Roux F, Singer W, Haenschel C, Sireteanu R, Rodriguez E. The development of neural synchrony reflects late maturation and restructuring of functional networks in humans. *Proc Natl Acad Sci U S A*. 2009 Jun 16; 106(24): 9866-71.
12. Post RM, Leverich GS, Xing G, Weiss RB. Developmental vulnerabilities to the onset and course of bipolar disorder. *Dev Psychopathol*. 2001; 13: 581-598.
13. Beesdo K, Knappe S, Pine DS. Anxiety and anxiety disorders in children and adolescents: developmental issues and implications for DSM-V. *Psychiatr Clin North Am*. 2009; 32: 483-524.
14. Varchol L, Cooper H. Psychotherapy approaches for adolescents with eating disorders. *Curr Opin Pediatr*. 2009; 21: 457-464.
15. Vigod SN, Stewart DE. Emergent research in the cause of mental illness in women across the lifespan. *Curr Opin Psychiatry*. 2009; 22: 396-400.
16. Rajji TK, Ismail Z, Mulsant BH. Age at onset and cognition in schizophrenia: meta-analysis. *Br J Psychiatry*. 2009; 195: 286-293.
17. Spear LP. Heightened stress responsivity and emotional reactivity during pubertal maturation: Implications for psychopathology. *Dev Psychopathol*. 2009; 21: 87-97.
18. Angst J, Cui L, Swendsen J, Rothen S, et al. Major depressive disorder with subthreshold bipolarity in the National Comorbidity Survey Replication. *Am J Psychiatry*. 2010; 167: 1194-1201.
19. Chang KD. Course and impact of bipolar disorder in young patients. *J Clin Psychiatry*. 2010; 71: 2-5.
20. Lock J, Fitzpatrick KK. Advances in psychotherapy for children and adolescents with eating disorders. *Am J Psychother*. 2009; 63: 287-303.
21. Albano AM, Krain A. Anxiety and anxiety disorders in girls. In: Bell DJ, Foster SL, Mash EJ, editors. *Issues in clinical child psychology. Handbook of behavioral and emotional problems in girls*. Kluwer Academic / Plenum Publishers; New York: 2005. 79-116. doi: 10.1007/0-306-48674-1_3.
22. Silverman WK, Carter R. Anxiety disturbance in girls and women. In: Worell J, Goodheart CD, editors. *Handbook of girls' and women's psychological health: Gender and well-being across the lifespan*. Oxford University Press; New York: 2006. 60-68.
23. Beidel DC, Turner SM. At risk for anxiety: I. Psychopathology in the offspring of anxious parents. *J Am Acad Child Adolesc Psychiatry*. 1997 Jul; 36(7): 918-24.
24. Masi G, Mucci M, Favilla L, Romano R, Poli P. Symptomatology and comorbidity of generalized anxiety disorder in children and adolescents. *Compr Psychiatry*. 1999 May-Jun; 40(3): 210-5.
25. Treadwell K, Flannery-Schroeder EC, Kendall PC. Ethnicity and gender in a sample of clinic-referred anxious children: Adaptive functioning, diagnostic status, and treatment outcome. *Journal of Anxiety Disorders*. 1995; 9: 373-384.
26. Carter R, Wendy K, Silverman JJ. Sex Variations in Youth Anxiety Symptoms: Effects of Pubertal Development and Gender Role Orientation. *J Clin Child Adolesc Psychol*. 2011; 40(5): 730-741. doi: 10.1080/15374416.2011.597082.
27. Alfano CA, Ginsburg GS, Kingery JN. Sleep-related problems among children and adolescents with anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2007 Feb; 46(2): 224-32.
28. Brown TA, Marten PA, Barlow DH. Discriminant validity symptoms constituting the DSM-II-R and DSM-IV associated symptom criteria of generalized anxiety disorder. *Journal of Anxiety Disorders* 1995; 9: 317- 328.
29. Brown TA, Barlow DH. Structural relationships among dimensions of DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. *Journal of abnormal psychology* 1998; 107: 179-192.
30. Rapee R. Generalized anxiety disorder: a review of clinical features and theoretical concepts. *Clinical Psychological Review* 1991; 11: 419-440.
31. Wittchen HU, Carter RM, Pfister H, Montgomery SA, Kessler RC. Disabilities and quality of life in pure and comorbid generalized anxiety disorder and major depression in a national survey. *Int Clin Psychopharmacol* 2000; 15(6): 319-328.
32. Wittchen HU. Generalized anxiety disorder: Prevalence, burden, and cost to society. *Depress Anxiety* 2002; 16(4): 162-171.
33. Hoffman DL, Dukes EM, Wittchen HU. Human and economic burden of generalized anxiety disorder. *Depress Anxiety* 2006; 1(1): 1-19.
34. Wagner KD. Generalized anxiety disorder in children and adolescents. *Psychiatr Clin North Am* 2001; 24: 139-153.

35. Wittchen HU, Nelson CB, Lachner G. Prevalence of mental disorders and psychosocial impairments in adolescents and young adults. *Psychol Med*, 1998; 28: 109-126.
36. Hoehn-Saric R, Hazlett R, McLeod D. Generalized anxiety disorder with early and late onset of anxiety symptoms. *Comprehensive Psychiatry* 1993; 34: 291-298.
37. Offord DR, Boyle MH, Campbell D, Goering P, Lin E, et al. One-year prevalence of psychiatric disorder in Ontarians 15 to 64 years of age. *Can J Psychiatry*. 1996 Nov; 41(9): 559-63.
38. Wittchen H-U, Zhao S, Kessler R, Eaton W. DSM-III-R generalized anxiety disorder in the National Comorbidity Survey. *Archives of General Psychiatry*, 1994; 51: 335-364.
39. Bijl RV, van Zessen G, Ravelli A, de Rijk C, Langendoen Y. The Netherlands Mental Health Survey and Incidence Study (NEMESIS): objectives and design. *Soc Psychiatry Psychiatr Epidemiol*. 1998 Dec; 33(12): 581-586.
40. Bhagwanjee A, Parekh A, Paruk Z, Petersen I, Subedar H. Prevalence of minor psychiatric disorders in an adult African rural community in South Africa. *Psychological Medicine* 1998; 28: 1137-1147.
41. Kendler KS, Walters EE, Neale MC, Kessler RC, Heath AC, Eaves LJ. The structure of the genetic and environmental risk factors for six major psychiatric disorders in women. Phobia, generalized anxiety disorder, panic disorder, bulimia, major depression, and alcoholism. *Arch Gen Psychiatry*. 1995; 52(5): 374-83.
42. Guthrie EA, Black D, Shaw CM, Hamilton J, Creed FH, Tomenson B. Embarking upon a medical career: psychological morbidity in first year medical students. *Med Educ* 1995; 29: 337-41.
43. Moffat KJ, McConnachie A, Ross S, Morrison JM. First-year medical student stress and coping in a problem-based learning medical curriculum. *Med Educ* 2004; 38: 482-91.
44. Toews JA, Lockyer JM, Dobson DJ, et al. Analysis of stress levels among medical students, residents, and graduate students at four Canadian schools of medicine. *Acad Med*. 1997; 72: 997-1002.
45. Hashmat S, Hashmat M, Amanullah F, Aziz S. Factors causing exam anxiety in medical students. *J Pak Med Assoc*. 2008; 58(4): 167-70.

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Role of 25-Hydroxyvitamin D in threatened Preterm Labor: a case-control study

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Abstract

Background & Aim: Vitamin D is a steroid hormone and recent studies have shown that vitamin D may be involved in triggering uterine contractions and preterm labor. The aim of this study was evaluating serum 25-hydroxyvitamin D levels in pregnant women with threatened preterm labor.

Patients and Methods: In this case-control study, 120 pregnant women with gestational age of 28 to 37 weeks referred to Shahid Sayyad Shirazi Hospital of Gorgan in 2012 were studied. The subjects were placed in two groups, case group (with symptoms of labor onset) and control group (no symptoms). Serum 25-hydroxy vitamin D was measured for each sample. The collected data were analyzed using SPSS-18 statistical software and t-test and Pearson's correlation coefficient.

Results: There was a significant difference between cases and controls regards to the mean serum vitamin D levels (21.63 ± 11.46 ng/ml vs. 18.77 ± 6.19 ng/ml, P -value=0.013), parathyroid hormone (PTH) ($P=0.002$) and alkaline phosphatase (ALP) ($P=0.001$), but no significant difference regards to the serum levels of calcium and phosphorus. In both groups, there was a significant correlation between preterm labor and serum ALP ($P<0.05$), while no correlation with vitamin D, calcium, phosphorus and PTH ($P>0.05$).

Conclusion: The results of this study showed that serum vitamin D levels in pregnant women with threatened preterm labor are higher than women without symptoms, although no significant correlation was reported.

Key words: Serum 25-Hydroxyvitamin D Levels, Pregnant Women, Threatened Preterm Labor

Introduction

Vitamin D₃ is a steroid hormone in human body, which Serum 25 (OH) vitamin D₃ levels has been often considered as an index of it (1). Along with

the classic tissues, vitamin D receptor (VDR), the nuclear receptor for 1,25 (OH)₂ vitamin D₃ and the vitamin D – activating enzyme, 1- α hydroxylase are expressed in other tissues, prominently in placenta and deciduas (2). Their expression enhances in the first trimester of pregnancy, while some studies reported the abnormal expression of 1- α hydroxylase enzyme in mothers with pre-eclampsia. The significant changes in maternal calcium and vitamin D homeostasis occur during pregnancy in order to meet the fetal calcium needs for skeletal growth and bone mineral accretion. Increase in intestinal calcium absorption during pregnancy probably occurs through the increase in 1,25 (OH)₂ vitamin D₃ levels which enhances 50-100 % and by 100 % during the second and third trimester, respectively (3).

The main mechanism of increase in 1-25 (OH)₂ vitamin D still remains unclear. According to the previous studies, concentrations of parathyroid hormone (PTH) that stimulates hydroxylation of 25 (OH) D and consequently, its conversion to 1,25 (OH)₂ vitamin D does not change during pregnancy (4). Vitamin D is synthesized in the skin by UV_B radiation of sunlight. Low sun exposure, without vitamin D supplementation, may lead to increase vitamin D deficiency rate in women (5, 6).

Vitamin D deficiency in pregnancy may result in adverse events for the mother and the fetus (7). Neonatal complications include higher risk of growth restriction, respiratory tract infections and eczema. Furthermore, it causes altered glucose homeostasis and it may increase the risk of gestational diabetes mellitus, pre-eclampsia and bacterial vaginosis (8, 9). Women with vitamin D deficiency often do not show any symptoms but osteomalacia has been observed in some cases (10).

Vitamin D deficiency is prevalent in sun exposure-deprived populations and its adverse effects on the mother, the fetus and the growing infants have been considered as a major public health

concern(11-13). Thus, taking into account the possible role of vitamin D in preterm labor, the aim of the present study was evaluation of the maternal serum 25(OH) vitamin D levels in pregnant women with preterm labor.

Patients and Methods

This case-control study was conducted on 120 pregnant women of 28 to 37 weeks gestation (determined by using the last menstrual period date and Ultrasound examination before the 22nd weeks of pregnancy) admitted in Sayyad Shirazi Hospital of Gorgan, Iran. Pregnant women aged between 18 to 35 years were included into the study using inclusion and exclusion criteria as followings: not having any pregnancy disorders such as pre-eclampsia, bleeding, poly hydramnios, decolman (premature separation of placenta), multiple fetus and parity less than 4, any history of chronic diseases, diabetes mellitus or gestational diabetes, chronic hypertension, pre-eclampsia, drug or alcohol addiction, fetal deformity, poly hydramnios, placenta previa, uterine leiomyomas, abdomen surgery during current pregnancy, uterine malformation, cervical impotence, history of trauma, fever, any acute or chronic infection, body mass index (BMI) higher than 35, intra-uterine fetal death (IUFD), taking vitamin D or calcium supplement and corticosteroids. Review board of Golestan University of Medical Sciences and Ethical Committee approved the study. Informed written consent was obtained from each patient. The study comprised two groups, subjects with labor signs (cervical effacement, dilation and ruptured membranes) as the study group (N=60) and the subjects without labor signs as control group (N=60).

Serum 25- hydroxyl vitamin D levels were evaluated testing by enzyme immunoassay method

using IDF kit (ELISA, England). Values of 30-100 ng/ml, 10-29 ng/ml and less than 10 ng/ml were considered as normal, in sufficiency and severe deficiency of 25-hydroxy vitamin D, respectively.

Collected data were analyzed using SPSS-18 software. T-test was used in order to compare the mean values in two normal and independent groups. Pearson's correlation coefficient and linear regression analysis were used in order to assess the relation between serum vitamin D and preterm labor.

Results

Results showed that mean serum vitamin D levels was 21.36 ± 11.46 ng/ml in cases and 80% showed insufficient level while 6.7% had deficient values of 25-(OH) vitamin D, respectively. But in the control group, the mean serum 25-(OH) vitamin D level was 18.77 ± 6.19 ng/ml, and 95% had insufficiency while 1.7% showed deficiency of vitamin D, respectively. A significant difference was observed in Vitamin D levels between two groups. (P-value=0.013)

Moreover, mean values of calcium, phosphorus, parathyroid hormone (PTH) and alkaline phosphatase (ALP) concentrations were also higher in the study group compared to the controls. Table 1.

Data analysis of the case group showed that there was significant correlation between serum vitamin D levels and gestational age ($p=0.016$) and parity ($p=0.025$), while there was no significant correlation between serum vitamin D levels and maternal age, educational status, gravidity, previous abortion, maternal height, weight and BMI, gender of neonates and birth height and weight ($p>0.05$)

In the control group, there was no significant correlation between serum vitamin D levels and demographic variables (maternal age, gestational age, educational status, parity, gravidity, abortion

Table 1. Comparing serum levels of vitamin D, Ca, P, PTH and ALP between cases with threatened preterm labor and controls

Serum levels of variables (mean±SD)	Cases	Controls	P-value
25(OH)D (ng/ml)	21.63±11.46	18.77±6.19	0.013
Ca (mg/dl)	9.05±0.7	9.06±0.87	NS*
P (mg/dl)	3.87±1.10	3.68±1.17	NS
PTH (pg/ml)	30.67±19.19	22.17±12.12	0.002
ALP (IU/l)	371.153±153.11	224.31±84.18	0.001

*Not significant

history, maternal weight, height and BMI, birth height and weight and neonate's gender).

Pearson analyses demonstrated that there is a significant correlation between serum vitamin D levels and maternal age ($P=0.031$) and parity ($P=0.03$), while there is no significant relation between serum vitamin D level and gestational age, parity, and maternal BMI ($p>0.05$) in cases. Figure 1.

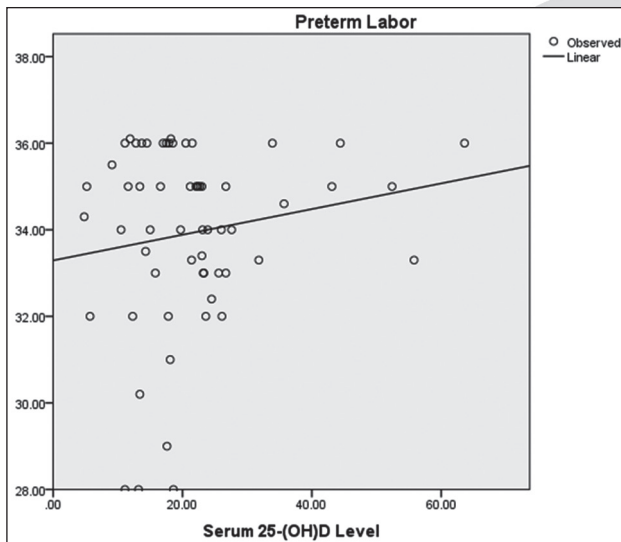


Figure 1. Correlation between serum 25-(OH) vitamin D and preterm labor in the case group

Discussion

The findings of this study demonstrated that mean value of 25-(OH) vitamin D concentration was higher in the study group than the control group. Moreover, mean values of Ca, P, PTH and ALP concentrations were also higher in the study group compared to the controls (not significant).

It is likely that 25-OH vitamin D affects uterine contractions via parathyroid hormone related peptide (PTHrP). Calcium and parathyroid hormones also influence vitamin D status during pregnancy, while there is no association between serum vitamin D level and prolactin, estrogen and placental lactogen (14, 15).

In this study, mean values of parathyroid hormone, Ca, P, alkaline phosphatase were not significantly different between two groups. However, Serum calcium ion concentration and its effect on 25(OH) vitamin D were not investigated. Our findings have shown that the pregnant women with preterm labor signs had higher serum vitamin D concentrations compared to the control group

There are few studies on the association between labor onset and vitamin D status. Scholl et al. study showed that the risk of cesarean delivery decreased in pregnant women with serum vitamin D levels higher than 37nmol/L (16). There are controversies in other studies. In Ota et al. study, 47.4% of pregnant women had low vitamin D (less than 30 ng/ml), and the prevalence of Anti Phospholipid Antibody (APA) was significantly higher in the subjects with low values of vitamin D compared to the subjects with normal values (39.7% vs. 22.9%, P -value<0.05). Thus, there was an association between vitamin D deficiency and high risk of abortion and preterm labor (17).

Boldnar et al. study demonstrated that preterm birth (<35 week gestation) occurred in 49.4 % of women with low level of 25- hydroxy vitamin D (<75 nmol/L) in comparison with 26.2 % of pregnant women with normal level of vitamin D (>75nmol/L) ($p<0.01$) (18). As a result, it is conceivable that low maternal 25 hydroxy vitamin D status in late second trimester could be associated with increased risk of preterm birth.

Results of Shiabata et al. study showed that neither intact parathyroid hormone nor calcium concentration were not associated to 25-hydroxy vitamin D that is in agreement with the results of our study. Furthermore, Shibata et al. showed lower levels of 25-hydroxy vitamin D in mothers with threatened premature delivery compared to those with normal delivery and they suggested that low vitamin D status influences on bone metabolism and was associated to the threatened premature delivery rate (19). On the contrary, our findings showed that higher vitamin D status increases the risk of preterm labor. In agreement with our findings, Ahrari et al. reported that mean serum vitamin D level was higher in the pregnant women with preterm labor compared to the pregnant women with normal delivery (20).

Moreover, studies have shown heterogeneous results regarding the prevalence of vitamin D deficiency. Maghbooli et al. reported a prevalence of 66.8% vitamin D deficiency (<35 nmol/L) (21). There have been other reports of 76% prevalence in Iran (22). Ahmed et al. reported 82.1 % of population had vitamin D deficiency (23). In the present study, vitamin D deficiency was observed in 86.7 % of the mothers in the study group and

96.7% of the control group that is relatively high in comparison to previous similar studies.

Considering to the controversial findings of the previous studies we cannot suggest a significant role of vitamin D in labor onset and preterm labor through evaluation of serum 25-hydroxy vitamin D status. It is likely that evaluation of serum active- form of vitamin D or 1,25 dihydroxy vitamin D is more helpful to explain the possible role of vitamin D in preterm labor occurrence.

Moreover, demographic variables such as age, ethnicity and socioeconomic status probably influence vitamin D status, consequently, its association to preterm labor. Thus, the controversies between the findings of the previous studies are likely due to the demographic differences in the population.

Conclusion

Our findings showed that serum vitamin D status is higher in pregnant women with threatened preterm labor compared to the normal delivery. Since many studies emphasized on the role of vitamin D deficiency in preterm labor, further investigation to approve the findings of the present study is required.

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References

1. Das G, Crocombe S, McGrath M, Berry J, Mughal M. Hypovitaminosis D among healthy adolescent girls attending an inner city school. *Archives of disease in childhood*. 2006; 91(7): 569-72.
2. Evans KN, Bulmer JN, Kilby MD, Hewison M. Vitamin D and placental-decidual function. *Journal of the Society for Gynecologic Investigation*. 2004; 11(5): 263-71.
3. Whitehead M, Lane G, Young O, Campbell S, Abeyasekera G, Hillyard CJ, et al. Interrelations of calcium-regulating hormones during normal pregnancy. *British medical journal (Clinical research ed)*. 1981; 283(6283): 10.
4. Bezerra FF, Laboissière FP, King JC, Donangelo CM. Pregnancy and lactation affect markers of calcium and bone metabolism differently in adolescent and adult women with low calcium intakes. *The Journal of nutrition*. 2002; 132(8): 2183-7.
5. Congdon P, Horsman A, Kirby P, Dibble J, Bashir T. Mineral content of the forearms of babies born to Asian and white mothers. *British medical journal (Clinical research ed)*. 1983; 286(6373): 1233.
6. Holick MF. McCollum Award Lecture, 1994: vitamin D--new horizons for the 21st century. *The American journal of clinical nutrition*. 1994; 60(4): 619-30.
7. Marya R, Rathee S, Dua V, Sangwan K. Effect of vitamin D supplementation during pregnancy on foetal growth. *Indian journal of medical research*. 1988; 88: 488-92.
8. Schöttker B, Ball D, Gellert C, Brenner H. Serum 25-hydroxyvitamin D levels and overall mortality. A systematic review and meta-analysis of prospective cohort studies. *Ageing research reviews*. 2013; 12(2): 708-18.
9. Specker B. Vitamin D requirements during pregnancy. *The American journal of clinical nutrition*. 2004; 80(6): 1740S-7S.
10. Seki K, Makimura N, Mitsui C, Hirata J, Nagata I. Calcium-regulating hormones and osteocalcin levels during pregnancy: a longitudinal study. *American journal of obstetrics and gynecology*. 1991; 164(5): 1248-52.
11. Ginde AA, Sullivan AF, Mansbach JM, Camargo Jr CA. Vitamin D insufficiency in pregnant and nonpregnant women of childbearing age in the United States. *American journal of obstetrics and gynecology*. 2010; 202(5): 436. e1-. e8.

12. Luxwolda MF, Kuipers RS, Kema IP, van der Veer E, Dijck-Brouwer DJ, Muskiet FA. Vitamin D status indicators in indigenous populations in East Africa. *European journal of nutrition*. 2013; 52(3): 1115-25.
13. Holmes VA, Barnes MS, Alexander HD, McFaul P, Wallace JM. Vitamin D deficiency and insufficiency in pregnant women: a longitudinal study. *British Journal of Nutrition*. 2009; 102(06): 876-81.
14. Ardawi M, Nasrat H, BA'Aqueel HS. Calcium-regulating hormones and parathyroid hormone-related peptide in normal human pregnancy and postpartum: a longitudinal study. *European journal of endocrinology*. 1997; 137(4): 402-9.
15. Xue Y, Karaplis AC, Hendy GN, Goltzman D, Miao D. Genetic models show that parathyroid hormone and 1, 25-dihydroxyvitamin D3 play distinct and synergistic roles in postnatal mineral ion homeostasis and skeletal development. *Human molecular genetics*. 2005; 14(11): 1515-28.
16. Scholl TO, Chen X, Stein P. Maternal vitamin D status and delivery by cesarean. *Nutrients*. 2012; 4(4): 319-30.
17. Ota K, Dambaeva S, Han A-R, Beaman K, Gilman-Sachs A, Kwak-Kim J. Vitamin D deficiency may be a risk factor for recurrent pregnancy losses by increasing cellular immunity and autoimmunity. *Human Reproduction*. 2013: det424.
18. Bodnar LM, Rouse DJ, Momirova V, Peaceman AM, Sciscione A, Spong CY, et al. Maternal 25-hydroxyvitamin D and preterm birth in twin gestations. *Obstetrics & Gynecology*. 2013; 122(1): 91-8.
19. Shibata M, Suzuki A, Sekiya T, Sekiguchi S, Asano S, Udagawa Y, et al. High prevalence of hypovitaminosis D in pregnant Japanese women with threatened premature delivery. *Journal of bone and mineral metabolism*. 2011; 29(5): 615-20.
20. Ahrari K, Alizadeh SA. Relation of 25-hydroxy vitamin d and onset of labor. *Kowsar medical journal*. 2010; 15(1): 0.
21. Maghbooli Z, Hossein-Nezhad A, Shafaei AR, Karimi F, Madani FS, Larijani B. Vitamin D status in mothers and their newborns in Iran. *BMC pregnancy and childbirth*. 2007; 7(1): 1.
22. Hatami G, Ahmadi S, Motamed N, Eghbali SS, Amirani S. 25-OH Vitamin D serum level in pregnant women in Bushehr-2012. *ISMJ*. 2014; 16(6): 410-8.
23. Shahla A, CharehSaz S, Talebi R, Azad E. Vitamin D deficiency in 15-40 years old females in Urmia. *The journal of urmia university of medical sciences*. 2005.

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Scimitar Syndrome-A late onset associated with asthma clinic - Case report

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Abstract

Scimitar syndrome is a rare congenital anomalous pulmonary venous drainage of the right or left lung into vena cava inferior. It may be diagnosed in newborn, in late childhood or adult period. Cases diagnosed in early childhood have significant clinics of pulmonary findings but late onset group may have subtle clinics and also be diagnosed accidentally.

We report a child having recurrent respiratory complaints and treated as asthma for a long time but diagnosed as Scimitar syndrome during the follow up.

Key word: Asthma, congenital anomaly, pulmonary, scimitar syndrome

Introduction

Scimitar syndrome (hypogenetic lung syndrome, Halasz syndrome, congenital pulmonary venolobar syndrome) is characterized with abnormal drainage of pulmonary vein into vena cava inferior (VCI) or rarely into right atrium. In this syndrome, resembling of the pulmonary vein which is mostly drained into VCI after descending near the right edge of the heart, to scimitar (scimitar sign) in posteroanterior (PA) lung radiographics is considered to be a characteristic appearance (1). But this typical radiological sign is not seen in most of the cases. The prevalence of the syndrome is very rare as 2/100000 in live births and female/male ratio is 2/1 (2). Anomalous pulmonary venous drainage of all or a portion of the right lung is accompanied by different congenital anomalies. Other important components of the syndrome are, hypoplasia of the right lung, dextroposition of the heart, hypoplasia of the right pulmonary artery, pulmonary sequestration, abnormal arterial feeding of the right lobe of the lung from infradiaphragmatic aorta and atri-

al septal defect (ASD). The major complications according to the age of onset and severity of the clinical findings of this disease are recurring lung diseases, congestive heart failure, and pulmonary hypertension (3).

In this article, a case with the history of with recurrent lower respiratory tract infections and diagnose as Scimitar Syndrome with radiographic examinations was mentioned.

Case Report

A thirteen years old girl was brought to the hospital with the complaints of recurring respiratory distress, grunting and cough which was started in her babyhood and continued periodically. She had lower respiratory infections after when she was 7 months old and then repeated every 2-3 months. She had these infections every month last 3 years. During this period, she had the diagnoses of bronchitis, bronchiolitis, asthma and pneumonia and was given antibiotics and bronchodilator therapies for many times. Her prenatal history was normal. When she was 3 years old, adenoidec-tomy was performed because of the complaints of grunting and respiratory distress. Lung sounds were equal but coarsening and expiratory sounds were prolonged in her physical findings.

In laboratory findings hemoglobin level was 12.1 g/dL but weight blood count, platelet count was normal. At the same time in her pulmonary function tests (PFT) are low, FEV1 (forced expiratory volume in one second) was 72%, FVC (forced vital capacity) was 69%, FEV1/ FVC was 100%. In PA radiographics (Figure 1) there was an atypical view of asymmetrical fullness in the left hilar area. There was a huge venous structure at the base of the right lung that drained into vena

cava inferior and in the neighborhood there were foci of focal emphysema in thorax computed tomography (CT) (Figure 2).

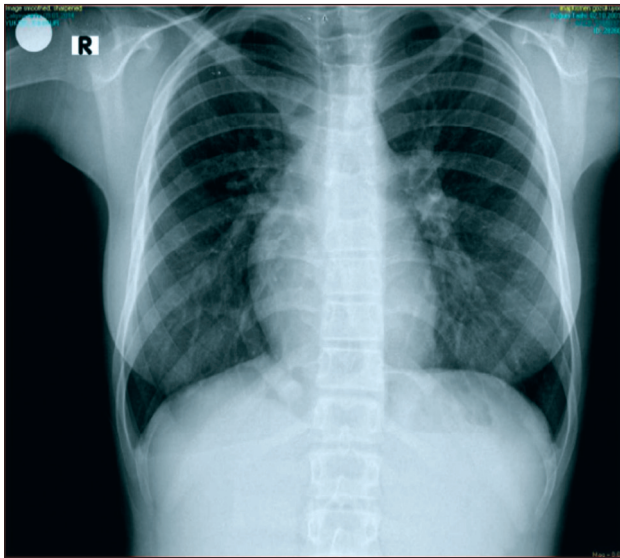


Figure 1. Slight shift of the heart to the right in PA graphic and Scimitar like linear radio opacity near the right side of the heart

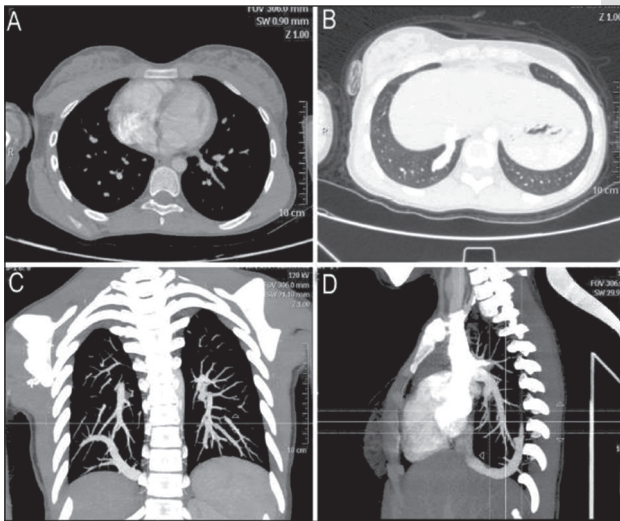


Figure 2. A. Right shift in the images of contrast-enhanced axial tomography. B-D. Connection of right inferior pulmonary vein with inferior vena cava in the images of axial, coronary and sagittal plane tomography.

In three dimensional thorax angiographic CT there was an aberrant pulmonary vein at the base of right lung and the largest dimension of pulmonary vein through costodiaphragmatic recess was 11 mm. and it was draining into vena cava inferior adjacent to liver. This view was compatible with scimitar syndrome. Both lung perfusion scintigraphy

was normal. While her electrocardiogram was normal, drainage of 3 of the pulmonary veins into left atrium and drainage of aberrant pulmonary vein into hepatic vein were observed in her echocardiography. She was diagnosed as Scimitar syndrome and was referred to cardiothoracic surgery department and operation decision was planned.

Discussion

Congenital malformations containing anomalous venous return were first described in 1836 by Cooper (4). Neil et al. first described this syndrome with the name of "Scimitar" (5). Syndrome is described as Scimitar syndrome because of the abnormal course of pulmonary vein which drains the right lung, and has a hyperdense shape like scimitar (Turkish sword) in posteroanterior radiographics. This vein continues parallel to the edge of the right heart and extends toward the diaphragm. Generally there is no sign of Turkish sword in the cases diagnosed in babyhood. About 70% of cases diagnosed in childhood and adulthood have signs of Turkish sword in PA radiographics (6). It is showed that abnormal pulmonary venous return is more often and less frequently to hepatic, portal or azygos veins or to the right atrium, left atrium, or coronary sinus Even though, primitive connection developed in intrauterine period at the 4-5th weeks should be regressed in normal evolution after the connection is evolved between pulmonary vascular bed and systemic veins (7). In our case it was shown that three pulmonary veins drained into left atrium and aberrant pulmonary vein were drained into hepatic vein. Hepatic vein is the biggest visceral vein drains into VCI. Hepatic portal vein and arteria hepatica propria carry the blood from the liver to VCI. When return to coronary sinus is formed, intracardiac anomalies like ASD may accompany. Dupius et al. classified the patients as infantile group who were diagnosed in the first year of life and as adult group who were diagnosed after infantile period. Risk of death after surgery was significantly more in infantile group (2). Clinical situation is more serious in babyhood and tachypnea, congestive heart failure and pulmonary hypertension develop in the first two months of life. Clinical status is better and less deadly in childhood and adulthood period.

Our case was in the adulthood period and did not have complaints that were described above except recurrent lung infections. Main factors determining the prognosis in the patients diagnosed with Scimitar syndrome are lung infections, pulmonary hypertension, congenital heart diseases (CHD), and right heart failure. CHD may accompany in 75% of neonates, and 36% of children with this syndrome. The most seen CHD is secundum ASD. Ventricular septal defect, patent ductus arteriosus, aortic stenosis, aortic arch anomalies, Shone complex and tetralogy of Fallot can be seen. And also anomalies of lung lobes, airways, pulmonary sequestration, dextrocardia and abnormal feeding from abdominal aorta can be observed (8). Pulmonary hypertension can develop because of left to right shunt. Major components of the syndrome are hypogenetic lungs, anomaly of right lung and partial abnormal pulmonary venous return, pulmonary sequestration, agenesis of pulmonary artery, systemic arterializations without sequestration and duplication of diaphragm. Minor components that seen very rare were tracheal trifurcation, eventration of diaphragm, partial absence of diaphragm, cyst of phrenic nerve, horseshoe lung, and absence of left pericardium (9). In our case there was no pulmonary and intracardiac involvement.

There is no need of any treatment in the patients diagnosed with Scimitar syndrome if there is no serious pulmonary left-right shunt or pulmonary pressure is normal. Surgical treatment is necessary in the patients having congestive heart failure and pulmonary hypertension and pulmonary flow/systemic flow (Qp/Qs) ratio is >1.5 (10). With surgical correction abnormal venous drainage is corrected to the left atrium and additional pulmonary, intracardiac anomalies are corrected. In conclusion Scimitar syndrome should be evaluated in children with recurrent pulmonary infections, asthma clinic and respiratory distress. In diagnosis only some of the patients may have typical radiological findings so advanced imaging techniques should be done in the suspected cases.

References

1. Dupuis C, Charaf LAC, Brevière GM, Abou P, Rémy-Jardin M, Helmius G. The adult form of scimitar syndrome. *Am J Cardiol.* 1992; 70: 502-7.
2. Gudjonsson U, Brown JW. Scimitar syndrome. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu.* 2006; 56-62.
3. Gao YA, Burrows PE, Benson LN, Rabinovitch M, Freedom RM. Scimitar syndrome in infancy. *J Am Coll Cardiol.* 1993; 22: 873-82.
4. Cooper G. Case of malformation of thoracic viscera. *London Med Gaz* 1836;18:600-2.
5. Neill CA, Ferencz C, Sabiston DC, Sheldon H. The familial occurrence of hypoplastic right lung with systemic arterial supply and venous drainage "scimitar syndrome". *Bull J Hop Hosp.* 1960; 107: 1-15.
6. Yıldız CE, Korkmaz AA, Babaoğlu K, Onan B, Güden M, Çetin G. Anormal pulmoner venöz dönüşün karmaşık formu; scimitar sendromunda yeni nesil görüntüleme ve cerrahi yaklaşım. *Türk Ped Ars.* 2013; 173-5.
7. Takeda S, Imachi T, Arimitsu K, Minami M, Hayakawa M. Two cases of scimitar variant. *Chest.* 1994; 105: 292-3.
8. Midyat L, Demir E, Askın M, Gülen F, Ülger Z, Tanaç R, et al. Eponym. Scimitar syndrome. *Eur J Pediatr.* 2010; 169: 1171-7.
9. Rutledge JM, Hiatt PW, Wesley Vick G 3rd, Grifka RG. A sword for the left hand: an unusual case of left-sided scimitar syndrome. *Pediatr Cardiol.* 2001; 22: 350-2.
10. Wang CC, Wu ET, Chen SJ, Lu F, Huang SC, Wang JK, et al. Scimitar syndrome: incidence, treatment, and prognosis. *Eur J Pediatr.* 2008; 167: 155-60.

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Metabolic Syndrome According to ATP3 Guidelines in a Public Sector Diabetic Clinic in Pakistan

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Abstract

The metabolic syndrome (MetS) is a clustering of components that reflects over nutrition, sedentary lifestyles, and resultant excess adiposity.

Objectives: To identify distribution of psychosocial risk factors of metabolic syndrome in community presented to a Public sector Diabetic clinic.

Study Design: Case Control study.

Place: Diabetic Clinic, Mayo Hospital Lahore Pakistan.

Study Period: 6 months.

Subjects and Methods: A case control study was conducted. Purposive sampling was used to conduct the study. Sample selection was made on laid down criteria after taking due consent. Interviews were conducted through a pretested questionnaire. Data was collected, compiled and analyzed through SPSS version 19. The demographic characteristics were described using frequency tables and percentages. Association of risk factor was computed by multivariate logistic regression and it was used to calculate odds ratio and their 95% confidence intervals.

Results: Metabolic syndrome was found to be more among people 40 years of age and above, mostly married females, those with an education above high school and living in urban residents. Our research showed that smoking, fat rich diet, irregular timing of meals and lack of exercise were the risk factors for metabolic syndrome.

Key Words: metabolic syndrome, psychosocial factors, community, ATP3 criteria.

Introduction

The *metabolic syndrome* (MetS) is a clustering of components that includes abdominal obesity, insulin resistance, dyslipidemia, and elevated blo-

od pressure and is associated with other co-morbidities such as prothrombotic state, proinflammatory state, nonalcoholic fatty liver disease, and reproductive disorders. These factors reflect over-nutrition, sedentary lifestyles, and resultant excess adiposity.¹ The National Cholesterol Education Program's *Adult Treatment Panel III* report (ATP III) identified the metabolic syndrome as² the presence of any three of the following five factors for the diagnosis of Metabolic Syndrome: abdominal obesity, hypertriglyceridaemia (triglycerides ≥ 1.7 mmol/L), low HDL cholesterol (HDL cholesterol ≤ 1.03 mmol/L for men and ≤ 1.29 mmol/L for women), elevated blood pressure (systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 85 mmHg or current use of antihypertensive drugs) and impaired fasting glucose (fasting plasma glucose ≥ 5.6 mmol/L).³

The pathophysiology of metabolic syndrome includes development of insulin resistance and obesity leading to diabetes and ultimately cardiovascular disorders. Moreover, adiponectin; ⁴ a fat derived hormone; is an anti atherogenic agent, the deficiency of which combined with increased levels of TNF- α or PAI-1⁵ induced by the accumulation of visceral obesity may be the major factors in causing atherogenic as well as metabolic disorders.

Prevalence of the metabolic syndrome as defined by National Cholesterol Education Program, Adult Treatment Panel III (NCEP, ATP III) and other criteria ranges from about 11 to 41 per cent in different regions of India.⁶ In a large family study of type 2 diabetes in Finland and Sweden, the risk for coronary heart disease and stroke was increased threefold in subjects with the syndrome ($P < 0.001$).⁷ ATP III viewed CVD as the primary clinical outcome of metabolic syndrome.² Using CT scanning for the analysis of adipose tissues, a

research study has clarified that visceral adipose tissue accumulation may have a major role in the occurrence of diabetes mellitus, hyperlipidemia, and hypertension and also atherosclerotic diseases. Therefore, visceral obesity may have a key role in the development of multiple risk factors.⁸

According to a study, insulin resistance was reported to be present in nearly 30 per cent of children and adolescents in India, more so in women. Furthermore, approximately 20-25 per cent of urban South Asians have evidence of metabolic syndrome. This could be due to rapid nutritional and lifestyle transition in urbanized areas.⁶ Despite the high prevalence of metabolic syndrome in South Asian countries, alleviation of risk factors such as lifestyle modification, adequate exercise and balanced nutrition may prevent this disease. Therefore, there is an urgent need to conduct a study regarding the underlying risk factors of metabolic syndrome. This study was aimed to identify the association of psychosocial risk factors associated with metabolic syndrome. The results would be implicated towards devising health education, to prevent rising burden of metabolic syndrome and health promotion.

Materials and methods

A case control study was conducted in Lahore, Pakistan to identify frequency of risk factors associated with metabolic syndrome according to ATP3 guideline.

Study population: Cases included adults above 18 years who were suffering from Metabolic Syndrome. They were willing to participate and fulfill the criteria laid down by ATP III guidelines for metabolic syndrome.

The Controls were selected for comparison and they were adults of age more than 18 years, either gender and did not have metabolic syndrome according to ATPIII guidelines.

Sample size calculations were obtained at 95% CI and 80% power of test and sample was 98 that was rounded to 100.

Purposive sampling technique was used to recruit study cases and controls from all eligible individuals. The ethical issues were addressed. Permission from Ethical Review board was obtained. Prior informed consent was also obtained from all selected study subjects and information was kept confidential.

Study Variables

- Metabolic syndrome defined on ATPIII guidelines.

Three out of five of the following conditions must be present during case selection: Abdominal obesity determined by elevated waist circumference (greater than 40 inches (102 cm) for men and greater than 35 inches (88 cm) for women), elevated blood pressure (equal to or greater than 130/85 mm Hg or use of medication for hypertension), elevated fasting Plasma glucose (equal to or greater than 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycemia), high serum triglycerides (equal to or greater than 150 mg/dL (1.7 mmol/L)) and low high-density cholesterol levels (less than 40 mg/dL (1.03 mmol/L) for men and less than 50 mg/dL (1.29 mmol/L) for women).

- Smoker: A smoker was a person who had smoked at least 100 cigarettes and now smokes at least one cigarette every day.
- Stress: Perceived stress scale was used. Score 21 and above was taken as stress presence.
- Lack of Exercise: Not performing aerobic activity for at least 30 minutes per day, five times a week.
- Irregular timing of meals: The meals are not taken according to scheduled time.
- Fat rich Diet: A daily diet where more than 35% calories are obtained from fat.

Results

A case control research study was conducted in a study population aged 40 years and above, mainly married (97%), living in urban areas (54%), educated (57% with high school education) and having their income above Rs.15000 (64%). The female population consisted mostly of housewives (57%). In a multivariate analysis of risk factors regarding the prevalence of metabolic syndrome, a statistically significant result was found to be present among smokers (OR= 7.5, 95% CI- 1.697, P< 0.05), those with fat rich diet (OR= 5.652, 95% CI: 1.389, P= 0.016), those who had irregular timing of meals (OR= 1.3, 95% CI: 3.603, P= 0.002). Lack of exercise (OR= 5.656, CI: 1.499, P= 0.011) was also a significant risk factor for metabolic syndrome.

Variables		Frequency	Percentage
Gender	Male	41	41
	Female	59	59
Education	Educated	57	57
	Non educated	43	43
Occupation	Jobless	12	12
	Housewives	57	57
	government	5	5
	Private job	9	9
	Others	17	17
Income	Below 15000	36	36
	Above 15000	64	64
Marital status	Married	97	97
	Unmarried	3	3
Address	Urban	54	54
	Rural	46	46

Multivariate analysis:

S.No	Risk factor	Adjusted Odds ratio	95% Ci Upper	Lower	Pvalue
1	Smoking	7.509	1.697	33.23	.008
2	Fat rich diet	5.652	1.389	23.005	.016
3	Irregular timings of meals	1.3	3.603	4.72	.002
4	Lack of exercise	5.656	1.499	21.337	.011

Discussion

Metabolic syndrome is a constellation of various components such as insulin resistance, obesity, dyslipidemia and hypertension.¹ Over the past few years, this syndrome has become a serious public health concern⁹ as it is considered a driver of current epidemics of diabetes¹⁰ and cardiovascular disorders.¹¹ A rising trend has been seen in its prevalence worldwide especially in developing South Asian countries of which Pakistan^{9, 12} shares a major burden. According to some studies, the prevalence of MetS in Pakistan ranges from 18% to 46% using different criteria for its diagnosis.¹² There is a dire need to establish the risk factors of this health issue so that it can be prevented. Hence, the aim of our study was to identify the distribution of MetS and its associated psychosocial factors. The prevalence of these risk factors varies among different regions and sections of population. As our study was conducted in a public diabetic clinic so it caters to these variations in a comprehensive way.

Aging has been associated with escalation of insulin resistance, other hormonal alterations, and

expansion in visceral adipose tissue,¹³ all of which are important in the pathogenesis of the metabolic syndrome. Therefore increasing age predisposes to the development of MetS as shown by our study as well. Out of 100 subjects, metabolic syndrome was diagnosed more in people above and equal to 40 years. Many of the researches conducted worldwide and in Indian subcontinent showed that women had a higher prevalence of metabolic syndrome.⁹ Ford et al. showed that in USA, 23.9% females and 21% males had MetS.¹⁴ This study depicted similar trends wherein MetS was present in 59% women and 41% men. More rigorous cutoffs applied in women for waist circumference and HDL may partly explain this variation.¹⁵ Another study illustrated that postmenopausal diabetics had greater chances of developing MetS as compared to premenopausal diabetics¹⁶ attributable to variation in sex hormones and aging.

A major contributing factor to the rising incidence of MetS is marked shift in lifestyle in South Asian countries due to urbanization, dietary westernization and increase in per capita income.⁶ Our research-

ch corroborates this observation as metabolic syndrome was widespread in educated people (57%), urban residents (54%) and those having income above Rs.15000 (64%). Educational status can be considered as a surrogate measure for socioeconomic status because it can envisage the future job opportunities and lifestyle patterns.¹⁷ Wealthy and educated people living in cities are more likely to be doing office jobs involving less physical activity leading to obesity and thus MetS. Conversely, some studies have found an inverse relationship between education¹⁸ and MetS. This could be due to the negligent attitude of less educated people towards health issues. As diabetes is a chief risk factor of metabolic syndrome and vice versa, so both diseases show a parallel rise in their prevalence due to urbanization. Shera et al. depicted regional prevalence of diabetes in Pakistan: 22.04% in urban and 17.15% in rural areas.¹⁹

Furthermore, sedentary lifestyle²⁰ poses an increased risk for diabetes and cardiovascular diseases and also modifies the severity of other risk factors. Prasad et al. revealed that 43% of subjects with metabolic syndrome were physically inactive.¹⁵ Similarly, current study showed that lack of exercise (p value=0.011) was a key risk factor of MetS. In addition, housewives (57%) being sedentary were the major victims of MetS according to our results. As physical activity levels are decreasing in South Asians²⁰ thus there is an upward trend of MetS in this region.

In addition, central obesity is found to be more common in Asians.²¹ It was revealed by a National Health Survey of Pakistan that 25% of our population is obese.²¹ This is an alarming situation because abdominal obesity is an important component of metabolic syndrome and even plays a vital role in its development.²² Our study substantiated this causal relationship as 71% of our cases had weight above 60 kg and 84% had height above 5 feet. Moreover, Fat-rich diet (p value=0.016) was identified to be the most important risk factor of MetS. It contributes to excessive weight gain leading to increased insulin resistance²³ and thus MetS.²⁴ Researches have shown that not all Insulin resistant people are clinically obese but they commonly have predominant upper body fat.²⁵ In this abnormal fat distribution, there is an unusually high release of non-esterified fatty acids from adipose tissue

leading to lipid accumulation in muscle and liver which ultimately predisposes to insulin resistance and dyslipidemia.²⁶ Central obesity, insulin resistance and dyslipidaemia also tend to be higher in smokers.²⁷ Accordingly, there is a greater incidence of metabolic syndrome in smokers as compared to non-smokers.²⁸ Our study showed similar results in which smoking ($OR=7.5$, 95% CI- 1.697, $P<0.05$) was a major risk factor of MetS. In fact, Chioloro et al. explained that Nicotine, carbon monoxide and other constituents of cigarette smoke increase insulin resistance²⁹ ultimately leading to diabetes and MetS. A dose response relationship has been illustrated between smoking and incidence of diabetes.³⁰ Cessation of smoking provides substantial benefit in stopping the progression of this disease.

In recent times, multiple socio-demographic and psychosocial studies including the current research have been conducted on metabolic syndrome in order to establish its risk factors and to devise a prevention plan. The reason MetS has been heavily researched upon is its resultant morbidity and mortality. As suggested by a study, people with metabolic syndrome have five times greater risk of developing type 2 diabetes mellitus.³¹ Another study has established the association of MetS with cardiovascular diseases.³² In particular, South Asians have an unusually greater tendency to develop type 2 diabetes³³ and coronary heart disease.³⁴ Misra illustrated that body composition³⁵ of South Asians with high percentage of body fat, ³⁵ abdominal obesity³⁵ and insulin resistance, ³⁶ is prone to development of metabolic syndrome. More than 10% of adult population of Pakistan suffers from diabetes with a rising trend. It is predicted that in the next 20 years, Pakistan will rank the 4th globally for diabetes prevalence unless the current situation is controlled.

The psychosocial risk factors identified in this study are modifiable; therefore, the burden of metabolic syndrome in South Asia can be reduced by preventive measures. A multidimensional prevention program should be initiated with the active participation of the Government, physicians, patients and the society, in general. Most importantly, a public awareness campaign ought to be commenced to make people aware that they are more susceptible to MetS. Thus, they should be taking aggressive measures such as increasing physical

activity and taking balanced diet at regular intervals to maintain ideal weight. Recent data³⁷ and WHO^{38, 39} recommend that BMI for Asians should be maintained between 19-23 kg/m². Exercise is a mandatory part of prevention plan as it helps to control obesity and maintain optimal weight.⁴⁰ It also helps alleviate obesity-associated risk factors: facilitating visceral adipose tissue loss; overcoming insulin resistance; improving dyslipidemias,^{41, 42} hence, lowering the risk of MetS.

Strengths of the present study include representative sampling methodology; use of standardized data collection protocols and achieving the objectives of our study: to establish the distribution and risk factors of metabolic syndrome. We were able to ascertain the demographic prevalence as MetS was found more in females, age above 40 years and in urban population. Our research also showed that lack of exercise, fat rich diet, smoking and stress were the major contributing factors of MetS. Lastly as we conducted a case control study so establishment of these risk factors can be more credible as compared to an observational study in which only causal inferences can be made.

However, we also encountered some study limitations such as recall bias of the behavioral risk factors. Moreover longitudinal follow up studies are important to identify unmeasured risk factors of the deadly sequelae of MetS for their comprehensive control among a wider Asian community sharing similar lifestyle and culture. Our study was based on ATP 3 guidelines which define metabolic syndrome based on the statistics of developed countries whereas the cutoffs for the components of MetS need to be modified for their implementation in Asian countries. Various studies have established the role of visceral fat in producing insulin resistance but we did not use any modality to specifically measure the visceral fat in body.

Conclusion

Metabolic syndrome was found more in married females, age above 40yrs and those with an education above matric and urban people.

The Research showed that smoking, fat rich diet, irregular timings of meals, and lack of exercise were the risk factors significantly associated with metabolic syndrome.

References

1. Cornier M A, Dabelea D, Hernandez TL, Lindstrom RC, Steig AJ, Stob NR, et al. *The Metabolic Syndrome*. *Endocrine reviews*. 2008 Dec; 29(7): 777-822
2. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C. *Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition*. *Circulation*. 2004 Jan 27; 109(3): 433-438.
3. Moy FM, Bulgiba A. *The modified NCEP ATP III criteria maybe better than the IDF criteria in diagnosing Metabolic Syndrome among Malays in Kuala Lumpur*. *BMC Public Health*. 2010; 10: 678. doi: 10.1186/1471-2458-10-678.
4. Maeda N, Shimomura I, Kishida K, Nishizawa H, Matsuda M, Nagaretani H, et al. *Diet-induced insulin resistance in mice lacking adiponectin/ACRP30*. *Nat. Med*. 2002 Jul; 8(7): 731-737.
5. Montague CT, O'Rahilly S. *The perils of portliness: causes and consequences of visceral adiposity*. *Diabetes*. 2000; 49: 883-888.
6. Misra A, Misra R, Wijesuriya M, Banerjee D. *The metabolic syndrome in South Asians: Continuing escalation & possible solutions*. *Indian J Med Res*. 2007 Mar; 125: 345-354.
7. Isomaa B, Almgren P, Tuomi T, Forsen B, Lahti K, Nissen M, et al. *Cardiovascular morbidity and mortality associated with the metabolic syndrome*. *Diabetes Care*. 2001 April; 24(4): 683-689.
8. Matsuzawa Y, Funahashi T, Kihara S, Shimomura I. *Adiponectin and metabolic syndrome*. *Arterioscler. Thromb. Vasc. Biol*. 2004 Jan; 24(1): 29-33.
9. Hydrie MZ, Shera AS, Fawwad A, Basit A, Hussain A, "Prevalence of metabolic syndrome in urban Pakistan (Karachi): comparison of newly proposed international diabetes federation and modified adult treatment panel III criteria". *Metabolic Syndrome and Related Disorders*. 2009; 7(2): 119-124: 2009.
10. Zimmet P, Alberti KG, Shaw J. *Global and societal implications of the diabetes epidemic*. *Nature*. 2001; 414: 782-787.
11. Sundstrom J, Riserus U, Byberg L, Zethelius B, Lithel H, Lind L. *Clinical value of the metabolic syndrome for long term prediction of total and cardiovascular mortality: prospective, population based cohort study*. *BMJ*. 2006; 332(7546): 878-881.

12. Basit A, Shera AS. "Prevalence of metabolic syndrome in Pakistan". *Metabolic Syndrome and Related Disorders*. 2008; 6(3): 171–175.
13. Boden G, Chen X, DeSantis RA, Kendrick Z. Effects of age and body fat on insulin resistance in healthy men. *Diabetes Care*. 1993; 16(5): 728–733.
14. Ford ES, Giles WH, Ali H. Increasing prevalence of Metabolic Syndrome among the US adults. *Diabetes Care* 2004; 27: 2444–2449.
15. Prasad DS, Kabir Z, Dash AK, Das BC. Prevalence and risk factors for metabolic syndrome in Asian Indians: A community study from urban Eastern India. *J Cardiovasc Dis Res*. 2012 Jul-Sep; 3(3): 204–211.
16. Afzal S, Bashir MM. Prevalence of Metabolic syndrome in pre and post menopausal diabetics. *Biomedica*. 2008; 24: 26–30.
17. Lidfeldt J, Nyberg P, Nerbrand C, Samsioe G, Scherstén B, Agardh CD. Socio-demographic and psychosocial factors are associated with features of metabolic syndrome. The Women's Health in the Lund Area (WHILA) study. *Diabetes Obes Metab*. 2003; 5(2): 106–12.
18. Kim MH, Kim MK, Choi BY, Shin YJ. Educational disparities in the metabolic syndrome in a rapidly changing society – the case of South Korea. *Int J Epidemiol*. 2005; 34(6): 1266–73.
19. Shera AS, Jawad F, Maqsood A. Prevalence of diabetes in Pakistan. *Diabetes Res Clin Pract* 76: 219–222, 2007.
20. Prasad DS, Das BC. Physical inactivity: A cardiovascular risk factor. *Indian J Med Sci*. 2009; 63: 33–42.
21. Jafar TH, Chaturvedi N, Pappas G. "Prevalence of overweight and obesity and their association with hypertension and diabetes mellitus in an Indo-Asian population". *CMAJ*. 2006; 175(9): 1071–1077.
22. Zimmet P, Alberti K, George MM, Kaufman F, Tajima N, Silink M, et al. "The metabolic syndrome in children and adolescents - an IDF consensus report". *Pediatric Diabetes*. 2007; 8(5): 299–306.
23. Riccardi G, Giacco R, Rivellese AA. Dietary fat, insulin sensitivity and the metabolic syndrome. *Clinical Nutrition*. 2004; 23: 447–456.
24. Renaldi O, Pramono B, Sinorita H, Purnomo LB, Asdie RH, Asdie AH. "Hypoadiponectinemia: a risk factor for metabolic syndrome". *Acta Medica Indonesiana*. 2009; 41(1): 20–24.
25. Nielsen S, Guo Z, Johnson CM, Hensrud DD, Jensen MD. Splanchnic lipolysis in human obesity. *J Clin Invest*. 2004; 113: 1582–1588.
26. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the Metabolic Syndrome. American Heart Association/ National Heart, Lung and Blood Institute Scientific Statement, *Circulation*. 2005; 112: 2735–2752.
27. Geslain-Biquez C, Vol S, Tichet J, Caradec A, D'Hour A, Balkau B. The metabolic syndrome in smokers: the D.E.S.I.R. study. *Diabetes Metab*. 2003; 29(3): 226–234.
28. Park YW, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988–1994. *Arch Intern Med*. 2003; 163: 427–436.
29. Chioloro A, Faeh D, Paccaud F, Cornuz J. Consequences of smoking for body weight, body fat distribution, and insulin resistance. *Am J Clin Nutr*. 2008; 87(4): 801–809.
30. Will JC, Galuska DA, Ford ES, Mokdad A, Calle EE. Cigarette smoking and diabetes mellitus: evidence of a positive association from a large prospective cohort study. *Int J Epidemiol*. 2001; 30(3): 540–546.
31. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; National heart, lung, and blood institute; American heart association; World heart federation; International atherosclerosis society; And international association for the study of obesity. *Circulation*. 2009; 120(16): 1640–1645.
32. Mancia G, Bombelli M, Corrao G, Facchetti R, Maddotto F, Giannattasio C, et al. Metabolic syndrome in the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) study: daily life blood pressure, cardiac damage, and prognosis. *Hypertension*. 2007; 49: 40–47.
33. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. *Diabetes Care*. 1998; 21: 1414–31.
34. Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation*. 1998; 97: 596–601.
35. Misra A. Body composition and the metabolic syndrome in Asian Indians: a saga of multiple adversities. *Natl Med J India*. 2003; 16 : 3–7.

36. Mohan V, Sharp PS, Cloke HR, Burrin JM, Schumer B, Kohner EM. Serum immunoreactive insulin responses to a glucose load in Asian Indian and European Type 2 (noninsulin-dependent) diabetic patients and control subjects. *Diabetologia*. 1986; 29: 235-7.
37. Guettier JM, Georgopoulos A, Tsai MY, Radha V, Shanthirani S, Deepa R, et al. Polymorphisms in the fatty acid-binding protein 2 and apolipoprotein C-III genes are associated with the metabolic syndrome and dyslipidemia in a South Indian population. *J Clin Endocrinol Metab* 2005; 90: 1705-11.
38. Deurenberg-Yap M, Deurenberg P. Is a re-evaluation of WHO body mass index cut-off values needed? The case of Asians in Singapore. *Nutr Rev*. 2003; 6: 80-87.
39. Misra A. Revision of limits of body mass index to define overweight and obesity are needed for the Asian ethnic groups. *Int J Obes Relat Metab Disord*. 2003; 27: 1294-6.
40. National Institutes of Health, The Practical Guide: Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. Bethesda, MD: National Institutes of Health 2000; NIH publication 00-4084.
41. Choiniere R, Lafontaine P, Edwards AC. Distribution of cardiovascular disease risk factors by socioeconomic status among Canadian adults. *CMAJ*. 2000; 162: 13- 24.
42. Rosengren A, Wilhelmsen L. Physical activity protects against coronary death and deaths from all causes in middle-aged men. *Ann Epidemiol*. 1997; 7: 69- 75.

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Abstract

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Key words: Camera ready paper, Journal.

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Table 1. Page layout description

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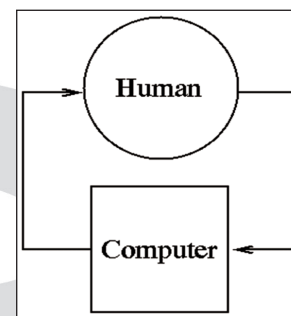


Figure 1. Text here

Conclusion

Be brief and give most important conclusion from your paper. Do not use equations and figures here.

Acknowledgements (If any)

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References

1. Sakane T, Takeno M, Suzuki N, Inaba G. Behcet's disease. *N Engl J Med* 1999; 341: 1284–1291.
2. Stewart SM, Lam TH, Beston CL, et al. A Prospective Analysis of Stress and Academic Performance in the first two years of Medical School. *Med Educ* 1999; 33(4): 243–50.

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