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Sadržaj / Table of Contents

Diagnosis of Aspergillus in Bronchoalveolar lavage of Patients at Risk for Invasive Aspergillosis with galactomannan enzyme assay

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Abstract

Background: Aspergillosis is induced by aspergillus species, especially a.fumigatus that has emerged as an important etiologic agent of this mentioned infection. In the present study, an evaluation was conducted for assessment of the Enzyme immunoassay [EIA] method for finding of Aspergillus galactomannan antigen in Broncho alveolar lavage [BAL]. Due to the lack of reliable information on the evaluation of galactomannan levels in patients with suspected invasive aspergillosis, this work is the first study of its kind in Tehran based on the information available in the international databases.

Methods: In this cross-sectional study, 89 Broncho alveolar lavage [BAL] fluid samples were acquired from all patients to identify reports with finding suggestive of infection and lung infiltration and who were undergoing bronchoscopy in shariati hospital at risk for Invasive aspergillosis [IA] by pulmonologist between June 2013 and march 2014. The specimens by direct and culture methods, galactomannan EIA were tested in the laboratory of mycology Tarbat Modares University. The data were analyzed using XLSTAT software by plotting ROC Curve.

Results: 27 samples EIA positive were identified and in the meantime, 18 samples were positive in Culture assays. The sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) for a BAL GM level of ≥1.0 were 94.4%, 85.9%, 98.4%,and 62.9%, respectively.

Conclusions: Results of the study along with other studies done show that the Galactomannan testing of good sensitivity and specificity for the diagnosis of invasive aspergillosis and High negative predictive value (NPV) to rejection of invasive aspergillosis is possessed.

Key words: Aspergillosis, galactomannan, enzyme immunoassay, Bronchoalveolar lavage

Introduction

Aspergillosis is induced by aspergillus species, especially a.fumigatus, that has emerged as an important etiologic agent of these mentioned infection. Aspergillus species cause a wide range of diseases such as allergic, chronic necrotizing aspergillosis, keratitis, fungal sinusitis and invasive aspergillosis especially in at risk patients(1).

Prior studies have been revealed a rising growth of aspergillosis is recipient patient compared with healthy individual. These patients are at a high risk of developing systemic aspergillosis. Serious risk factor for invasive aspergillosis (IA) is chemotherapy in mentioned patients. Early and correct diagnosis of aspergillosis is very necessary in an early phase of the infection in at risk population. Conventional methods with other clinical feature could help. However culture has a very low sensitivity and we requires immunological and molecular marker for early diagnosis. Invasive aspergillosis (IA) is a leading cause of infection among patients undergoing hematopoietic stem cell transplantation, solid organ transplantation, and treatment for hematological malignancies.

Although the spread of IA is different among host groups, the fatality rate caused by this disease is high and ranges from 58 to 99% in immunocompromised patients. Aspergillus fumigatus remains the main cause of IA; however, at least 20 other species, including A.flavus, A.terreus, A.niger, A.nidulans and A.versicolors have been stated as the cause of human infection.

In some centers, A.terreus is becoming a progressively usual cause of IA. This species is a concern because it is less susceptible to amphotericin

B in vitro than A.fumigatus and it can be considered as the cause of fulminant invasive infections in immunocompromised patients (2). Prior studies have mentioned the potted plants as a significant source of fungi in hospitals (3).Most literatures on the clinical impact of Aspergillus. spp infections and epidemiology embrace patients with cancer, hematological malignancies, solid organ transplant and stem cell transplantation. However, other studies demonstrate that Aspergillus spp. may cause invasive disease in other categories of patients without obvious immunodeficiency, including patients in intensive care units (ICUs).

If the recognition is hold in abeyance, the swift diffusion of the infection and further disease may result in antifungal treatment having no impact on the disease consequence. Deferment in treatment also causes higher regress rates and therapy costs. A common cost of treatment with voriconazole is over $30000(4). Although A.fumigatus is the most popular etiologic factor, being responsible for approximately 90% of human infections, it is not considered as the only pathogen in this regard. A.flavus, A.terreus, A.niger, and A.nidulans can also lead human infections(1).

Platelia® Aspergillus is an enzyme immunoassay that uses rat monoclonal antibodies, which identify ß (1→5)-linked galactofuranose (6). The Platelia™ Aspergillus EIA is a one-stage immune enzymatic sandwich microplate experiments which finds galactomannan in human Fluids. The experiment uses the rat EBA-2 monoclonal antibodies, which are directed against Aspergillus galactomannan. The monoclonal antibodies are used(7), to coat the wells of the microplate and bind the antigen, and (8) to find the antigen bound to the hypersensitive microplate (conjugate reagent: peroxidase-linked monoclonal antibodies), and can be completed in about 4 hours.

Materials and Methods

In the present study, an evaluation was conducted for assessment of the EIA method for detection of Aspergillus galactomannan antigen in BAL samples from all patients to identify reports with finding suggestive of infection and lung infiltration who were undergoing bronchoscopy in *shariati hospital* at risk for IA. According to the hedayati et al.(9) study and possible outbreaks of aspergillosis in Iran, 89 enough samples were evaluated under the supervision of a statistician. Finally EIA results were compared with clinical diagnosis and common diagnostic tests, such as microscopy and culture method. According to the Searching in international databases, there are no credible data on GM detection in BAL samples among the patients at risk for Invasive Aspergillosis in the capital of Iran. The ethics committee of *Tarbiat Modares University* approved this research.

Specimen processing: Eighty-nine Broncho alveolar lavage [BAL] fluid samples were acquired from all patients to notice the the infection and lung infiltration. A cross-sectional study was conducted. The patients were undergoing bronchoscopy by pulmonologist between June 2013 and March 2014 within a week after the recognition of lung infiltrates and lung collapse symptoms in *shariati* hospital, Iran.

The samples were accumulated in sterile vials without medium conservation and sent to the medical mycology Laboratory in *Tarbiat Modares* University within 2 h. Upon receipt, each sample was separated to two parts: one was directly processed for routine microbiological culture the second was under ELISA for GM.

To detect filamentous fungi were carried out on Sabouraud dextrose agar (Merck, Germany) with chloramphenicol and Czapec Dox agar (Merck, Germany) and incubated at 28-32°C. During this period, fungi grown were identified by standard mycological techniques based upon macroscopic feature, slide culture and direct microscopic examination.

EIA Procedure: The Platelia Aspergillus GM EIA (Bio-Rad Laboratories, France Lot No: 62796) was used to detect the presence of GM on uncentrifuged BAL fluid specimens. All control (negative, positive, cut-off) and BAL fluid (300 µL BAL + 100 µL EDTA acid solution) were treated. Then were heated tubes for 3 minutes in a 100°C water bath. Were centrifuged 10 minutes at 10,000g, Was provided a chart (plate map) for cognizance of control sera and test samples in the microplate, was added 50 µL of ready-to-use Conjugate and 50 µL of treated controls and test samples supernatant to each well, were incubated the microplate with plate sealer for 90 minutes at 37°C, was prepared Washing Solution, was aspirated and washed 5 times,

Rapidly was added 200 µL of Substrate-Chromogen Reaction Solution to each well avoiding disposal to bright light, was incubated the microplate without plate sealer in the dark at room temperature (18-25°C) for 30 minutes, was added 100 µL of ready-to-use Stopping Solution to each well. Were read the OD of each well at 450/620 nm.

The presence or absence of galactomannan antigen (GM Ag) in the assay samples is specified by computation of an index for each patient samples.

$$I = \frac{\text{OD sample}}{\text{Mean Cut-off Control OD}}$$

Data analysis

The Patients with IA were classified as having probable or possible IA on the basis of modified EORTC/MSG criteria. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated on a per-patient basis for BAL GM testing and standard mycological techniques based upon culture methods. The optimal cutoff for BAL GM testing was determined by receiver operating characteristic (ROC) analysis using XLSTAT software. (Figure 1)

Results

Patients with underlying conditions such as diabetes, lymphoma, Hodgkin's disease, lupus, organ transplantation, use of broad-spectrum antibiotics, kidney problems leading to dialysis were 29 cases and 60 patients with high fever, the lesion of lung lobes and other radiological findings, acute problem respiratory, bronchiectasis, hemoptysis, view the CT halo sign and air crescent sign, BAL fluid specimen were taken according to the recommendation of pulmonologist and Were enrolled in this study. According to EORTC/MSG criteria, out of 51 (57.3%) patients, were classified as Possible/ Probable IA and 38 (42.7%) as Non IA (Table 1).

All 89 BAL fluid samples were assayed with macroscopic, slide culture, microscopic characterization and Galactomannan ELISA assay. No sign of aspergillosis existed among sixty-two of the patients, and samples from these patients embraced negative results in cultures and other experiments. And according to the results of Galactomannan ELISA assay are expressed "galactomannan index" (GMI= OD sample/ Mean OD Cut-off Control), by comparison to the "cutoff" control. In clinical studies (5, 10-12), the GM assay higher GMI (1.0 or 1.5), was used in BAL fluid to obtain sensitivity ranging from 85 to 100% (9, 12). Therefore GMIs of 1.0 or higher are regarded as positive in this study. Thus due to the GMI Obtained, 27 samples ELISA positive Were identified (Charts 1), and 18 samples were positive in Culture assays (Table 2). Of the 18 samples with culture positive results, 7 samples Aspergillus fumigatus and 11 samples Aspergillus flavus were identified by routine methods respectively. To determine the most appropriate OD index cutoff to define positivity, a ROC curve was calculated The diagnostic accuracy as given by the area under the ROC curve was 0.987 (Figure 1). However, sensitivity and specificity measure the analytical validity of the test (the accuracy and precision) respectively 94.4% and 85.9% was determined. For an evaluation of the clinical validity, we rely on the predictive values and the diagnostic odds ratio. The positive predictive value (PPV) of the GM BAL fluid assay is (62.9%) at an OD index cutoff of 1.0. However, the latter cutoff is associated with a very high negative predictive value (NPV) (98.4%) (Table 3).

Table 1. Characteristics of patients

Patient characteristic	Value for the parameter (no. of patients [%])
Total population	**89 (100%)**
Mean of age (years)	**35 ± 2**
Male	**42 (47.2%)**
Female	**47 (52.8%)**
NO of dead's (%)	**5 (5.6%)**
Distribution by main underlying condition	
Hematologic malignancy	**8 (9%)**
Recipient Solid organ	**16 (18%)**
Admitted to the Intensive care units (ICUs)	**18 (20.2%)**
Hemodialysis Patients	**2 (2.2%)**
Chronic obstructive pulmonary disease (COPD)	**23 (25.8%)**
Corticosteroids consumer	**2 (2.2%)**
Bone marrow transplant	**10 (11.2%)**
Solid cancer	**8 (9%)**
Diabetes	**2 (2.2%)**
Invasive aspergillosis status (EORTC/MSG criteria)	
Possible/ Probable	**51 (57.3%)**
Non Invasive aspergillosis	**38 (42.7%)**

Table 2. Performance of BAL GM for diagnosing aspergillosis

Characteristics / Name of tests		IA[3]	Non IA	Total
BAL[1] Culture	Positive	11 (21.5%)	7 (18.4%)	18 (20.2%)
	Negative	40 (78.5%)	31 (81.6%)	71 (79.8%)
BAL GMI[2]	Positive	16 (31.4%)	11 (28.9%)	27 (30.3%)
	Negative	35 (68.6%)	27 (71.1%)	62 (69.7%)

1.BAL: bronchoalveolar lavage; 2.GMI: galactomannan index ; 3.IA: Invasive aspergillosis

Table 3. Performance characteristics of the Platelia galactomannan enzyme immunoassay in bronchoalveolar lavage fluid

GM[1] index	Sensitivity	Specificity	PPV[2]	NPV[3]
≥1.0	94.4%	85.9%	62.9%	98.4%

1. GM = galactomannan 2. PPV= positive predictive value; 3. NPV= negative predictive value;

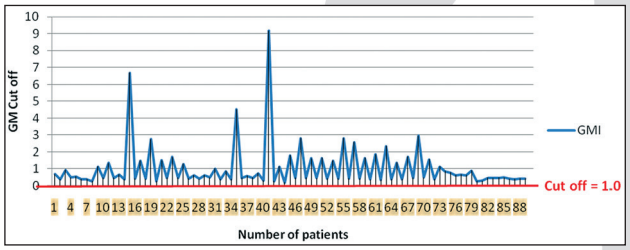

Chart 1. Distribution of Galactomannan Index

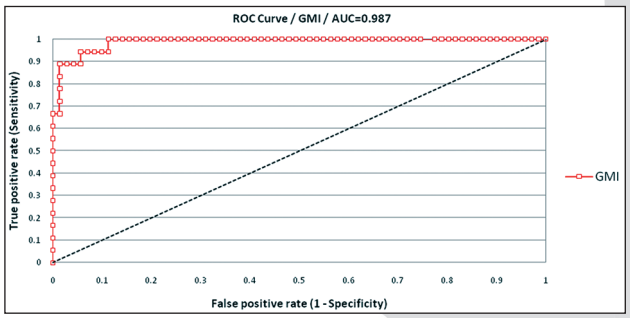

Figure 1. ROC curve for the Platelia EIA in BAL fluid samples

Discussion

The definitive diagnosis of IA often requires invasive techniques such as biopsy of tissue for histology and culture are needed for decisive recognition of IA (8). However, the diagnostic efficiency of customary culture-based methods of BAL fluid may have a relatively low sensitivity for finding of A. fumigatus in patients with IA (1, 13). The compound diagnostic experiments are more sensitive and specific, such as GM EIA and real-time PCR, would permit primary recognition of IA, would enhance clinical results through opportune beginning of antifungal therapy, and would allow averting antifungal treatment when test results are negative. Moreover, both the GM EIA and real-time PCR assay may provide more rapid results than traditional culture-based methods. These findings show that GM EIA is effective tool in the analysis of BAL fluid for identification of IA. Using these assays in related to culture-based recognition techniques could simplify a subtle diagnosis and more-timely beginning of targeted therapy and could result in fewer invasive methods. Of course, antifungal treatment abated the sensitivity of the GM EIA to 92% whereas the sensitivity of BAL fluid culture has reduced to 16% by antifungal therapy, these findings are consistent with the observation that antifungal therapy may lower the residual fungal burden in lung tissue and therefore deduct the sensitivity of these assays (10, 13-15). Meanwhile because of cross-reactivity between antibiotics and GM antigen such as amoxicillin-clavulanic acid, piperacillin-tazobactam and amoxicillin (7, 16-22), the feature of the GM assay may be deducted in certain patient populations receiving these antibiotics.

Decisive diagnosis needs histopathological record of deep-tissue invasion or an affirmative culture from ordinary sterile sites. However, invasive diagnostic methods can be perilous for asthenic neutropenic patients and cultures for this fungus are determined by low sensitivity. Valid noninvasive methods to recognition IPA are vital for the optimal management of these high-risk patients. Promising replacement with culture or biopsy include enzyme related to enzyme linked immunosorbent assay (ELISA) detection of the galactomannan (GM) antigen in serum and other bio-

logical fluids,e.g., Bronchoalveolar lavage (BAL) fluid and PCR based methods for the detection of Aspergillus-specific DNA is desirable. New quantitative experiments using real-time PCR have also been expanded for the recognition of IA (5).

In this regard, the application of more specific test, such as real-time PCR, may significant secondary information to enhance diagnostic accuracy. It should be considered that a positive result may occur in patients infected with fungi containing a cross reactive galactomannan. The monoclonal antibody used reacts with β-1-5-linked galactofuranose in the galactomannan of Wallemia, Paecilomyces, Trychophyton, Penicillium, Alternaria, Botrytis, Cladosporium (23, 24), all which could have a positive result in the method. (6, 25). The Histoplasma galactomannan at high concentrations (~1μg/ml) is detected in this method. (26-28). False-positive results also were reported in patients with P. marneffei (26, 27), Geotrichum (29-31), Neosartorya (Aspergillus udagawae) and cryptococcosis (32,33, 34).

Results of the study along with other studies show that the Galactomannan testing of high specificity and sensitivity for the diagnosis of invasive aspergillosis , But this test is not able to detect Aspergillus species. Also physician-driven decisions for performing bronchoscopy and the timing of bronchoscopy are potential sources of bias. This is certainly the case for patients not treated according to integrated care pathways. As a consequence, samples may have been collected at various time points during the course of the infection and at various stages of fungal disease. On the other hand, the variable amount of instilled and collected fluid may affect GM concentrations and consequently, the sensitivity of the assay. By considering that some Aspergillus species have shown resistance to antifungal agents, so the use of other diagnostic tests, essential seems. However, due to the conditions in clinical laboratories and the existence of ELISA reader at all laboratories and on the other hand do not need expertise required in the diagnoses based on direct and culture methods and also the high cost and the necessary specialty in molecular techniques, Galactomannan detection method by ELISA on serum and BAL samples, the best way to screen or diagnosis of invasive aspergillosis in non-specialized diagnostic and therapeutic centers and consequently the early detection of disease.

Compare the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) with other studies in recent years such as Jorien D'Haese et al (35)and M. Hong Nguyen et al studies(36), shows that GM test has a relatively high sensitivity and specificity and NPV in the aforementioned studies with our study is consistent and higher than PPV (respectively 81%, 93.6% and 42.9%, 100% and in our study 62.9%, 98.4%). However, in Hedayati, et al.(9) study has been done in Iran, it is inconsistent because in the mentioned study, PPV percent is higher than NPV (89% and 87.3%).

Conclusions

Results of the study along with previous studies show that the Galactomannan test having a good sensitivity and specificity for the diagnosis of invasive aspergillosis and high negative predictive value (NPV) in order to reject the invasive aspergillosis.

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Pegboard task in Duchenne muscular dystrophy

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Abstract

Duchenne muscular dystrophy (DMD) is the most common form of muscular dystrophy. It is a progressive hereditary genetic disorder linked to the X chromosome, characterized by progressive weakness and degeneration of the skeletal muscles.

Objective: The aim of the study was to analyze the engine performance of people with Duchenne muscular dystrophy using the pegboard task.

Methods: The study was conducted with two groups: one with 38 male carriers of Duchenne muscular dystrophy (DMDG) with an average age of 19¬ ± 6 years and another 38 subjects of normal development (TDG) and an average age 19¬ of ± 8 years. The study analyzed the performance of each group in the realization of the grooved pegboard task with both hands. The time for completion of the task was used as a performance measure and was measured at the time of each completed row, and then the sum total of all rows was calculated.

Conclusion: An improvement in the engine performance in both groups was demonstrated through the pegboard task.

Key words: Duchenne muscular dystrophy, motor control, grooved pegboard test.

Introduction

Duchenne muscular dystrophy occurs in approximately one in 3,500 male live births.[1] It is considered the most common form of muscular dystrophy. It is an inherited recessive genetic disease characterized by the absence of dystrophin protein in muscle fiber membrane resulting from mutation of the gene Xp21.[2]

It is essentially characterized by the progressive and irreversible weakening of the skeletal, respiratory and cardiac muscle, leading to severe physical disability with reduced expectations of life.[3] Functional changes usually start in the first three years of life, with gradual muscle weakness symmetrical and bilateral, initially in the pelvis and legs and progressing to the trunk muscles, shoulder girdle, upper limbs, neck and respiratory muscles.[4]

Because of the progressive nature of the disease, the patient is confined to a wheelchair from approximately the age of 10 to 13. With the evolution of the disease, people become increasingly dependent for activities of daily living (ADL), requiring greater assistance and care.[1]

Because of motor alterations present in DMD, it is important that we use knowledge-derived motor control, with the intention of seeking consistent scientific evidence and contributing to the development of differentiated intervention programs for this population. According to a 2006 study [5] an intrinsic property of human motor control is a trade-off between speed and accuracy that allows tracking of motor habits in tasks that require manual dexterity.[6] Changes in motor development are characterized by deficits in several areas, such as: fine motor, overall balance, body schema and spatial-temporal organization.[7]

Several pieces of research have been performed on aspects of muscular dystrophy; specifically, postural adjustments [8], physical training [9], multidisciplinary clinical evaluations [10], therapeutic treatments [11], pharmacological treatments [12-14], gross motor function and functional disability in mobility, self-care and social function.[15, 16]

However, there is a growing interest in motor control in muscular dystrophy, with proposals to ensure greater functionality.[4, 17]

As regards DMD, the ability to adjust the coordination and the application of the muscle strength needed to perform a task is critical at any given

time of disease progression. Inability to perform actions quickly and accurately simultaneously hinders the performance of motor tasks.

To afford the person with DMD greater functionality in everyday tasks, the existence of studies investigating simple motor skills and their performance in terms of functional effectiveness is critical; they which can serve as evidence for practical application in rehabilitation programs considering the needs and specificities of disease progression. Faced with this information, the aim of our study was to analyze DMD suffers' engine performance in a simple handicraft task and compare it with that of people who had typical development. As a hypothesis it was expected that people with DMD will complete the proposed task, however with worse performance when comparing to the group with typical development.

Method

Seventy-six subjects were selected, 38 males with Duchenne muscular dystrophy (GDMD) with a mean age of 19¬ ± 6 years and a control group of 38 subjects with typical development (GTD). The groups were matched for age and sex with GDMD (mean age 19 ± 8 years).

The sample was created for convenience. The inclusion criteria were: to the DMD group were considered eligible all patients with a diagnosis of Duchenne Muscular Dystrophy, confirmed by molecular method and/or protein expression, in treatment at the Brazilian Association of Muscular Dystrophy (Associação Brasileira de Distrofia Muscular – ABDIM). For the TD group were eligible males without any neuromuscular alteration, age-matched to the participants of the DMD-group.

Exclusion criteria for participants in both groups were: presence of associated comorbidities, non-acceptance of participation in research by the participant and/or legal guardian through the non-signing of the consent form, and/or term of agreement.

The task used the grooved pegboard test (Lafayette Instrument Company, 1-800-428-7545 Model No. 32025), a manual dexterity test consisting of a surface with 25 holes distributed in five rows with five holes per row, and a concave surface where the pins are placed to start the task. The pins must be removed one by one and sequentially inserted into the concave surface to complete the 25 holes in the shortest time possible. If the patient cannot adequately hold the pin and the overthrow during the execution of the task, the patient himself should pick it up and put it back with the other pins on the concave surface and restart the task; three consecutive failures meant that patient data were not considered for the study (Figure 1).

The time for completion of the task was used as a performance measure and was measured with a digital timer for each completed row from left to right and then the sum total of all five rows was calculated. The pegboard task was performed with the patient sitting in a chair in front of a table and with the preferred hand. In the GDMD group 15% (n = 5) of the participants used the left hand and 85% (n = 33) used the right hand, and in the GDT

Figure 1. Representation of the task of carrying out the sequence

group this figure was 8.5% (n = 3) and 91.5% (n = 35), respectively.

This study was approved by the Research Ethics Committee of the Faculty of Medicine of ABC-FMABC under the protocol CAAE: 39122214.6.0000.0082 on March 25, 2015.

Data analysis

The dependent variables were the time in seconds which participants took to complete each row of the pegboard (Row 1, Row 2, Row 3, Tier 4 and Tier 5) and the total time (sum of all ranks). Data were analyzed by ANOVA with factor 2 (Groups: DMD, TD) for two (rows) with repeated measurements for the last factor. For the comparison of the total time between groups Student's t-test was performed. Post hoc comparisons were performed with Tukey's HSD test ($p < 0.05$).

Results

Data for statistical analysis are shown in Table 1. In the analysis of the movement time among the ranks ANOVA showed a significant reduction in the time between the rows 1-2 both DMD group (M = 27,4s - 25,6s) as the TD group (M = 16.7s - 15,6s). Between rows 2 and3 and 3 and 4 reduction was not significant (Figure 2).

Between the rows 4-5 was found significant effect for rows and interaction between rows and groups, in which only the DMD group reduced the time between the rows 4-5 significantly (F = 23.3s - 20.1s) whereas for the TD group there was no significant difference (M = 13.7s - 13.9s) (Figure 2).

For the analysis of total time between groups, Student's t-test showed that DMD patients showed significantly greater movement time (M = 120.1s) than the TD group (M= 75.2s) ($p < 0.001$) (Figure 3).

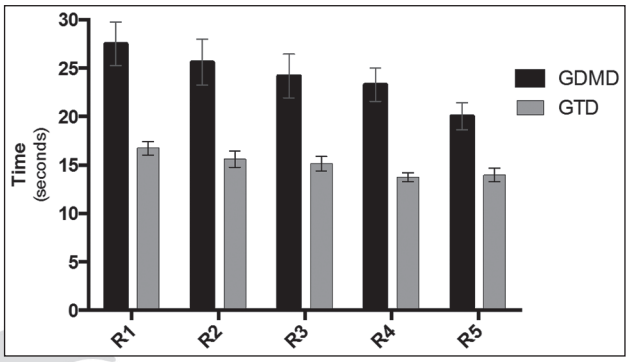

Figure 2. Refers to row 1 to 5 of the pegboard task
DMD: Group with Duchenne muscular dystrophy ; DT: Group with Typical Development ; R1 – R5: refers to rows 1 to 5 of the pegboard task.

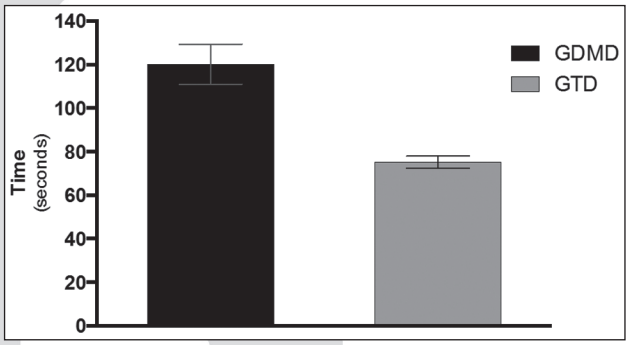

Figure 3. Comparison Chart of the total time for both groups
DMD: Group with Duchenne muscular dystrophy; TD: Group with typical development.

Discussion

The objective of this study was to investigate the motor performance in patients with Duchenne muscular dystrophy and those with typical development and compare it by means of a grooved pegboard test.

Between the different factors studied in motor control area, currently a greater attention is given to speed and accuracy of movement. This interest is justified by the fact that most craftsmanship

Table 1. Statistics regarding the analysis between the rows in the pegboard

Variables	Main effect: Rows			Main effect: Groups			Interaction: Rows x Groups		
	(df) F-ratio	*p*-value	η^2	(df) F-ratio	*p*-value	η^2	(df) F-ratio	*p*-value	η^2
R1 *versus* R2	(1, 74) 5.69	.020	.07	(1, 74) 25.9	<.001	.26	-	-	-
R2 *versus* R3	-	-	-	(1, 74) 17.6	<.001	.19	-	-	-
R3 *versus* R4	-	-	-	(1, 74) 24.12	<.001	.25	-	-	-
R4 *versus* R5	(1, 74) 5.39	.023	.07	(1, 74) 25.9	<.001	.26	(1, 74) 7.03	.010	.09

df: degrees of freeedom; R1 – R5: refers to row 1 to 5 of the pegboard task.

requires accurate and fast performance. However, the movement time will vary with each individual, depending on the level of motor control and the acquisition of each one, which shows the ability to adapt and the individuality of the human nervous system in relation to different tasks.[18]

Before the proposed task, it is important to know that the ability to grab an object precisely between the thumb and index finger allows humans to perform a wide range of manipulations and gentle movements. The biomechanical advantage of the thumb opposition, combined with the cortical control and sensory feedback, allows an amazing variety of hand movements.[19] Control of grip strength during manipulation of objects provides insights into the importance of afferent sensory information that is applicable for the control of all voluntary movements.[19]

In the literature to date we found intervention programs designed mainly to improve walking in children with DMD. With the continuous improvement in life expectancy, however, upper limb function also deserves specific attention in rehabilitation and research programs. By showing the strong relationship between muscle strength, range of motion and distal upper limb motor function, this study suggests the importance of maintaining adequate levels of muscular strength, especially with regard to the upper extremity range of motion, for long-term preservation of the function distal motor of the upper limbs. The role of intervention programs, such as resistance training, is a matter of debate in the literature because of the possible adverse effects on the integrity of the muscles involved.[20]

The results of our study suggest that the greater the number of repetitions performed, the better the performance, so practice is important for people with DMD. Our study corroborates a 2014 work [21], which states that the better the motor control, the larger the increase in manual dexterity and the faster the motor speed. The test subjects demonstrated an increased performance during the execution of the task presented, the authors state that this may be owed to a wide range of psychomotor functions, including hand-eye coordination, manual dexterity and motor speed. As well as performing in our study, an improvement on performance from the first row to the last row.

The measurement of time and compensatory movements for functional tasks is not often used to assess children with Duchenne muscular dystrophy (DMD). As muscle weakness progresses, new synergies (compensatory movements) are selected to perform the tasks, requiring time.[22]

According to a study undertaken in 2010 [23], muscle weakness in patients with DMD is symmetrical and starts from proximal to distal, with more pronounced weakness of the pelvic girdle than of the shoulder girdle, preceding the weakness of the muscles of the trunk and limbs, making the task of running for the GDMD more difficult, as evidenced by the task execution results. It was found that the GDT group performed better compared with the average for GDMD F1 - F5. Even so, the GDMD group presented a significant result between tiers 1 and 5, reducing task execution time compared with the GDT group, which showed lower evolution, even if they completed the task in less time than the GDMD group.

Data indicates that for the GDMD group both the preferred and not preferred hand showed reduction of the time during task; however, the preferred hand showed a greater decrease in evolution. The GDT group achieved discrete evolution.

Despite the poorer performance of the DMD group, the more they practice along the rows, the more is the improvement of performance in relation to speed on this population.

The motor loss of this population is an inevitable condition, requiring the professionals who assist in the care of these patients to maintain motor conditions as long as possible.

Conclusion

The present study showed improved motor performance in both groups, as shown by the decrease in execution time over the rows. The GDMD group performed better than the GTD group, despite taking a longer time.

Authors' contributions

All authors participated in the acquisition of data and revision of the manuscript. All authors determined the design, interpreted the data and drafted the manuscript. All authors read and gave final approval for the version submitted for publication.

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A Comparison of Residents of Emergency and Orthopedic Medicine in Diagnosing Salter Harris Fracture Type I in Distal Fibula

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Abstract

Objectives: The objective of this study was to determine the difference between Ems and Ops residents about diagnosis of Distal Fibular Salter Harris I Fractures.

Methods: In this study we chose 10 graphs from distal fibula that included 5 normal graphs and 5 graphs with SH1 fracture. Also we choose 60 residents including 30 Ems and 30 Ops residents. Then the graphs were shown to them and they were asked to write their diagnosis of every graph.

Results: According to our scoring system every true answer had 1 point and every false had 0 point. So the maximum score would be 10 and the least score would be 0. We found that 36% of Ems residents and 42% of Ops residents could have a true diagnosis. There is no significant difference between these two groups.

Conclusions: We believe that both of two groups (Ems & Ops) have problems in diagnosis of Salter Harris 1 fracture. Also there is no difference between Ems residents with or without previous orthopedic rotation, that means these training rotations were not useful. So, we could suggest for more practical orthopedic rotations for this group of residents.

Key words: Residents, Emergency, Orthopedic

Introduction

The most common type of growth plate injuries includes those which are caused acutely as the result of strikes to the body. These injuries are called growth plate fractures. Growth plate injuries are most commonly caused in arm, thigh and leg bones. Salter Harris classification is the common classification of growth plate fractures. Salter Harris fracture is a kind of fracture in which growth plate or epiphysis plate is involved. It is a common injury among children in the manner that it includes 15% of long bones fractures in children [1]. Salter Harris fracture type I is more common among children. This injury passes directly through growth plate and does not involve the bones around the plate. The graphs of these patients are usually normal. These injuries recover fast and they are rarely coupled with any side effect [2]. Diagnosis of growth plate fractures in children is of a great importance because mismanagement in such injuries can result in complications in the growth process including disturbed reformation of right axis of bones. Radiologic procedure is used to accurately diagnose these fractures [3-7]. Diagnosis of fractures in distal fibula is based on the history, physical examination and observation of ankle graph. Salter Harris fracture system is used to diagnose the type of fracture. Considering the nature of cartilage radiolucent, Salter Harris fracture type I has usually a normal graph and several residents face problems in the initial management of this lesion and its accurate diagnosis. In this study, capabilities of orthopedic and emergency medicine residents in accurate diagnosis of this lesion are evaluated. Despite the relatively high prevalence of this lesion in pediatric trauma emergency and lack of any consensus in its management among the corresponding specialty services, few studies have already been made in this regard. Therefore, it is required to conduct a comprehensive study by considering effective variables. (8-15)On the other hand, considering the mutual effect of the approach adopted by orthopedic and emergency medicine services on final management of patients, it is required to make a comparison ‘between the diagnostic views of these two

groups and to evaluate their agreement in this field. Another point about demographic features of residents is their former job records. As for the emergency medicine residents, this includes completion of orthopedic rotation which seems to influence on their capabilities in facing such cases (15-20).

Methodology

Demographic features of these individuals include age, sex, level of current education, former job records (as general physician) for both groups and the record of passing rotation orthopedics for residents of emergency medicine. 10 simple graphs related to distal fibula were selected among which 5 graphs were normal and 5 graphs were related to Salter Harris fracture type I. Arrangement of graphs was random and did not follow any special order. No explanation concerning the history or positive and negative points was provided to the residents in the clinical examination and diagnosis was announced only based on the observation of corresponding graph. Moreover, no time restriction was considered for responding. It should be noted that the questioner of this study was unaware of actual diagnosis of any graph. Before beginning the test, some explanations were first provided to the residents concerning the content of the study and its objective and they were invited to cooperation. Test place for residents of emergency medicine was located at the emergency department and for orthopedic residents was located at the orthopedic clinics located at educational hospitals of Shahid Beheshti University. Each resident was asked to exactly observe each graph and to say if the observed image was normal and if it had any fracture. In case of diagnosing any fracture, the respective resident was required to specify the type of fracture as well; SH1, SH2, SH3, SH4, SH5. It should be noted that in each case, the intended resident was separately tested and it was not possible for the residents to consult. Moreover, none of the residents was aware of the diagnoses of his/her other colleagues. During the test, most of the residents stated non-access to history and clinical examination as major disadvantages of the study. After descriptive review of answers given by the residents of emergency medicine and orthopedics to the graphs suspected to Salter Harris fracture, a score was defined for each resident based on the number of correct/incorrect answers. For this purpose, 1 positive score was considered for each correct answer but no score was given to incorrect answers. It should be noted that no negative score was given to incorrect answers. Therefore, the scoring system designed in the present study is a 10-score system in which the minimum and maximum zeros are zero and 10, respectively. Moreover, in addition to comparison of two groups, comparisons were also made inside each group concerning demographic variables. The most important demographic variable reviewed and analyzed in this study was the completion of orthopedic rotation course by emergency medicine residents. In this way, the answers given by emergency medicine residents were analyzed with respect to completion/non-completion of orthopedic rotation course. The collected data was recorded based on the given answers and was then analyzed by Chi square formula and spss software.

Results

In the present study, 30 students of emergency medicine specialty course and 30 students of orthopedic specialty course were included in the study. Mean and standard deviation ages for emergency medicine and orthopedic residents were 32/8 ± 2/6 years and 29/9 ± 2/8 years with an age range of 26 to 42. After age classification of residents into two groups, namely under the age of 32 and older than or equal to 32, it was observed that most emergency medicine residents (63.3%) were older than 32 years old while the highest frequency of orthopedic residents (76.7%) were in the age group under 32. Chi square test showed that there is a significant difference between mean ages of the two groups (21= 0.002). 70% (p persons) of emergency medicine residents were male and 30% (9 persons) were female. However, 96.7% (29) orthopedic residents were male and the two groups had a significant difference with respect to sex (p=0.006). 53.3% of emergency medicine students (16 residents) were in the first year, 30% (9 residents) were in the second year and 16.27% (2 residents) were in the third year while the frequency of the first, second and third years of orthopedic specialty included 40% (12 residents), 46.7% (14 residents) and 13.3% (4 residents), respectively.

However, Chi square test did not show any significant difference between the two groups (p=0.41). Mean and standard deviation of work records of emergency medicine and orthopedic residents were 3/3±1/9 and 1/9±1/4 years, respectively which showed a significant difference between the two groups (p<0/0001) based on Mann-Whitney test. It should be noted that among the emergency medicine students, 12 residents (40%) had passed rotation course. As it was said, in this paper, a 10-scoe system was considered for the answers given by the residents. Based on this scoring system, mean and standard deviation of the score obtained by emergency medicine and orthopedic residents were 3/6±1/7 and 4/2±1/7 scores, respectively and Mann-Whitney test did not show any significant difference between the means of the two groups (p=0/16). As it is seen, on the average only 36% of the diagnoses made by emergency medicine residents are correct. Moreover, this figure is 42% for orthopedic residents. This is the diagnostic mean for the residents of emergency medicine and orthopedics. It should be noted that even completion of orthopedic rotation course had no significant effect on the level of accurate diagnosis of emergency medicine residents, in the manner that mean and standard deviation of diagnostic score for the trained and untrained groups were 3/8±1/7 and 3/6±1/7, respectively which have no significant difference (p=0.67) .

Discussion and Conclusion

This study was conducted by comparing two groups consisting of orthopedic and emergency medicine residents concerning their capability to diagnose Salter Harris I fractures in distal fibula. In addition to comparison of this capability between the two groups, demographic factors such as age, sex, work records and current educational level inside each group as well as effect of those factors on the capability of residents to accurately diagnose the graphs have been evaluated as well. On this basis, it becomes clear that considering age index, mean and standard deviation of age for emergency medicine residents was 32/8±2/6 and for orthopedic residents it was 29/9±2/8 with an age range of 26 to 42. After age classification of specialty students into two groups, namely under the age of 32 and older than or equal to the age of 32, it was observed that 63.3% of emergency medicine residents were older than 32 while the highest frequency (76/7%) was for orthopedic residents that was in the age group of under 32 years of age. Chi square test showed that there was a significant difference between the mean age of two groups (p=0.002). As to the sex index, 70% (21) residents of emergency medicine were male and 30% (9) residents were female. But 96.7% (29) orthopedic residents were male and the two groups had no significant difference with respect to sex (p=0.006). As to the current educational level, 53.3% of emergency medicine students (16 residents) were in the first year, 30% (9 residents) were in the second year and 16.7% (2 residents) were in the third years. This was while the frequency of the first, second and third students of orthopedic specialty program were 40% (12 residents), 46.7 (14 residents) and 13.3% (4 residents). However, Chi square test did not show any significant difference between the two groups (p=0.41). It should be noted that emergency medicine residents pass during their training a course called Orthopedic Rotation. At first, it was imagined that passing this course would have a clear effect on the capability of these residents to accurately diagnose the graphs; however, the analysis made on this variable provided conflicting results. On this basis, mean and standard deviation of diagnostic scores for the trained and untrained groups included 3/8±1/7 and 3/6±1/7, respectively and they have no significant difference (p=0.67) . In this study, after comparing the orthopedic and emergency medicine groups we found that 36% of emergency medicine residents and 42% of orthopedic residents were able to accurately diagnose the graphs. As it is seen, there is no significant difference between the two groups and it can be said that both groups face difficulties in diagnosing this lesion. The reasons for such low diagnosis capability can be attributed to the followings.

1. Ambiguous nature of Salter Harris I fractures in the graphs
2. Importance of clinical examination of patients
3. Incapability of residents in accurate examination of graphs

1) Ambiguous nature of Salter Harris I fracture in the graphs: Salter Harris I fracture appears across growth plain. Since cartilage in the graphs has a radiolucent nature, radiologic image of this lesion is a challenging issue. In other words, diagnosis of normal graph, fractures type I and IV in the growth plain factures always face challenges [8]. This is because the radiologic image obtained in these three cases is very similar and distinction of them requires viewpoint of a physician as well as history and examination of patient.

2) Importance of clinical examination of patient: As it was said, the graph obtained from Salter Harris fracture type I is considered in the differential diagnosis with normal graph and fracture type IV. Therefore, as most of the residents declared, clinical examination is the main diagnostic index. However, in the current study it is not possible to examine the patient and provide an exact diagnosis. This can somehow be attributed to this restriction. Based on the examination of injured area and existence/non-existence of tenderness, the physician will make a more accurate decision and more serious lesions (fracture) will not be missed.

3) Inability of residents to accurately examine the graphs: Another major issue which is also considered in this study is the capability of residents to diagnose the graphs. As it was said, none of the two groups could show any acceptable capability in this regard. In this way, it can be said that both groups had a poor performance in diagnosing Salter Harris fracture type I. As to the residents of emergency medicine, considering the possibility of passing orthopedic rotation course during residence period, it can be said that by holding applied and integrated courses, they can better diagnose this graph. Another issue which can here be inferred is the lack of any significant difference between the training and non-trained groups among the emergency medicine residents. This finding can set forth the disadvantage of previous rotation courses and the necessity of a review in the educational strategy of these courses. As compared to other studies performed by Arezoo Zomorrodi et al in which emergency medicine residents propounded Salter Harris fracture type I with a more suspicion and had a more tangible agreement on this issue, in the present study there is no preference for emergency medicine residents and again there is no basic difference between the two groups.

Conclusion

In this study, we found that orthopedic and emergency medicine residents face difficulties in diagnosing Salter Harris fracture type I in distal fibula and have no difference with respect to comparison (36% emergency medicine vs. 42% orthopedics). Another point which is inferred is the poor performance of medicine residents in diagnosing this type of lesion even despite passing orthopedic rotation course. Here, the necessity of holding additional and integrated courses for this group is considered.

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Prevalence of symptoms of allergic diseases in children in southern Ceara

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Abstract

Introduction: Diseases related to the respiratory system are most common in childhood and is increasing its prevalence rates in recent years, the increase of allergic diseases in children has been linked to several factors, with the triad asthma, rhinitis and eczema responsible for a high index of respiratory compromise in the group.

Objective: Verifying the prevalence of allergic diseases in children aged 6 and 7 years old.

Method: This is a cross-sectional study with a quantitative and descriptive approach. The research was conducted in a city of southern Ceara, in the period of March/April 2014, being the surveyed population made up of 116 children, where parents or guardians answered the questionnaire International Study of Asthma and Allergies in Childhood (ISAAC) about the most prevalent symptoms in allergic diseases. Data were tabulated and analyzed using SPSS (version 20).

Results: There were not observed statistically significant differences between the sexes regarding the presence of wheezing ever in life, in the last 12 months and regarding the number of crises. The same way there were no statistical significant differences observed for symptoms of rhinitis and the gender. The symptoms of eczema were not reported.

Conclusion: In the town of Brejo Santo-CE there were results of higher prevalence of allergic rhinitis and asthma in children aged seven and girls of six years old.

Key words: Prevalence; Allergic Diseases; Children.

Introduction

Allergic diseases have higher prevalence in children who have specific genetic characteristics, these being increased stimuli when there is exposure to allergens. It is understood that the immediate contact with the allergen would develop a greater risk for the disease throughout life in children who possessed allergy in childhood. The triad formed by asthma, rhinitis and eczema is responsible for the development of allergic diseases in childhood causing discomfort and decrease in the child's quality of life[1].

Asthma is a disease developed over time and can be associated with predisposing factors, adding to the environmental exposure, being the inflammation the main cause of the decrease in flow passage in the respiratory system[2]. The applicant inflammation and prolonged periods develop clinical signs that are identified simply and easily as dyspnea, cough and wheezing[3].

Allergic rhinitis (AR) can be interpreted as a disease triggered by antibodies in patients with specific genes causing inflammation and damaging the respiratory tract and nasal mucosa[4]. By having common characteristics such as runny nose, sensitized eye, allergic rhinitis supposedly manifests when the individual is exposed to allergens that react to such antibodies[5].

Report Cassol *et al.*[6] that atopic eczema (AE) during infancy manifested latently in children with prone genetic; and, when associated with other diseases, it is observed over exacerbated symptoms. This disorder will show a decrease in their symptoms over time[7]. Atopic eczema, to manifest itself in childhood, is presented between acute episodes and remissions; despite being a disease with high prevalence, studies on it are still scarce[8].

This research is justified by the major negative impacts on the life of patients with allergic diseases, as they determine a change in the patient's normal routine, and the implication of their symptoms in childhood is more troubled, because it generates difficulties in socialization and development of children.

Studies indicate that the incidence rates of allergic diseases in this age group are high and present special problems during the course of life[8]. Thus, it aimed to determining the prevalence of allergic diseases in school children of six and seven years old.

Method

It is a cross-sectional study with a quantitative approach. The survey was conducted in four schools of the public and the private network in the city of Brejo Santo–CE, during the months of March and April 2014.

The research population consisted of 200 children, students of the four aforementioned schools, but only 116 parents of students accepted to answer the questionnaire. The inclusion criteria for the study were: children aged between six and seven years old, being excluded children with neurological or cognitive impairment.

Visits were made to selected schools on different days, being delivered to students the Term of Informed Consent (IC) that should be signed by the parent or guardian, and a letter to parents explaining about the survey. It was later scheduled with the direction of the schools a meeting with parents to fill out the questionnaires concerning matters related to the symptoms of asthma, rhinitis and atopic eczema.

The instrument used was the standardized questionnaire International Study of Asthma and Allergies in Childhood (ISAAC) containing the epidemiology and symptoms of diseases present in the study. It consists of three modules with specific questions for each disease. The module I was relative to asthma, having eight questions; the second had six specific questions about rhinitis; and in the third, questions were related to eczema and have seven questions to be applied [9].

The study was approved by the Research Ethics Committee (CEP) of the College Santa Maria under the opinion nº 547.421. All participants signed the Informed Consent and the research was conducted by Resolution 466/12 governing research with human beings.

Data were tabulated and analyzed using SPSS (version 20). This was followed by descriptive analysis of frequency and percentage and chi-square inferential analysis of Pearson (χ^2) and Poisson regression. The latter was used to estimate the reason of prevalence, by means of the exponential of its effect. This was used in the robust estimator covariance matrix for errors most reliable standards. It was accepted as significant a minor error or equal to 5%, ie, $p \leq 0,05$.

Results

The results are given in three tables, the first and the second with descriptive statistics and associations with gender; already the third shows the prevalence ratios stratified by gender.

Among the participants there was observed fewer seven years old children (43,3%) and girls of six years old (30,4%). It has not been possible to establish a connection and / or difference between those who have had wheezing and the gender of the respondents, since it does not show any statistically significant difference. The same can be said for those who had wheezing in the last 12 months and in relation to the number of crises.

To sleep disturbance due to the crisis, even without statistically significant differences, it was possible to observe a slight difference in the sample, with 30% of boys with a night's sleep being disturbed at least once a week with wheezing, whereas 19,6% of girls. In general, the other variables showed no percentage difference between genders.

In table 2, one can observe the description of symptoms of rhinitis. In Table 1 could not assure statistically significant difference between gender and symptoms.

Table 3 shows the prevalence ratios (PR) of asthma and rhinitis stratified by sex. In children at six, asthma presented a slightly larger RP for boys (PR = 1,04; p = 0,77) and for girls (PR = 1,20; p = 0,19) but was not statistically significant. For rhinitis, the prevalence was higher for seven years old children, with boys with RP 1,15 (p = 0,24) and girls with PR of 1,28 (p = 0,07) but not with significant result.

Table 1. Description of the participants regarding the symptoms of asthma. Brejo Santo, CE, Brazil, 2014.

Symptoms	Male		Female		P
	N	%	n	%	
Have had wheezing?					
Yes	31	51,7	27	48,2	0,71
No	29	48,3	29	51,8	
Had wheezing in the last 12 months?					
Yes	15	25,0	14	25,0	1,00
No	45	75,0	42	75,0	
How many bouts of wheezing in the past 12 months?					
None	42	70,0	41	73,2	0,63
1 - 3	15	25,0	14	25,0	
4 - 12	3	5,0	1	1,8	
Frequency of disturbed sleep for wheezing in the past 12 months					
Never woke up with wheezing	42	70,0	44	78,6	0,27
Less than one night per week	18	30,0	11	19,6	
One or more nights per week	0	0	1	1,8	
In the last 12 months, his wheezing was so strong to the point of preventing his son could say more than 2 words to every breath					
Yes	3	5,0	4	7,1	0,63
No	57	95,0	52	92,9	
His son had asthma					
Yes	5	8,3	7	12,5	0,46
No	55	91,7	49	87,5	
In the last 12 months had wheezing after exercising					
Yes	2	3,3	4	7,1	0,43
No	58	96,7	52	92,9	
In the last 12 months, his son had a dry cough at night, without being cold or with respiratory infection					
Yes	24	40,0	20	35,7	0,63
No	36	60,0	36	64,3	

Table 2. Description of the participants regarding the symptoms of rhinitis. Brejo Santo, CE, Brazil, 2014.

Symptoms	Male		Female		P
	N	%	n	%	
Have had problems with sneezing or runny nose, when it wasn't cold or flu.					
Yes	21	35,0	20	35,7	0,94
No	39	65,0	36	64,3	
In the last 12 months, your son had a problem with sneezing or runny nose, when it wasn't cold or flu					
Yes	19	31,7	16	28,6	0,71
No	41	68,3	40	71,4	
In the last 12 months had this nasal problem been accompanied by watery eyes, or runny nose?					
Yes	19	31,7	11	19,6	0,14
No	41	68,3	45	80,4	
In the last 12 months, how many times their activities were hampered by this nasal problem					
Nothing	36	60,0	35	62,5	0,73
A little	21	35,0	18	32,1	
Moderated	2	3,3	3	5,4	
Very much	1	1,7	0	0	
Any time your son had hay fever?					
Yes	10	16,7	12	21,4	0,51
No	50	83,3	44	78,6	

Table 3. Reasons (RP) prevalence of asthma and rhinitis stratified by gender

		Male		Female	
		RP (IC 95%)	***P***	**RP (IC 95%)**	***p***
Asthma	7 years old*				
	6 years old	1,04 (0,81 – 1,34)	0,77	1,20 (0,91 – 1,59)	0,19
Rhinitis	7 years old	1,15 (0,91 – 1,46)	0,24	1,28 (0,97 – 1,69)	0,07
	6 years old*				

Discussion

The 43,3% rate as the correlation between the genders of the children surveyed have higher prevalence in boys aged seven are similar to the data found in the literature to the highest rate of asthma in males[3].

Allergic diseases have increased its prevalence starkly in recent times. Possible causes for this increase in the number of allergy suffering people may be related to increased exposure to allergens[10]. Worldwide asthma has shown different rates in its incidence and prevalence. This variation is analyzed according to the symptoms and answers related to applied questions. The use of data can be very important as will minimize the damage and in more severe cases and infer to minimize the crisis and a likely death of asthmatic[11]. According to the World Health Organization (WHO) there is an average of asthma of approximately 235 million people worldwide, making it the most common chronic asthma in children.[12]

In a study with children aged six to seven years old there were assessed 1.537 male children (48,3%) and 1.646 female (51,7%). It was found the highest proportion in boys, thus influencing a disadvantage for them in which discussed the symptoms of allergies; these results were obtained using the ISAAC questionnaire. It was evident also that 74,6% of children with asthma had allergic rhinitis and that from the age of six would be the age group where the disease manifested itself more forcefully[13].

With 25,2%, research shows that asthma is more prevalent in children of six and seven years old, compared to teens who have reached only 15,9% of cases[3]. For the presence of symptoms wheezing ever in life and in the last 12 months are different from literature data with prevalence in males resulting in 25,9% in the same, against 24,6% in girls. Rose *et al.*[14] claim that after the questionnaires noted that 54,1% of the participants of his research were boys, which had 51,2% of significant symptoms present, including the presence of wheezing in the last year. The prevalence of asthma in children would be related to common anatomical specifics different between the genders, being the kind of tone airway a contributing factor to the onset of the disease in males[15].

In this research it was observed that 30% of boys had disturbed sleep at least once a week while 19,6% of girls had the problem, going in agreement with most studies.

Felizola *et al.*[13] show that 12,1% of children under six and seven years old with diagnosed asthma had sleep impairments due to influential symptoms such as wheezing. Significantly higher prevalence was found in boys with regard to wheezing ever in life and in the last twelve months, the highest number of crises, focusing prejudice to sleep[1].

Regarding rhinitis, the variable that most approached a difference was the tearing or runny nose the past 12 months, and 31,7% of boys reported tearing or runny nose, compared with 19,6% of girls. Regarding eczema, no child showed the problem.

For their symptoms generate a great impact, rhinitis has defied numerous studies to minimize changes in child's life. Over 80% of patients have more severe cases, 40% of those with mild considered tables also reported thus loss in their life due to illness. Thus, it is very common and characterized in this study that 38% of rhinitis patients also had asthma and that 78% of asthma patients suffer from rhinitis associated[13]. The pathophysiological mechanism of asthma and rhinitis has been pointed out as one, as the treatment of rhinitis has direct implication in reducing the incidence and severity of asthma.[16]

The disturbances caused by RA still have an important effect that can cause other diseases related to the nervous system. And so patients with this disease tend not refer symptoms or exaggerate them, with a poor perception of allergy control[15,17]. She does not have an appropriate definition that allows easy identification. A very detailed clinical research is needed thereby allowing to diagnose the disease. The child's exposure rhinitis with the agents that produce a reaction and cause the development of symptoms is an important data for identification of the disease[18].

Allergic rhinitis affects a lot and in a negative way in the life of the child carrier and still at some point it emerges some effort so that its symptoms are minimized, with nasal congestion presenting biggest complaint, then the eyeball sensitized present in 37,8% children[19].

Ibiapina *et al.*[5] reported that the prevalence of rhinitis has varied to achieve 0,8% to 14,9% throughout the world, hence its symptoms can also vary; however most influential are still nasal congestion, sneezing, nasal itching and itchy eyes. The symptoms of sneezing and runny nose are high with 42,7% of the group studied presenting such problems. Already 12,3% had eye problems that limited somehow their life[20].

This research has not been any reported cases of atopic eczema among children evaluated. However, according to Nunes[7], studies suggest that eczema has increased its prevalence rates, not knowing for sure what the reason, the more it is assumed that environmental factors combined will lower socio-economic conditions would be likely indicators. The prevalence of AE ranged from 1,1% in Iran and 18,4% in Sweden featuring two extremes. Nunes[21] about eczema shows up very prevalent in infancy and childhood with apparent injury and characteristic areas, mainly present in the wrists, hands and knees. By having inflammatory causes ever-present immunologic changes affect the respiratory system making it touched[22].

By owning remarkable genetic characteristics sensitive gene to allergens such as food, dust and others, cause these abnormalities in the child's skin. It would be a protein deficiency the most acceptable cause for the allergy to develop[23]. In a study done by Naspitz *et al.*[24] it was found that 457 children, a total of 38,7% of girls and 61,3% of boys. Respiratory allergies develop after contact with inhaled allergens sporadically[25], and children of full age would be more sensitive due to longer exposure time causing serious problems to the respiratory system. Importantly, the symptoms can be overlooked or confused with other skin diseases common in childhood. According to Lustosa *et al.*[26] genetic factors and environmental exposure to allergens and non-specific factors contribute to the onset of atopic diseases.

This research evidenced that allergic diseases are prevalent and can suffer differences in prevalence according to the research area, as well as seasonal factors on such symptoms. In the town of Brejo Santo-CE there were results of higher prevalence of allergic rhinitis and asthma in children aged seven and girls of six years old, which suggests the attention of health professionals in developing programs that minimize the damage caused children's lives having these disorders.

Epidemiological data obtained in the study may help to develop a health plan through educational programs targeted to this audience, aiming not only treatment over prevention of children who have not yet developed.

Both rhinitis and asthma require adequate therapeutic treatment, because probably accompany the carrier all his life and when combined still promote more exacerbated damage. Albeit at lower levels when compared to the rates obtained in studies conducted in several countries a more watchful eye is needed for children to develop and become adults with minimum damage as possible to their life, when related to allergic diseases.

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Time trend analysis and ecological study of gastric cancer in Iran

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Abstract

Background: Trend and Pattern of stomach cancer vary in different geographical regions. Some of studies indicated that there is a relationship between stomach cancer and Socio economic status. The aim of this article is the study of the trend of stomach cancer in over time, and also the effect of economical factors on cancer incidence in Iran.

Materials and Methods: In this study, various sources of data were obtained through National Cancer Registry (2003-2010) and Statistical Center in Iran. Trend of cancer rate was estimated adjusted for sex, age groups and patient's residential locations.

A proxy value was calculated for all individuals using principal components analysis (PCA).The risk of cancer based on the population and score was assessed. This model controlled for different age groups and provinces in separate gender. All analysis done with Software stata 12.

Result: From the notional cancer registry of Iran, 49276 cases stomach cancer were obtained between 2003 and 2010.Age-standardized incidence rates were generally higher in men than in women and its trend vary in different provinces in Iran.

The negative binomial regression model showed risk of cancer incidence for men and women were 60% and 52%. All of age groups under 45 years had a lower risk. The highest IRR attributed to year 2008 for each sex. Our results showed, there is an Inverse relationship between stomach cancer and economic status in Iran.

Conclusion: Incidence of gastric cancer had an increasing trend in both sexes and economic status has a negative relation with incidence of gastric cancer. We believed further research in future is needed into the relation between ES and gastric cancer, especially based on individual data to avoiding ecological fallacy

Key words: gastric cancer, incidence, economic position, Time trend, Iran

Introduction

Cancer is one of the important Causes of death in all over the world. After Cardiovascular disease cancer is second reasons of death in developed countries and third Causes of death in developing countries. Based on GLOBOCAN estimates, Stomach cancer is the third leading cause of cancer death in both sexes worldwide and the fifth most common malignancy in the world, after cancers of the lung, breast, colorectal and prostate.[1]

An estimated 951,600 new stomach cancer cases (6.8% of the total) and 723,100 deaths (8.8% of the total) occurred in 2012.[1, 2]

More than 70% of cases (677,000 cases) occur in developing countries (456,000 in men, 221,000 in women), and half the world total occurs in Eastern Asia (mainly in China). [1]

Age-standardized incidence rates are generally about twice as high in men as in women and vary widely across countries. [3] Ranging from 3.3 in Western Africa to 35.4 in Eastern Asia for men, and from 2.6 in Western Africa to 13.8 in Eastern Asia for women. The highest estimated mortality rates are in Eastern Asia (24 per 100,000 in men, 9.8 per 100,000 in women), the lowest in Northern America (2.8 and 1.5, respectively. [1]

A steady decline in stomach cancer incidence and mortality rate has been observed in majority of more developed countries in Northern America and Europe since the middle of 20th century. [2, 4]

According to estimations of IARC in 2012 in IRAN about 53000 Persons lost the life because of cancer, this report has been estimated the incidence of cancer about 85000 Persons in that year. In IRAN in year 2012 , the incidence of stomach

cancer was 11.4% and counted as second Common cancer after breast cancer (11.5%), also stomach cancer with mortality 15.5% known as the fetal cancer in this country. [1]

Mortality stomach cancer is also the first cause of death due to cancer in both sexes in Iran.[5]

Gastrointestinal cancers are one of the most cancers; doctors believed that environmental and biological factors, and also food culture are Interference in cancer incidence. [6]

This differences in the world is because of the disagreement in the food templates, food storage, the availability of fresh produce, as well as prevalence of Helicobacter pyloric infection.[7, 8]

Access to health care and early diagnosis and treatment are economic and social factors that can affect on cancer, so cancer is a real social disease.[9]

The study indicated that the stomach and esophagus cancer are more in communities with low economic and social status.[9], it seems that it is because of the relationship between economic and social index, environmental exposure, contact career and also personal habits.[10, 11]

Some of studies indicated that there is an Inverse relationship between stomach cancer and Socio economic status.[12, 13]

The relationship between socioeconomic factors with cancer incidence or mortality has been largely investigated, with findings of strong correlations, particularly for lung and gastrointestinal cancer in men and cervical cancer in women .[10]

Trend and Pattern of cancer cases vary in different geographical regions. [13, 14]

The incidence of cancer has been slowly declining in the developed countries while increasing in the Less developed and developing countries has been increased. [15]

Patterns of gastric cancer in our country is Similar to the high-risk regions worldwide.[16] Gastric cancer is one of the most common malignancies in Iran and its incidence is particularly high in the northwest of the country. [17]

Considering the importance of this issue, the aim of this article is the study of the trend of stomach cancer in over time, and also the effect of economical factors on cancer incidence in Iran.

We hope these kinds of studies could be an appropriate for targeted interventions and be used for health planners and experts in public health.

Methods

Data sources

IRAN divided into 28 Province in 2003. In this study was used population data defined by each sex and 5-year age groups in years 2003, 2006 and 2011 from Iran Statistical Center and population was estimated by growth rate for other years.

The economic data were obtained from Iran Statistical Center based on census in 2006 and cancer data on pathology and population based cancer registry that have been Collected by Ministry of Health and Medical Education (MOH&ME) during period of 2003-2010. This Cancer registry data cover almost 80-90% of cancer cases**.**

Statistical analysis

Age standardized rate (ASR) per100, 000 men and women with 95% confidence intervals were calculated using the direct method of standardization using WHO standard population of 2000 [18]. ASR and trend of cancer rate during 2003–2010 were calculated for each sexes, province and Patient's residential locations.

Patient's residential locations were categorized into nine geographical regions that are recommended by MOH & ME including:

1. West South (Khuzestan): Ahvaz, Lorestan
2. North (Mazandaran): Mazandaran, Gilan, Golestan, Semnan, Babol
3. Central of North (Tehran): Tehran, Markazi, Qazvin, Qom,
4. Central part (Esfahan): Esfahan, Yazd, Chaharmahal-o-Bakhtiyari, Kashan
5. Middle West (Kermanshah): Kermanshah, Kordestan, Elam, Hahadan
6. South West (Lower part) (Fars): Shiraz, Bushehr, Bandar Abbas, Kohgiluyeh, Jahrom, Fasa
7. South East (Kerman): Kerman, Zahedan, Zabol, Rafsanjan
8. North East (Khorasan): Razavi Khorasan, Southern Khorasan, Northern Khorasan, Shahrood, Gonbad
9. North West (Azerbaijan): Tabriz, Azerbaijan, Ardabil, Zanjan

We also grouped provinces into 5 regions according to their median economic status and their

population. The risk of cancer in these regions was assessed. To produce economic groups, a proxy value was calculated for all individuals using principal components analysis (PCA) that explained 37% of the total variance. The variables were entered in PCA model included as follow:

house ownership ,room per person, area per capita, having independent bath ,kitchen, Light vehicles, landline, cell phone, computer for the household, fuel, piped water, heating system, Central heat and cold, building structure and manufactured year.

We enter provinces in 5 different category based on their population and proxy value. Each of Categories Included the below Province:

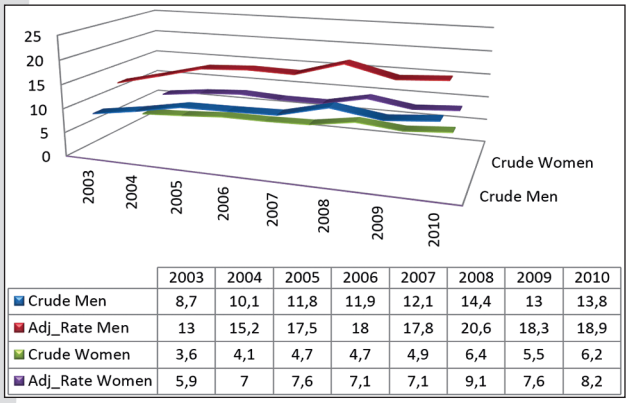
- Provinces of Region 1: Hormozgan, Kerman, Khorasan, Sistan va Baluchestan, Gilan
- Provinces of Region 2: Kermanshah, Western Azerbaijan, Kurdistan, lorestan, Ilam, Ardebil, Kohgiluyeh Va Boyer Ahmad, Bushehr, Zanjan,
- Provinces of Region 3: golestan, Hamedan, Khuzestan, fars, markazi, East Azerbaijan
- Provinces of Region 4: Mazandaran, Esfahan, Chaharmahal Va Bakhtiari, Semnan, Yazd, Qazvin
- Provinces of Region 5: Tehran

This classification used in trend model as a Justification variable that indicate economic situation. The negative binomial regression used to examine significant trend across 8 years and reported incidence rate ratio (IRR). This model controlled for different age groups and provinces. Because of the major difference in 2 genders, the analyses have done separately in both genders. In our study, 3 models were used in first model estimated the effect of calendar year controlled for age groups and age group 45 year was as base group. In second model, different economic regions interred in the model, indeed the trend controlled based on the economic situation in addition of age group. In the third model, the provinces entered into model and the incidence in different provinces compared to Sistan Va Baluchestan incidence as a base province. A p-value less than 0.05 was considered as significant. All analysis done with soft were stata;12

Result

Basis on the national cancer registry report, the study showed that there were 49276 stomach cancer cases in IRAN between 2003 - 2010, that 71.18 %(35076) and 28.82 %(14200) are men and women respectively. Survey in stomach cancer trend between years 2003 -2010 indicated that the most age-standardized incidence rate (ASR) attributed to year 2008 (15 per 100,000 in both sexes).

ASR in women increased from 5.9 in year 2003 to 9.1 per 100,000 women in year 2008. In year 2009 this rats decrease and then it increased in 2010. In men also the trend is going up in mentioned years. The ASR rate in 2008 reached maximum amount. The least of ASR in men is 13 and the maximum is 20.6 per 100,000 men. (Diagram1)



	2003	2004	2005	2006	2007	2008	2009	2010
Crude Men	8,7	10,1	11,8	11,9	12,1	14,4	13	13,8
Adj_Rate Men	13	15,2	17,5	18	17,8	20,6	18,3	18,9
Crude Women	3,6	4,1	4,7	4,7	4,9	6,4	5,5	6,2
Adj_Rate Women	5,9	7	7,6	7,1	7,1	9,1	7,6	8,2

Diagram 1. Trend of crude rate and ASR per 100,000 by gender from 2003 to 2010

The probability of cancer incidence has been increased with aging in both genders. Incidence rates in men after 70 years old increased significantly. The highest age-specific incidence related to age group 80 years and older and age group 70 years in men and women respectively.

According to the results the maximum ASR in nine geographical regions was attributed to North regions in year 2008 with 19.4 per 100,000 person and then North West regions with 17.9 per 100,000 persons in year 2005. Also the least ASR was 4.2 per 100000 person belong to Central (south part) and then South West (lower part) with 4.4 in 100,000 person in year 2003. (table 1)

There was the highest incidence rate in Ardebil Province (Northwest) for both sexes. ASR in men was varied from 21.1 in year 2003 to 43.9 per 100,000 in year 2008. The most incidence in coun-

try attributed to the years 2008 and 2010. The least incidence rate was in Sistan va Baluchestan province, minimum ASR was 2.8 and 1.1 in men and women in year 2003. The highest ASR in women was 19.9 in 100,000 women in Ardebil Province.

Three models used to evaluate significancy of incidence trend across 8 years. In model No. 1 that year variable along with age groups entered in the model, the highest incidence rate in both sexes was in 2008 compared to 2003. (More risk of cancer incidence 60% and 52% for men and women). All of age groups under 45 years had a lower risk (rather than45-49 years) and in over 50 years the risk goes up, and in 80-84 goes to the maximum rate. (Table 2)

In model No. 2, that Provincial different regions also entered, the effect of calendar year has been observed more, it means that the Provincial different regions is a negative confounding variable. When we considered it in the model, the incidence ratio went up as incidence rate ratio in 2008 near 100%. Provinces of Region 2 rather than region1 have more risk about 35-36%. There was no significant difference in men between Tehran and the provinces region1, but in women the risk was 11%more than the base region. (Table 2)

In model No.3 was entered all of the variables as year, age group and provinces, the highest IRR attributed to year 2008 for each sex compared to the baseline year 2003 (2.09 and 2.13 times compared to 2003 in men and women respectively)

All of provinces (except Boshehr and Hormozgan) have a Significant differences in cancer risk rather than Sistan va Baluchestan. The cancer risk in the Ardebil province, was 6.48 and 5.63 in men and women respectively next Kordestan and Mazandaran have most cancer risk than Sistan va Baluchestan province.

Table 1. ASR stomach cancer by place of Residence in Iran during 2003-2010

Place of Residence	2003		2004		2005		2006		2007		2008		2009		2010	
	ASR	95% CI	ASR	95% CI	ASR	95% CI	ASR	95% CI	ASR	95% CI	ASR	95% CI	ASR	95% CI	ASR	95% CI
Central (Central part)	5.3	4.6-6	7.7	6.8-8.5	7.3	6.5-8.1	8.1	7.3-8.9	8.5	7.7-9.4	9.2	8.4-10.1	10.9	10-11.8	10.9	10.1-11.8
South East	4.2	3.4-5.1	5.7	4.7-6.7	6.1	5.1-7.1	6.1	5.1-7	5.4	4.5-6.3	7.5	6.5-8.5	8.9	7.7-10	7.6	6.6-8.6
Middle West	9.8	8.7-10.9	11.5	10.3-12.7	13.5	12.3-14.8	13.2	12.1-14.4	13	11.8-14.1	17	15.7-18.3	12.4	11.4-13.5	14.5	13.415.7-
North East	5.7	5-6.5	16.1	14.8-17.4	15.2	14-16.4	15.1	14-16.2	14.4	13.3-15.5	18	16.8-19.2	17.4	16.3-18.6	18.2	17.1-19.4
West South	6.5	5.5-7.4	7.3	6.3-8.4	9.4	8.2-10.5	8	7-9	10.2	9.1-11.2	16.2	14.8-17.5	12.4	11.3-13.6	13	11.9-14.2
North	11.3	10.4- 12.3	15.6	14.5-16.8	17.7	16.6-18.8	14.9	13.9-15.9	15.1	14.1-16	19.4	18.3-20.5	15	14.1-16	17.2	16.2-18.2
South West (Lower part)	4.4	3.7-5	6.4	5.6-7.2	7.2	6.4-8.1	6	5.3-6.7	8.9	8-9.8	9.6	8.7-10.5	7.8	7-8.6	10.2	9.4-11.1
Central (North part)	5.5	5-5.9	10.1	9.5-10.7	13.2	12.5-13.9	9.5	9-10.1	8.5	8-9.1	14.9	14.3-15.6	12.1	11.5-12.7	12.2	11.6-12.8
North West	8	7.3-8.8	17.3	16.1-18.4	17.9	16.8-19	14.3	13.4-15.3	17.8	16.7-18.8	17.7	16.7-18.8	17.2	16.2-18.2	16.1	15.1-17

Table 2. Model 1 and 2 for evaluating the effect of calendar rate, age-group and different region on total cancer incidence rate in Iran during 2003-2010

year	model 1(men)				model 2(men)				model 1 (women)				model 2(women)			
	IRR	P>z	[95%		IRR	P>z	95% CI		IRR	P>z	95% CI		IRR	P>z	95% CI	
2004	1.17	0.01	1.04	1.30	1.49	0.00	1.36	1.63	1.16	0.02	1.02	1.31	1.50	0.00	1.35	1.66
2005	1.31	0.00	1.18	1.46	1.61	0.00	1.46	1.76	1.29	0.00	1.14	1.45	1.64	0.00	1.48	1.81
2006	1.33	0.00	1.20	1.49	1.53	0.00	1.39	1.68	1.17	0.01	1.04	1.33	1.41	0.00	1.27	1.56
2007	1.36	0.00	1.22	1.51	1.62	0.00	1.48	1.78	1.19	0.01	1.05	1.34	1.48	0.00	1.34	1.64
2008	1.59	0.00	1.43	1.76	1.98	0.00	1.81	2.16	1.52	0.00	1.35	1.71	1.97	0.00	1.79	2.18
2009	1.34	0.00	1.21	1.50	1.64	0.00	1.50	1.79	1.25	0.00	1.10	1.41	1.61	0.00	1.46	1.78
2010	1.43	0.00	1.29	1.59	1.77	0.00	1.62	1.94	1.39	0.00	1.24	1.57	1.81	0.00	1.65	2.00
Age group																
(0-4)	0.00	0.99	0.00	.	0.00	0.99	0.00	.	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
(5-9)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
(10-14)	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.01
(15-19)	0.01	0.00	0.01	0.01	0.01	0.00	0.01	0.01	0.01	0.00	0.00	0.01	0.01	0.00	0.01	0.01
(20-24)	0.02	0.00	0.02	0.03	0.02	0.00	0.02	0.03	0.05	0.00	0.04	0.06	0.05	0.00	0.04	0.06
(25-29)	0.05	0.00	0.04	0.06	0.05	0.00	0.04	0.06	0.12	0.00	0.10	0.14	0.12	0.00	0.11	0.15
(30-34)	0.14	0.00	0.12	0.16	0.14	0.00	0.12	0.16	0.22	0.00	0.18	0.26	0.23	0.00	0.20	0.27
(35-39)	0.27	0.00	0.23	0.31	0.27	0.00	0.23	0.30	0.37	0.00	0.32	0.44	0.38	0.00	0.33	0.44
(40-44)	0.57	0.00	0.49	0.65	0.55	0.00	0.49	0.62	0.58	0.00	0.50	0.68	0.58	0.00	0.51	0.66
45-49	1	-	-	-	1	-	-	-	1	-	-	-	1	-	-	-
(50-54)	2.22	0.00	1.95	2.53	2.17	0.00	1.94	2.41	1.76	0.00	1.52	2.03	1.80	0.00	1.60	2.02
(55-59)	3.27	0.00	2.87	3.71	3.29	0.00	2.95	3.66	2.68	0.00	2.32	3.09	2.78	0.00	2.47	3.11
(60-64)	5.50	0.00	4.84	6.24	5.51	0.00	4.96	6.12	4.64	0.00	4.03	5.35	4.74	0.00	4.24	5.30
(65-69)	7.75	0.00	6.83	8.79	7.62	0.00	6.86	8.46	6.31	0.00	5.49	7.26	6.45	0.00	5.77	7.20
(70-74)	12.81	0.00	11.31	14.52	12.74	0.00	11.49	14.12	8.89	0.00	7.74	10.22	9.18	0.00	8.24	10.23
(75-79)	13.35	0.00	11.78	15.14	13.12	0.00	11.82	14.56	10.36	0.00	9.00	11.92	10.80	0.00	9.67	12.08
(80-84)	17.32	0.00	15.24	19.68	17.27	0.00	15.52	19.22	10.90	0.00	9.40	12.63	11.17	0.00	9.92	12.58
+85	10.48	0.00	9.15	12.01	10.80	0.00	9.60	12.15	7.03	0.00	5.96	8.29	7.49	0.00	6.54	8.58
region																
2					1.36	0.00	1.27	1.45					1.35	0.00	1.26	1.46
3					1.11	0.00	1.04	1.19					1.09	0.01	1.02	1.17
4					1.20	0.00	1.12	1.29					1.11	0.01	1.02	1.19
5					1.00	0.95	0.90	1.11					1.11	0.04	1.00	1.22

Table 3. Model 3 for evaluating the effect of calendar rate, age-group and different province on total cancer incidence rate in Iran during 2003-2010

Model3								
	men				women			
year	IRR	P>z	[95%		IRR	P>z	[95%	
2004	1.54	0.00	1.42	1.67	1.61	0.00	1.45	1.79
2005	1.70	0.00	1.57	1.84	1.77	0.00	1.60	1.97
2006	1.59	0.00	1.47	1.72	1.50	0.00	1.35	1.66
2007	1.70	0.00	1.58	1.84	1.60	0.00	1.44	1.77
2008	2.09	0.00	1.94	2.26	2.14	0.00	1.94	2.37
2009	1.78	0.00	1.65	1.93	1.77	0.00	1.59	1.95
2010	1.91	0.00	1.77	2.07	1.97	0.00	1.79	2.18
age group								
(0-4)	0.00	1.00	0.00	.	0.00	0.00	0.00	0.01
(5-9)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01
(10-14)	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.01
(15-19)	0.01	0.00	0.01	0.01	0.01	0.00	0.00	0.01
(20-24)	0.02	0.00	0.02	0.03	0.05	0.00	0.04	0.06
(25-29)	0.05	0.00	0.04	0.06	0.12	0.00	0.10	0.15
(30-34)	0.13	0.00	0.12	0.15	0.22	0.00	0.19	0.26
(35-39)	0.27	0.00	0.24	0.30	0.38	0.00	0.33	0.43
(40-44)	0.55	0.00	0.50	0.61	0.57	0.00	0.50	0.65
45-49	1	-	-	-	1	-	-	-
(50-54)	2.15	0.00	1.96	2.35	1.78	0.00	1.58	1.99
(55-59)	3.26	0.00	2.98	3.57	2.72	0.00	2.43	3.05
(60-64)	5.44	0.00	4.99	5.94	4.69	0.00	4.20	5.23
(65-69)	7.51	0.00	6.89	8.19	6.38	0.00	5.73	7.11
(70-74)	12.67	0.00	11.65	13.79	9.07	0.00	8.15	10.09
(75-79)	13.11	0.00	12.03	14.28	10.73	0.00	9.62	11.97
(80-84)	17.05	0.00	15.60	18.63	10.94	0.00	9.73	12.32
+85	10.89	0.00	9.84	12.06	7.67	0.00	6.67	8.81

Continues

province	men				women			
	IRR	P>z	[95%		IRR	P>z	[95%	
sistan	1	-	-	-	1	-	-	-
Markazi	2.74	0.00	2.29	3.27	2.13	0.00	1.65	2.75
Gilan	4.21	0.00	3.56	4.97	3.23	0.00	2.55	4.08
Mazandaran	4.95	0.00	4.20	5.84	3.71	0.00	2.94	4.68
East Azerbaijan	3.56	0.00	3.02	4.20	2.76	0.00	2.19	3.49
West Azerbaijan	4.25	0.00	3.60	5.02	3.48	0.00	2.76	4.40
Kermanshah	2.75	0.00	2.31	3.28	2.59	0.00	2.02	3.31
Khuzestan	2.35	0.00	1.98	2.79	2.47	0.00	1.95	3.13
Fars	2.29	0.00	1.93	2.70	2.21	0.00	1.75	2.80
Kerman	2.25	0.00	1.89	2.68	2.18	0.00	1.70	2.79
Khorasan	4.07	0.00	3.47	4.79	3.03	0.00	2.41	3.80
Isfahan	2.37	0.00	2.01	2.80	2.03	0.00	1.61	2.57
Kurdistan	4.98	0.00	4.20	5.90	4.01	0.00	3.14	5.11
Hamedan	3.21	0.00	2.69	3.81	2.63	0.00	2.06	3.37
Chaharmahal and Bakhtiari	2.53	0.00	2.07	3.08	1.82	0.00	1.35	2.46
Lorestan	3.51	0.00	2.95	4.18	3.41	0.00	2.67	4.36
Ilam	2.28	0.00	1.82	2.84	2.35	0.00	1.69	3.25
Kohgiluyeh Va Boyer Ahmad	3.92	0.00	3.21	4.78	2.86	0.00	2.12	3.86
Bushehr	1.02	0.85	0.80	1.32	0.85	0.41	0.59	1.24
Zanjan	3.86	0.00	3.22	4.62	3.12	0.00	2.40	4.04
Semnan	4.12	0.00	3.41	4.97	3.30	0.00	2.51	4.32
Yazd	2.51	0.00	2.08	3.04	2.46	0.00	1.89	3.21
Hormozgan	0.91	0.42	0.72	1.15	1.11	0.52	0.81	1.51
Tehran	2.77	0.00	2.36	3.25	2.71	0.00	2.17	3.39
Ardabil	6.48	0.00	5.47	7.68	5.63	0.00	4.43	7.16
Qom	3.07	0.00	2.54	3.70	2.25	0.00	1.71	2.96
Qazvin	3.53	0.00	2.94	4.22	3.04	0.00	2.35	3.93
Golestan	4.04	0.00	3.40	4.81	3.17	0.00	2.47	4.06

Discussion

In this study, we analyzed time trend of gastric cancer in Iran for an eight-year period from 2003 to 2010. We further tried to investigate the relation between economic status and gastric cancer in an ecological design. Our results indicated that the maximum and minimum age-standardized incidence rates were calculated as 15 and 9.7 per 100,000 person-years in 2008 and 2003, respectively. A further result showed a negative relation between socioeconomic status and incidence of gastric cancer.

Numerous studies investigated association between socioeconomic status and gastric cancer.

Some of them are based on individual measures [12, 19, 20], while other studies used area-based. In addition, some studies analyzed trend of gastric cancer incidence [25-28]. In previous study, Haidari et al (2012), reported trend of gastric cancer incidence in Iran and found that the age-standardized incidence rate has increased from 2.8 in 2000 to 9.1 per 100,000 person-years in 2005[25]. In our research, age-standardized incidence rate in 2005 was estimated as 12.9 per 100,000 person-years. This gap can be explained by using different reference population to estimating the denominator of the rates.

Kaneko and Yoshimura (2000) worked on trend of gastric cancer incidence in Japan by histological type (HT) according to the Lauren classification. The result of their study showed that during 1975-1989 there was a decreasing and stable trend in intestinal and diffuse type, in the same order. It was believed that time trend analysis by HT might be useful for etiology [29]. Therefore, it would be better to analyzing time trend by HT in future studies. Dai et al (2008) reported 21-year trend of gastric cancer in Tianjin, China. In essence, they found there was a decreasing trend in both males and females aged above 45. However, in males and females aged under 45, were estimated increasing and stable trend, respectively[28]

Kavousi et al (2014), studies high-risk clusters of gastric cancer in Iran, where Ardabil, Kurdistan, Mazandaran and Gilan provinces were reported as high-risk areas[30]. In our study, Gilan province belongs to region 1 and Kurdistan and Ardabil provinces belong to region 2, based on PCA to estimate economic score and have had a significant relation with higher incidence of gastric cancer. Zandic and Reich (2005) explained the relationship between socioeconomic factors and stomach cancer in Slovenia. In fact, they have found that geographical variation of stomach cancer incidence could be explained by socioeconomic factors disparities[24]. Van loon et al (1998) worked on the Netherland Cohort Study data, and reported a lower stomach cancer risk for well-educated men, after adjusting for age. They also found this association would be smaller after adjusting for smoking, family history of stomach cancer and intake of alcohol, coffee, vitamin C and carotene[12]. Therefore, ecological design might not be adequate for assessing relationship between ES and gastric cancer. Uthman et al (2103) assessed association between socioeconomic position (SEP) and incidence of gastric cancer in a systematic review and meta-analysis design. According to their study, increased risk of gastric cancer is associated with low SEP[23].

Limitations

One of the limitations in our study is under estimation of gastric cancer new cases. It would be due to insufficient registration. In the present study, data were obtained from Iran's Ministry of Health and Medical Education (MOHME). Unfortunately, MOHME would be able to register only 80% to 90% of new cases. However, the aforementioned problem does not affect trend of gastric cancer incidence. The second limitation was ecological design of the study, which harbored some weaknesses. If fact, ecological designs suffer from ecological fallacy due to confounder factors.

Conclusion

In conclusion, in our study incidence of gastric cancer had an increasing trend in both sexes. Additionally, was showed ES has a negative relation with incidence of gastric cancer. The results of this study would be beneficial to policy makers pave the way for evidence-based decision-making. We believed further research in future is needed into the relation between ES and gastric cancer, especially based on individual data to avoiding ecological fallacy.

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Metabolic Alkalosis in Children with chronic kidney disease

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Abstract

Metabolic alkalosis is a rare finding in the setting of chronic kidney disease. Here we present three children with chronic renal failure who developed metabolic alkalosis.

Key Words: Children, Metabolic Alkalosis, Chronic Kidney disease.

Introduction

Metabolic acidosis is the most common acid-base abnormality in children with chronic kidney disease (CKD). It is mostly due to the inability of impaired kidneys to excrete hydrogen ions[1]. Metabolic alkalosis is quite unusual in patients with chronic kidney disease and the management could be challenging to the physician[2]. Here, we present 3 children with chronic renal failure who developed metabolic alkalosis.

Patient 1.

An 11 year old boy was admitted to the emergency department (ED) due to severe nausea and vomiting since 4 days ago. He was case of cerebral palsy and was diagnosed with chronic renal failure due to complications of neurogenic bladder. His renal failure was managed conservatively without dialysis.

Since 2 years ago he had episodes of severe frequent vomiting that was fully investigated and finally a diagnosis of cyclic vomiting was made.

On admission to the ED, he seemed moderately dehydrated. His urine output had decreased and could keep nothing in his stomach.

On examination, he was restless and could not communicate with anyone.

His blood pressure was 110/70 mmHg with a pulse rate of 95 beats/min. his respiratory and abdominal examination was unremarkable.

Blood results are shown in table 1.

Table 1. Blood measurements of the patients

	Patient 1	Patient 2	Patient 3
Urea mg/dl	151	195	105
Cre mg/dl	4.5	7.1	3
Na meq/l	123	115	130
K meq/l	2.5	3.2	4.2
Hb g/dl	11	8	7
Ca mg/dl	8.1	6.5	7
P mg/dl	4.5	7.1	4.5
Mg mg/dl	2.2	2.3	1.7
PH	7.49	7.55	7.61
Hco_3 meq/l	31	32	38

The patient was rehydrated with IV saline 0.9% and received IV antiemetic (Ondansetron). His vomiting settled within 72 hours and the electrolyte and blood gas abnormalities improved with IV rehydration (table 1). He was discharged after 7 days and his kidney function was back to its baseline level without dialysis.

Patient 2.

A 7 year old boy was admitted to the hospital due to severe frequent vomiting and decreased urine output. He was case of neonatal asphyxia and resultant neurologic problems. On admission he was quite restless. His blood pressure was 90/60 mmHg, pulse rate 73 beat /min in sinus rhythm

and respiratory rate was 26/min. he was moderately dehydrated and had marked increase in urea and creatinine levels and marked metabolic alkalosis on blood gas. Table 1.

Abdominal and respiratory examinations were unremarkable and on neurologic examination he had developmental delay and spastic paralysis.

The patient received intravenous saline 0.9% and was rehydrated. His metabolic alkalosis was better (pH=7.46, HCO3= 28) but urea and creatinine levels remained elevated. He was candidate for peritoneal dialysis and this therapy was started for him.

On investigations he was found to have neurologic bladder and resultant chronic kidney disease.

Patient 3.

A 10 year old girl, case of chronic kidney disease due to reflux nephropathy who was under peritoneal dialysis since 6 months ago was referred to the hospital due to metabolic alkalosis. Physical examination revealed an alert and oriented girl. Blood pressure was 80/50 mmHg, pulse 100/min and respiratory rate 26/min. abdominal and respiratory examinations were normal and no murmurs were heard on heart auscultation. Initial serum values are shown in table 1.

Her drug history included: calcium carbonate tablets 500 mg, 3 times a day, rocaltrol (vitamin D) pearl 1.25 mg once a day, ferrus sulpate tablets and vitamin supplements. She also received recombinant erythropoietin 2000 units twice a week and shohl's solution (1 liter contains 100 gram sodium citrate and 140 gram citric acid, each milliliter equals to 1 mili equivalent of bicarbonate)

After complete evaluation of the patient it was noticed that she had received shohl'e solution with a dose much greater than the prescribed dose because of the caregiver's mistake.

5 days after correction of the dose of the drug her blood gas was normal and she was discharged from the hospital.

Discussion

Kidneys are the key organs in maintenance of acid-base balance in the body [3] .Association of renal failure and metabolic acidosis is a well known fact but combination of advanced renal failure and metabolic alkalosis is most unusual.

Metabolic alkalosis is the increase in serum bicarbonate concentration. But it should be noted that an elevated serum bicarbonate concentration may also be a response to primary respiratory acidosis but this increase needs normal kidney function and thus is not seen in patients with advanced renal failure[1].

There are two mechanisms by which CKD patients may develop metabolic alkalosis[4]:

1. Hydrogen ion loss from gastrointestinal tract which can result from vomiting or nasogastric suctioning or loss of intestinal secretions like high output ileostomies[7] or some unusual causes of diarrhea[5].
2. Alkali intake or administration.

Because renal causes are eliminated in these patients, identification of the underlying cause of metabolic alkalosis in these patients is simplified[4].

The cause of metabolic alkalosis in our first and second patients was clearly gastrointestinal hydrogen ion loss.

Each one millimole hydrogen ion lost in the emesis, generates one millimole of bicarbonate in body fluids and in a patient without kidney function, bicarbonate concentration of extracellular fluid increases leading to metabolic alkalosis[6].

In our third patient the cause of metabolic alkalosis was gain of exogenous $HCO3^-$. In patients with normal kidney function, administration of even large doses of sodium bicarbonate generally results in very rapid renal excretion of the alkali load without much increase in plasma bicarbonate concentration[8] but external alkali load accumulates rapidly in patients with impaired kidney function due to impaired alkali secretary capacity.[9]

Management of patients with metabolic alkalosis should focus on removing the cause. Administration of isotonic saline solution improves intravascular volume in hypovolemic patients and also dilutes body alkali stores and if kidney function exists helps in bicarbonate excretion.

In general metabolic alkalosis has few symptoms but in cases of severe alkalemia, confusion, lethargy, hypoventilation, seizure and coma may develop which mandate emergency interventions[10]. These patients may require hemodialysis or peritoneal dialysis.[11]

Our first patient responded to intravenous saline administration but in the second and third patient peritoneal dialysis was performed. Successful management of metabolic alkalosis in CKD patients with peritoneal dialysis has been reported before[12, 13]

Conclusion

Renal failure presents with a variety of electrolyte and acid base abnormalities. Although metabolic acidosis is the most common acid- base abnormality in these patients in some instances metabolic alkalosis may also occur which include severe loss of gastrointestinal fluids and excess alkali administration. Management sometimes requires hemodialysis or peritoneal dialysis.

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Abstract

In this paper the instructions for preparing camera ready paper for the Journal are given. The recommended, but not limited text processor is Microsoft Word. Insert an abstract of 50-100 words, giving a brief account of the most relevant aspects of the paper. It is recommended to use up to 5 key words.

Key words: Camera ready paper, Journal.

Introduction

In order to effect high quality of Papers, the authors are requested to follow instructions given in this sample paper. Regular length of the papers is 5 to 12 pages. Articles must be proofread by an expert native speaker of English language. Can't be accepted articles with grammatical and spelling errors.

Instructions for the authors

Times New Roman 12 points font should be used for normal text. Manuscript have to be prepared in a two column separated by 5 mm. The margins for A4 (210×297 mm2) paper are given in Table 1.

Table 1. Page layout description

Paper size	A4
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Regular paper may be divided in a number of sections. Section titles (including references and acknowledgement) should be typed using 12 pt fonts with **bold** option. For numbering use Times New Roman number. Sections can be split in subsection, which should be typed 12 pt *Italic* option. Figures should be one column wide. If it is impossible to place figure in one column, two column wide figures is allowed. Each figure must have a caption under the figure. Figures must be a resolution of 300 DPI, saved in TIFF format, width 10 cm min. For the figure captions 12 pt *Italic* font should be used. (1)

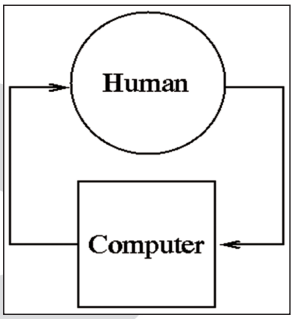

Figure 1. Text here

Conclusion

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

Acknowledgements (If any)

These and the Reference headings are in bold but have no numbers.

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