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Evaluation of Calcium, Phosphorus, Parathormone and Vitamin D Concentration in Morbid Obesity patients referred to four Hospitals in Tehran, Iran

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Abstract

Background and Aims: Obesity is a condition of excessive general or localized body fatness, of which may affect person's health. Definition of obesity is not easy, but as a simple prediction of obesity, it is assumed that a person with body mass index (BMI) equal or greater than 30 KG/square meter can be identified as obese. About 5-10% of obese people, suffer from morbid obesity and this Patients are at risk of deficiency of various nutrients. This study was aimed to evaluate the serum concentrations of Calcium, Phosphorus, vitamin D and Parathormone, considering age, gender, BMI and other body measures, in order to make pre-treatment monitoring of these markers among morbid obese patients.

Methods: A retrospective cross sectional study was designed. All obese patients with morbidity were included in the study. These patients had been referred to four hospitals (Hazrat-Rasoul, Moheb, Milad, Bahman) of Tehran between the year 2007 and 2011 by census.

Serum calcium, phosphorus, parathormone, vitamin D concentrations as well as other body parameters such as weight, height, BMI, hip and waist circumferences, body composition and liver sonography were measured, besides, demographic information such as type of job, smoking, alcohol consumption was also questioned.

Results: 335 obese patients' record with morbidity was documented. Calcium had no significant correlation with BMI, age or gender (P value=0.6). A significant correlation was noted between age and vitamin D concentration, with a rather observable positive coefficient. Vitamin D defficincy was reported in 88.7% of the subjects. Moreover, Vitamin D had a reverse correlation with BMI representing the Spearman's of -0.141.

Out of 335 studied participants, 326 underwent liver sonography and 198 (60.7%) suffered from fatty liver without any significant correlation with vitamin D levels. Parathormone was checked in 247 patients and presented a mean of 69.57±48.07 mg/dl. Except BMI, PTH had no correlation with other studied markers. The Spearman's coefficient for BMI was 0.196, which indicated a positive modest relationship between BMI and blood PTH concentration.

Conclusion: The above mentioned evaluated markers had a significant relation with the obesity. Consideration of these markers will probably play a vital role in the prevention and treatment of morbid obesity while more protection from malnutrition and osteoporosis.

Key words: Morbid obesity, Vitamin D, Calcium, Phosphorus

Introduction

Obesity is defined by body mass index (BMI) equal to30 kg/m^2 or more; is a medical condition in which excess amount of fats are accumulated in the body either generalized or localized (1). It is a body weight more than 20% of the ideal weight for each person (presented by National Institute of Health; NIH). Dramatically, morbid obesity, defined by BMI more than 40 or body weight 45 kg more than the ideal weight, is an absolute global health warning (2). NIH declared that severe obesity is clinically a chronic serious condition with complications in multiple organs of the body.

Among the developed nations, an estimated 66% of U.S. adults are overweight and 32% are obese. Among obese people, totally 5-10% is morbid cases (3, 4). Because of the increase prevalence worldwide overweightness or obesity has

recently been observed as a common issue. The international trend is often called "globosity."(1)

Currently 30% to 50% of Iranian adults, 20 years and above are overweight or obese (16). Genetic pattern, high calorie diets, lack of physical activity, eating habits, psychic pressures and some diseases, such as hypothyroidism play a vital role in obesity. (5)

It has been reported that approximately 400,000 people die worldwide, each year due to improper intake of diet and physical activity or relevant consequences. Recently it has been disclosed that United States, Canada and Europe have the highest rate of obesity, and Egypt and Mexico go on next steps (6).

Obesity in females is significantly more than the males, because of adulthood fluctuations, hormonal changes, marriage and pregnancy (7). Hypothyroidism is the most common cause of obesity, in which the metabolism rate of the body decreases results in higher fat tissue formation from food calories on one hand, and water retention, edema and weight gain, on the other hand (1).

Pituitary and adrenal glands (by means of increased steroid hormone secretion), as well as poly cystic ovaries, insulinoma, and hypothalamic disorders are also involved in morbid obesity, yet, mental and neurologic disorders, such as stress, aggressiveness and depression are also responsible for causing obesity (8,9). The relationship between obesity and serum vitamin D (25 OH) was first observed in 1971 that attributed it to the sequestration of vitamin D in fat tissues (17-20).

Following the publication of these results, numerous epidemiological studies have examined the role of vitamin D in modifying body weight. Most of these studies reported the involvement of vitamin D in regulating body weight, total, visceral and subcutaneous fat mass (21-24).

Many authors have pointed out that obese people avoid consuming fat and fat-soluble vitamins; this would be helpful to monitor vitamin D, calcium, phosphorus and parathormone in all of obesity treatment types (including dietary, medicine or surgery).

Although the mentioned items could are greatly changed after each of treatments, this is important to be noticed that long-term obesity, by low rate of sun exposure or less intake, can be a promised cause of deficiency or insufficiency of vitamin D and calcium.

High dietary calcium intakes are associated with decrease in the prevalence of overweightness and obesity. The mechanism for this effect appears to be related to depression of the PTH and 1,25 hydroxy vitamin D, which leads to inhibition of lipogenesis and increased lipolysis; and also increased excretion of fecal fat caused by soap formation (25).

This study was aimed to evaluate serum concentrations of Calcium, Phosphorus, vitamin D and PTH (Parathormone) considering age, gender, BMI and other body measures in order to make pre-treatment monitoring of the markers more prominent, at least among educated societies. This would be a preliminary study to compare serum markers before and after treatment to find the changes and causative factors in order to achieve the best ways of dealing with the obesity.

Materials and Methods

Patients and measures: Through a retrospective cross-sectional study we recruited all the morbid obese referrals of four hospitals in Tehran (Hazrat-Rasoul, Moheb, Milad, Bahman hospitals) between 2007 and 2011 by census. All the charts were reviewed considering morbid obesity, defined by body mass index (BMI)≥40. In order to control confounding factors, such as nutritional status, supplements intake and exposure to sunlight, the cases were examined by a nutritionist.

After examination, serum calcium, phosphorus, parathormone, and vitamin D concentrations as well as body measures including weight, height, BMI hip and waist circumferences, body composition and liver sonography were recorded, besides demographics (job, smoking, alcohol consumption) were also documented.

Due to the nature of any census descriptive studies, there was no randomization on case selection and all patients referred to hospitals for treatment of obesity were included in this study. People with any other diseases, which interrupt serum concentrations of studied markers, were excluded.

Ethics: No intervention was done through this research work and the Helsinki's treaty was thoroughly respected in order to keep patients' information secret and give them feedback.

Statistics: Data was collected by self-designed questionnaire and analyzed by SPSS 18. Normal distributed variables were successfully analyzed through classical tests, such as Chi-square and independent t-test, while others by non-parametric methods. The significance was considered as a p value less than 0.05 when confidence interval of 95% existed. Means, minimum, maximum values, and standard deviations were noted for quantitative measures as well.

Results

Overall 335 morbid obese patients' records were recruited, out of which 286 (85.4%) were female and the rest were male and the mean age was 39.64±10.54 years. All patients were between 17 and 67 years old. As it can be seen in table 1, the mean weight, height and BMI was 122.3±22.69 kg, 163.54±8.81 cm and 45.63±7.07 respectively. We unfortunately missed the hip and waist circumference measures in 170 patients.

About the smoking, the result of this study shown 230 (68.6%) non-smokers, 46 (13.8%) quit smoking, 49 (14.6%) passive smokers and 20(3%) smokers. The alcohol consumption had 9% prevalence among our presented participants.

The mean of blood calcium concentration was 9.41±0.59 mg/dl and there was no significant correlation of calcium concentration with BMI (P value=0.6), gender (P value=0.7) or age (P value=0.313). The mean of blood phosphorus concentration was 3.82±0.65 mg/dl and the same results in calcium, there was no significant correlation of phosphorus concentration with BMI, gender or age. Table 2 shows Calcium, Phosphorus, Parathormone and vitamin D detailed values.

Parathormone was checked in 247 patients and presented a mean of 69.57±48.07 mg/dl. Except BMI, PTH had no correlation with other studied markers (P value=0.002). The Spearman's coefficient was 0.196 in BMI, which indicates a positive modest relationship between BMI and blood PTH concentration.

Vitamin D serum level was determined, considering itslevels of 20mc/ml for deficiency and 30 mc/ml for insufficiency. About 39.1 % of the patients were vitamin D deficient, 39.6% had insufficient levels of vitamin D, and only 21.3% of subjects had the normal levels of vitamin D shown in table 3.

Table 1. Body measures of studied patients

	Number	Mean	S.D*	Minimum	Maximum
Weight	335	122.3	22.6	82.3	209.2
Height	335	163.5	8.8	146	192
BMI	335	45.6	7.7	35.14	80.62
Hip Cir.**	164	129.1	14	98	198
Waist Cir.	164	136.4	15.34	80	204

**Standard deviation*
***Circumference*

Table 2. Measures of studied markers according genders

	Calcium		Phosphorus		Parathormone		Vitamin D	
	Female	Male	Female	Male	Female	Male	Female	Male
Mean	9.7	9.4	3.8	3.8	69	72.2	22.1	18.7
S.D	5.4	0.49	0.6	0.55	47.4	52.2	28.9	11
Minimum	7	8	2	2.8	1	20	1	4
Maximum	12	10	7	5	400	298	215	50

**Standard deviation*

Table 3. People general vitamin D conditions through the study

Vitamin D condition	Number	Percentage
Deficient	92	39.1
Insufficient	93	39.6
Normal	50	21.3
Total	235	100

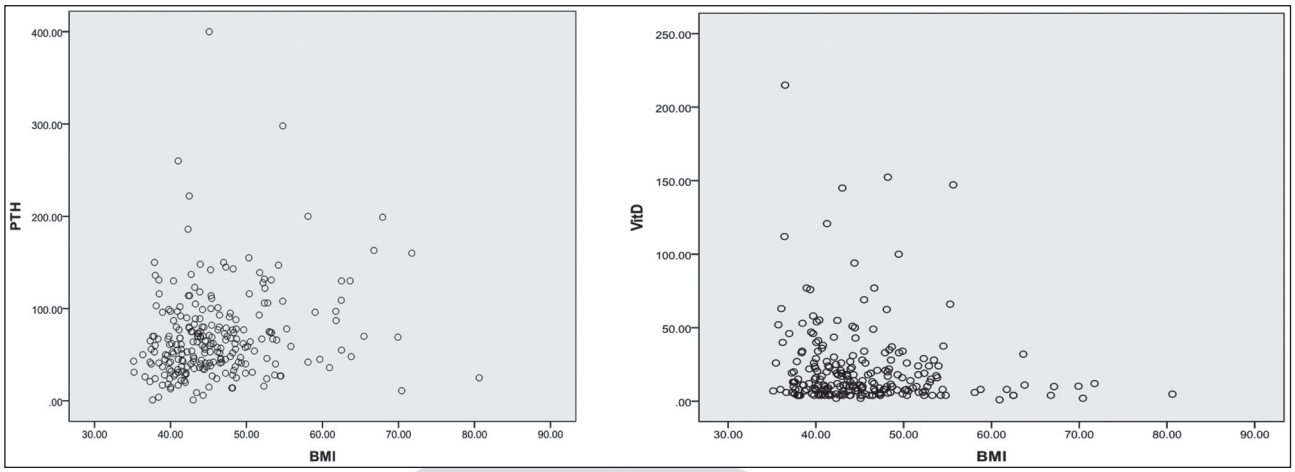

Figure 1. Linear regression diagrams related to the correlation between BMI and serum concentrations of PTH and Vit D

Moreover, a significant correlation was observed between age and vitamin D concentration (P value<0.05) with a rather observable positive coefficient (r=0.256).

Vitamin D had a reverse correlation BMI, representing the Spearman's of -0.141 (P value=0.03), which is completely different from that of PTH. Figure 1 illustrates linear regression diagrams of the two recent measures (PTH and vitamin D) in correlation with BMI, in addition to the relevant graph between BMI and patients' age.

Out of 335 studied participants, 326 underwent liver sonography and 198 (60.7%) suffered from fatty liver without any significant correlation with vitamin D levels. (P value>0.759).

Discussion

Respecting the main aim that was evaluating serum concentrations of Calcium, Phosphorus, parathormone and vitamin D among morbid obesity cases, 335 patients participated from 2007 through 2011.

Obesity is a multi-factorial disorder, coinciding usually with diabetes mellitus, hypertension, cardiovascular disorders, osteoarthritis and/or some malignancies (10). Obesity could be named, somehow, a new-world syndrome effecting people of all ages. In United States, its prevalence has been increased to 8% in men and 9% in women in a single decade (11).

In Tehran, a dramatic growth in the prevalence of obesity and overweightness was reported during 3 years in a single district (12). Among the four studied markers in the present study, Calcium and vitamin D concentrations have a vital role in the obesity. These two markers are vital for monitoring of obese patients before and after treatment, to identify any eficiency in terms of bone density (13).

The results of this study are comparable to Ruedus's study in which the mean calcium concentration was 9.73±5.02 (14) approximately equal to the value reported in our sutdy. Grethen et al., also reported lower blood Calcium levels in 48 obese women but did not find any difference in groups regarding age and sex (15) Based on the result of our study, serum PTH was an average of 69 mg/dl in female and male patients, which was consistent with results Valyna et al.

Hagstrom et al., explained that PTH is in direct correlation with total body and trunk fat mass, as well as local limb obesity (15). On the contrary, they realized that blood vitamin D concentration had a reverse relationship with abdominal obesity (2). We confirmed not exactly the above, but similar correlations with BMI instead of body fat mass (P value=0.002; r=0.196 and P value=0.03; r=-0.141, respectively).

Another work by Brock et al. showed that the most important risk factors of low vitamin D in obesity are including incorrect diet (resulting in mal-absorption), BMI more than 30 and lack of physical activity(3). Moreover, senility, female sex, black race, malnutrition and low sun exposure are the other risk factors, especially in China and Mongolia.

As it can be seen in table 2, despite low vitamin D levels, blood calcium concentration was maintained at normal range at the expense of higher PTH release in blood. That`s why obese people should be monitored for osteoporosis.

On the other hand, due to fat deficient diets intake by obese people, fat soluble vitamins other than vitamin D would be under challenged. More studies are needed in this regard in order to avoid harmful conditions in individuals and protect the patients from malnutrition and osteoporosis who prefer to be treated partially at home.

Limitations of our study:

Imperfect information in the charts was the most prominent challenge in the study, which led to a great pool of missing data. However, records without BMI, comorbidities and focused blood markers had to be excluded.

Acknowledgement

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Inflamatory marker in heart failure with preserved ejection fraction

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Abstract

Clinical studies have shown that, besides the biomarkers with proven role in both the diagnosis and prognosis of heart failure, such as pro-BNP and NT-pro-BNP, certain inflammatory markers may influence heart failure evolution.

Aim: As almost half of the heart failure patients are those with preserved ejection fraction, we aimed to assess the presence of inflammatory markers at the time of primary diagnosis of heart failure with preserved ejection fraction and to compare their values with the proven diagnostic and prognostic parameters (pro-BNP, NT-proBNP), as well as with the clinical status parameters (exercise capacity and quality of life).

Material and methods: Patients diagnosed for the first time with heart failure with preserved ejection fraction were included. We have determined pro-BNP and NT-pro-BNP inflammatory markers and after stabilisation of heart failure we have assessed the clinical status components. Patients were monitored for one year, and then all these parameters were assessed again.

Statistical analysis was performed using Pearson's correlation coefficient, multiple linear regression and Student's T-test for independent variables.

Results: Statistically significant correlations between TNF, pro-BNP, NT-proBNP and clinical status parameters were evidenced both at inclusion and after one year. Increased TNF values, with statistical significance was evident after 1 year in patients with metabolic syndrome, ($p = 0.004$) with obesity ($p=0,001$) and with renal chronic disease ($p=0,008$) Conclusion: Inflammatory markers may play a prognostic role in heart failure with preserved ejection fraction. Further research is needed to prove the efficiency of anti-inflammatory therapy in the management of heart failure with preserved ejection fraction.

Key words: inflammatory marker, biomarker, heart failure, preserved ejection fraction, clinical parameters.

Introduction

Certain inflammatory markers are known to greatly contribute to the onset and progression of various cardiovascular pathologies. Increases of inflammatory markers (TNF, IL6, PCR) with prognostic role in heart failure evolution were shown in case of systolic dysfunction heart failure (1,2).

A biomarker has to play a diagnostic role in disease staging, monitoring of therapeutic efficiency and prognosis. Biomarkers like pro-BNP and NT-proBNP play proven diagnostic and prognostic roles in heart failure.

Given that heart failure is a clinical syndrome caused by pressure and volume changes in cardiac chambers as a consequence of certain pathophysiological mechanisms secondary to the primary cardiovascular pathology, it is important to assess more substance categories which may play biomarker roles. (3, 4)

BNP and NT - proBNP are generally accepted as being useful in the diagnostic evaluation of patients with acute dyspnoea.

Furthermore, natriuretic peptides are successful auxiliaries not only for the diagnosis, but also for the exclusion of heart failure.

A meta-analysis of 40 de clinical studies highlighted that these markers play an important role in estimating the cardiovascular risk (5).

Moreover, this type of biomarker has been used as a guide marker in heart failure therapy and it was shown that the therapy guided by pro-BNP/ NTproBNP values produced much better results than other therapeutic strategies. (6)

The neurohormonal cascade plays a critical role in disease progression. Both the norepinephrines and renin-angiotensinogen-angioten-

sin system influence ventricular remodelling by acting on myocytes and extracellular matrix, but also on physiological mechanisms responsible for normal heart activity. Myocytes are able to synthesise TNF in myocardial necrosis, as well as in case of increased left ventricular filling pressure.

TNF-alpha impacts upon the myocardial remodelling process and heart failure evolution. Elevated serum levels of proinflammatory cytokines (IL-6 and TNF-alpha) have proven to be prognostic markers in patients with decompensated heart failure. TNF-α contributes to heart failure progression by its action on the oxidative stress that modulates certain proteins (e.g., by its action on sarcoplasmic reticulum proteins, particularly heavy chain myosin, it has a negative inotropic effect). (7) IL - 6 directly affects the connections between myocytes and fibroblasts, while increases in IL - 6 are associated with changes of cardiac extracellular matrix, onset of apoptosis, hypertrophy and eventually cardiac dysfunction. Due to these features, IL-6 is sometimes referred to as a "remodelling" marker. (8)

Aim

As almost half of the heart failure patients are those with preserved ejection fraction, we aimed to assess the presence of inflammatory markers at the time of primary diagnosis of ejection fraction heart failure and to compare their values with the proven diagnostic and prognostic parameters (pro-BNP, NT-proBNP), as well as with the clinical status parameters (exercise capacity and quality of life) and comorbidities.

Material and methods

Seventy-eight patients admitted to the Cardiology Clinic, who had clinical signs of heart failure and primary diagnosis of heart failure with preserved ejection fraction, were included in the present study.

Inclusion criteria :

Sinus rhythm

Clinical signs and symptoms of heart failure, according to Framingham criteria

FE ≥ 45 %

E/Ė ≥ 15

Pro-BNP >150pg/ml

Exclusion criteria:

Atrial fibrillation

Acute coronary syndrome within the last 30 days

Cardiac stimulator implant

Severe valvular heart diseases

Severe respiratory dysfunction

Chronic kidney disease ≥4 KDOQI

Mental disorders

Cancer

Presence of sinus rhythm was considered as mandatory criterion in order to eliminate the effect of atrial fibrillation on cardiac function (the diastolic one, especially), clinical symptomatology and heart failure evolution.

All the patients have signed Informed Consent forms.

Serum biomarker assessment

Laboratory constants were determined at patients' admission to clinic. Blood was taken via peripheral venous puncture after the subject has rested for at least 20 minutes. The blood was collected into tubes containing EDTA. Plasma was separated and stored at -20ºC until measured.

BNP was analysed in EDTA plasma using the Microparticle Enzyme Immunoassay (MEIA) Abbott AxSYM. AxSYM® BNP is a Microparticle Enzyme Immunoassay (MEIA) for the quantitative determination of human B-type natriuretic peptide (BNP) in human EDTA plasma on the AxSYM System. Reference laboratory value for BNP <100pg/ml.

NT-proBNP was measured by Electrochemiluminescence Roche. Reference laboratory value for NT-proBNP i<450pg/ml TNF was measured by chemiluminescent enzyme immunometric method by use of IMMULITE. Reference laboratory value for TNF < 8,1pg/ml.

IL-6 was measured by Electrochemiluminescence Roche, with normal value <7pg/ml.

Echocardiographic assessment

Ultrasound evaluation has been performed using a Vivid S5 cardiac ultrasound system, as follows:

- assessment of LVTD, LVTS and LV wall thickness in M-Mode,
- measurement of ejection fraction by Simpson method,

- assessment of transmitral diastolic flow (E and A waves, e/a ratio, EWDT- E wave deceleration time, IVRT - isovolumetric relaxation time), assessment of pulmonary venous flow,
- tissue Doppler with recording of early and late diastolic mitral annulus velocities (E´ - maximum early diastolic velocity and A´ - maximum late diastolic velocity)
- assessment of left atrium sizes – determination of LA area in apical 4-chamber

Quality of life assessment

Minnesota quality of life questionnaire (MLHFQ) was filled by patients the day before discharge, at inclusion and after 12 months . Minnesota Living with Heart Failure questionnaire comprises 21 items, each quantified on a 0-5 scale. Some of the items assess the physical status (8 items: 2-7, 12-13), while 5 items assess patient's emotional status (17-21).

The 6-minute walk test (6MWT) was performed the day before discharge. The patient walked for 6 minutes on a flat surface at his own pace. Blood pressure and heart rate were measured before the test; if BP>180/100mmHg or/and HR>120b/minute, the test was not performed.

Twelve months after patients' inclusion, inflammatory markers, along with proBNP, NT-proBNP and clinical status components were reassessed. Cardiovascular and non-cardiovascular cause admissions of patients were monitored within the same period of time.

Statistical analysis

Pearson's correlation coefficient and multiple linear regression have been used for the analysis of statistical series corresponding to the pair of statistical variables, the dependent variable being expressed as a linear combination of independent variables. The used algorithm was backward stepwise regression. The T-Test for 2 Independent Means was used for the statistical evaluation of a variable in different groups. A p value of < 0.05 was considered statistically significant.

Results

Table 1 shows biomarkers values at patients' inclusion and one year after. Regarding the correlation between biomarkers values at inclusion and between biomarkers and clinical status components, we can see a moderate correlation between TNF level and pro-BNP (r=0,652) and NT-proBNP (r=0,434) as well as between TNF level and clinical status components: quality of life score, as assessed by the Minnesota Questionnaire (MLHFQ) (r= 0,415) and exercise capacity as assessed by the 6 minute walking test (6MWT) (r= 0,424), all these correlations being statistically significant ($p<0.001$). As the IL6 values concerns, a weak correlation has been seen with NT-proBNP (r=0,330, p=0,004) value at inclusion, the other correlations having no statistical significance (Table 2). One year after the inclusion, statistically significant correlations between TNF, and pro-BNP and NT-proBNP remained the same, weaker correlations being recorded between them and clinical status parameters. Unlike at the inclusion time, a moderate, statistically significant correlation has been seen between IL6 and clinical status parameters at one-year follow-up (Table 3).

No statistically significant correlations of these parameters were evidenced between <65 and >65

Table 1. Biomarkers at inclusion and at 1 year follow-up

		pro-BNP	NT-proBNP	IL6	TNF	BNP1*	NTBNP1*	TNF1*	IL61*
N	Valid	78	78	78	78	77	77	77	77
	Missing	0	0	0	0	1	1	1	1
Mean		474.6649	751.6192	3.6493	10.9097	464.1038	725.8553	10.5808	3.4814
Std. Error of Mean		29.04282	51.03928	.27605	.38856	34.19101	57.78846	.49444	.26228
Median		408.0000	681.0000	2.8000	11.0000	353.0000	617.5000	9.9000	2.8000
Std. Deviation		249.83578	436.07980	2.35856	3.34249	292.12815	490.35133	4.22452	2.22556
Minimum		156.00	81.00	1.50	5.00	40.47	107.30	4.30	1.16
Maximum		1423.00	1862.00	10.00	20.00	1679.00	2200.00	21.90	10.00

**after 1 year*

Table 2. Correlations between TNF/IL6 and pro-BNP / NT-proBNP/ clinical parameters

	proBNP		NT-proBNP		IL6		MLHFQ		6MWT	
	r	p	r	p	r	p	r	p	r	p
TNF	0.652	p<0.001	0.434	p<0.001	0.179	NS	0.415	p<0.001	-0.424/	p<0.001
IL6	0.233	NS	0.330	p<0.004	-	-	0.274	NS	-0.226	NS

r = pearson correlation coefficient
6MWT = exercise capacity as assessed by the 6 minute walking test
MLHFQ= quality of life score assessed by the Minnesota Living with Heart Failure questionnaire

Table 3. Correlations between TNF/IL6 and pro-BNP / NT-proBNP/ clinical parameters, after 1 year

	ProBNP1		NT-proBNP1		TNF1		MLHFQ1		6MWT1	
	r	p	r	p	r	p	r	p	r	p
TNF1	0.718	p<0.001	0.579	p<0.001	-	-	0.352	P=0,004	-0.436	p<0.001
IL61	0.168	NS	0.297	NS	0.397	NS	-0.672	p<0.001	-0.715	p<0.001

r= Pearson correlation coefficient
1= marker or parameter value after 1 year
6MWT = exercise capacity as assessed by the 6 minute walking test
MLHFQ= quality of life score assessed by the Minnesota Living with Heart Failure questionnaire

Table 4. Features of patient groups according to NYHA class.

	Group I N=31	Group II N=47	p
Age	66 ±9.2	65± 9.	0.63
Female sex	23 (74.2%)	27 (57.4%)	0.75
Ischemic cardiopathy	23 (74.2 %)	26 (55.3%)	0.09
Hypertension	29 (94%)	42 (89%)	0.72
Diabetes	10 (32.3%)	14 (29.8%)	0.82
Obesity	17 (54.8%)	21 (44.7%)	0.37
Metabolic syndrome	23 (74%)	20 (42.5%)	0.0123
Renal chronic disease	16 (51.6%)	13 (27.7%)	0.032
ACE	14 (45.16%)	25 (53.19%)	0.49
ARB	10 (32.25%)	15(31.91%)	0.9760
Beta-blocker	20(64.51%)	44(93.61%)	0.001
Furosemide	29(93.54%)	15(31.91%)	p<0.0001
Spironolactone	27(87.09%)	24(51.06%)	0.001
Statins	9(29.03%)	15(31.91%)	0.7871

ACE = *Angiotensin-Converting Enzyme Inhibitors*, **ARB =** *Angiotensin Receptor Blockers*

age groups, nor between women and men, at both inclusion and 1-year follow-up.Two groups of patients were formed, according to NYHA class: NYHA III (group I) and NYHA II (group II). I must mention that no NYHA I or NYHA IV patients were included in the studied group. Table 4 shows the features of the two patient groups.

As one can see, there are no statistically significant differences between the two groups, except the presence of metabolic syndrome (p=0.0123) and chronic kidney disease (p=0.032).

As regards the type of therapy, significant differences are recorded for beta-blocker therapy (p=0.001) in favour of NYHA II group and diuretics therapy in NYHA III group (p<0.0001).

Values of inflammatory markers, NT-proBNP and pro-BNP, and clinical status parameters (quality of life and exercise capacity) in the two groups were compared at both inclusion and 1-year follow-up. Statistically significant differences were seen both at inclusion and after one year. (Table 5) Parameters evolution in the two studied groups has recorded statistically significant differences between TNF levels at inclusion and 1-year follow-up, respectively, for NYHA III patients (P<0.0001). (Table 6). In the NYHA II

Table 5. Evolution of biomarkers and clinical status parameters according to NYHA class

Parameter	Group 1 at inclusion	Group 2 at inclusion	p	Group 1 after 12 months	Group 2 after 12 months	p
TNF	11.76±2.79	10.29±2.53	p=0.27	13.96±3.39	7.71±1.09	p<0.00001
IL6	4.24±1.95	2.94±1.57	p<0.001	4.26±1.87	2.68±1.17	p=0.0018
proBNP	563.94±304.92	369.82±136.19	p=0.009	534.30±258.129	401.18±191.41	p=0.027
NT-proBNP	908.29±388.28	604.74±275.69	p=0.314	866.42±443.82	548.112±261.96	p<0.0001
6MWT	258.33±61.83	251.62±46.50	p=0.0769	236.87±58.175	258.43±81.57	p<0.0001
MLHFQ	53.81±10.41	46.52±9.05	p=0.0029	57.93±16.66	44.75±15.46	p=0.00097

6MWT = exercise capacity as assessed by the 6 minute walking test
MLHFQ= quality of life score assessed by the Minnesota Living with Heart Failure questionnaire

Table 6. Evolution of biomarkers and clinical status parameters in the NYHA III patient group

	At inclusion	After 1 year	p
TNF	11.76±2.79	13.96±3.39	p<0.00001
IL6	4.24±1.95	4.26±1.87	p=0.4189
proBNP	563.94±304.92	534.30±258.129	p=0.379
NTproBNP	908.29±388.28	866.42±443.82	p=0.419
6MWT	258.33±61.83	236.625±46.50	p=0.378
MLHFQ	53.81±10.41	57.93±16.66	p=0.353

6MWT = exercise capacity as assessed by the 6 minute walking test
MLHFQ= quality of life score assessed by the Minnesota Living with Heart Failure questionnaire

Table 7. Evolution of biomarkers and clinical status parameters in the NYHA II patient group

	At inclusion	After 1 year	p
TNF	10.29±2.53	7.71±1.09	p=0.009
IL6	2.94±1.57	2.68±1.17	p=0.403
proBNP	369.82±136.19	401.18±191.41	p=0.487
NTproBNP	604.74±275.69	548.112±261.96	p=0.484
6MWT	251. 62±46.50	258.43±81.57	p=0.433
MLHFQ	46.52±15.46	44,75±9,05	p=0.439

6MWT = exercise capacity as assessed by the 6 minute walking test
MLHFQ= quality of life score assessed by the Minnesota Living with Heart Failure questionnaire

patients group, significant differences were also seen between the TNF levels, as this has recorded a statistically significant decrease after 12 months (p=0.009). (Table 7)

There have been evaluated TNF and IL 6 values, depending on comorbidities. There were no statistically significant differences in the patients with ischemic heart disease or diabetes. Increased TNF values, with statistical significance was evident after 1 year in patients with metabolic syndrome, (p = 0.004) with obesity (p=0,001) and with renal chronic disease (p=0,008) (Figure 3). These were not accompanied by significant differences between the values of pro-BNP, NT-pro-BNP or clinical parameters.

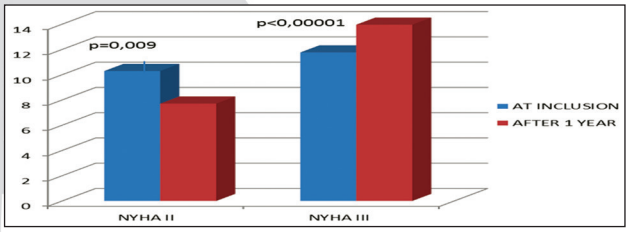

Figure 1. TNF evolution according to NYHA class

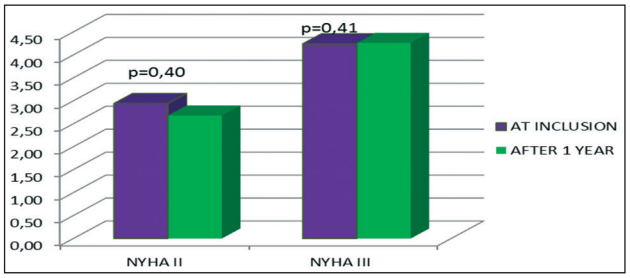

Figure 2. IL6 evolution according to NYHA class

Significant differences were highlighted for TNF value in women compared with men (p=0,002) at inclusion, without being accompanied by differences in other clinical or laboratory parameters.

The patients over 65 years had higher TNF value than patients under 65 (p = 0.0002), at baseline, without obvious other differences with statistical significance.

In univariable analysis, increased levels of these biomarkers (pro-BNP, NT-proBNP, TNF) were all associated with hospitalization.

However, none of these biomarkers remained significant as an independent predictor in multivariable analysis with hospitalization.

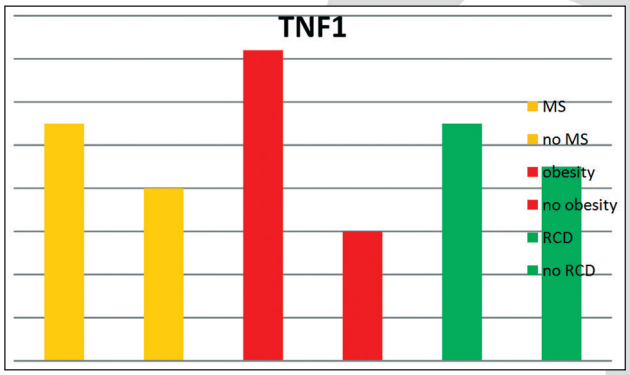

Figure 3. TNF value after 1 year, for patient with metabolic syndrome, obesity and renal chronic disease

TNF1= TNF value after 1 year; MS = metabolic syndrome, RCD = renal chronic disease

Discussions

There are discussions in the literature on the role of inflammatory markers in the evolution of certain chronic diseases (9).

Biomarkers were examined, especially in heart failure with systolic dysfunction. At the same time, the significance of these types of biomarkers can be completely different depending on the type of heart failure. In HFPEF, comorbidities such as metabolic syndrome or obesity can lead to increases in inflammatory markers that may influence the evolution of heart failure.

It is known that in heart failure with preserved ejection fraction, prevalence of comorbidities is much higher than in heart failure with systolic dysfunction. For this reason, we intend to compare the presence of inflammatory markers in various comorbidities (ischemic heart disease, diabetes, chronic kidney disease). Statistically significant differences were highlighted for TNF values, after 1 year follow-up, for patients with metabolic syndrome, obesity and renal chronic disease.

Weight loss leads to a significant decrease of inflammatory markers.

Up to the present time, several studies have shown the importance of inflammatory markers in atherosclerotic pathology, particularly in atheroma plaque progression and rupture. It is difficult sometimes to demonstrate whether inflammatory markers originate in the atheroma plaque process or this is due to systemic inflammatory processes, which would accelerate atherosclerosis and favour atheroma plaque rupture (10) However, in the present study, there were no statistically significant differences between the values of inflammatory markers in patients with ischemic heart disease.

The myocardium without pathological damage, do not secrete TNF. In affected myocardium TNF receptor expression is increased. At the same time, proved experimentally that TNF promotes hypertrophy myocyte, maintaining a normal systolic function of the left ventricle, followed by dilated cardiomyopathy and systolic dysfunction (11) . There is evidence that immune activation plays an important role in the pathogenesis of heart failure. It is important to consider CHF as a systemic illness.

There were statistically significant correlations for TNF with prognostic markers with evidence and with clinical status parameters. For patients in NYHA class II at baseline, reduced TNF was associated with an improvement in clinical status, while an increase in TNF levels in patients in NYHA class III at baseline, was accompanied by worsening clinical parameters.

At the same time, inflammatory markers, especially TNF, promotes progressive myocardial injury after activation by the stimulation of the immune system by myocardial injury or volume or pressure overload, the mediators responsible for inflammation and/or anti-inflammatory responses will provide new targets for therapeutic intervention.(12) Other types of treatment should be to taken into account because the current management is mainly oriented towards symptoms relief and studies utilizing drogs targeting for new pathophysiological pathways are awaited.

Some studies, have shown that pharmacologic blockade of the biologic effects of TNF was associated with improved functional status as well as with improved myocardial function. (13)

It has also been shown that the use of immunomodulators such as rofecoxib in patients with cardiovascular pathology, although it leads to a decrease in PCR and IL6 levels, has been associated with a significant increase in cardiovascular mortality. (14) Even though various therapies that act on most pathophysiological mechanisms of this clinical syndrome are currently used in heart failure treatment, patients' prognosis is still guarded.

First clinical trials assessing the efficiency of some TNF antagonists (Etanercept –TNFR-2 fusion protein) RENAISSANCE (in USA) and RECOVER (Europe) did not produced the expected results. This may also due to the fact that patients with severe heart failure were included and cases treated with low study doses were excluded from the statistical analysis. This type of medication seems to be only effective in patients with proved inflammatory activity.

Conclusion

Inflammatory markers are correlated with prognostic markers already proven in heart failure and clinical status parameters.

Proinflammatory status is influenced by some comorbidities (metabolic syndrome, obesity, renal chronic disease), is present in women and the elderly. TNF value can be predictor for heart failure evolution, particularly in patients with severe heart failure.

Considering the high number of comorbidities in the patients suffering from heart failure with preserved ejection fraction and that in this pathology is an increased incidence of females and older people , in which a proinflammatory status is also associated, the possibility to study inhibitor therapy upon inflammatory activity should not be neglected for these patients.

This study included a small number of patients and had a short follow-up. Further research may provide additional evidence for the value of these biomarkers in improvement of risk stratification of patients with HFPEF.

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Adjuvant role of electrotherapy in the management of gonarthrosis

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Abstract

Introduction: Osteoarthrosis is a degenerative articular pathology characterized by progressive destruction of the cartilage. Clinically it is manifested by pain, which is worsened by movement and progressive functional failure. The purpose of this study was to evaluate the effectiveness of electrotherapy (horizontal therapy) and manual therapy in patients treated with electrotherapy and manual therapy in combination with Non-Steroid Anti-Inflammatory Drugs (NSAID) for the treatment of primary gonarthrosis, compared with100 patients NSAID treatment alone.

Methods: Randomized prospective study in the 245 patients treated for gonarthrosis in the University Hospital Centre "Mother Teresa", Tirana, conducted in the period of April 2011– April 2012.

Results: 245 patients were involved in the study, aged 45-80 years old with mean age 62.5 years. Patients treated with electrotherapy had a reduction of pain (RR = 0.12, 95% CI: 0.06 - 0.022, P < 0.0001). 3 months after treatment with electrotherapy the amplitude of movement of articulation was increased (RR = 1.29, 95% CI: 1.07 - 1.54, P = 0.006).

Conclusion: We found that the most effective treatment of gonarthrosis for our patients was the combination of NSAID with electrotherapy and other modalities comparing with only NSAID treatment. NSAID combined with electrotherapy and manual therapy was more effective in pain management and in increasing the amplitude of the articulation than the monotherapy with NSAID. NSAID combined with electrotherapy and manual therapy has better economical effects because it prevents strain, which constitute an indication for surgical intervention.

Key words: Osteoarthrosis, Electrotherapy, horizontal therapy, range of motion (ROM), pain.

Introduction

Gonarthrosis most frequently defined as the change involving damage of the articular cartilage of the knee joint, emergence of abnormal knee tissue, reactive changes in synovial membrane, and pathological synovial fluid. Approximately 85% of the population near 65 years of age present radiographic evidences of osteoarthritis (1), and the knees are the joints most often affected by osteoarthrosis (2). Gonarthrosis, as a chronic disease of the knee joint most frequently causes pain and limited range of motion (3). The clinical severity of knee osteoarthritis is reflected in the WOMAC osteoarthritis index, which enables a valid, reproducible assessment of the degree of impairment by pain and loss of function (4). Gonarthrosis is diagnosed on the basis of clinical and radiological examinations (5). Osteoarthritis of the knees is not a curable disease at present, as the mechanism by which it arises and progresses remains incompletely understood. Therefore, the goal of treatment is to alleviate the signs and symptoms of the disease and, if possible, to slow its progression.

Gonarthrosis therapy is multidisciplinary. Conservative treatment is provided in stepwise fashion, as recommended by the European League against Rheumatism (6). Physiotherapeutic measures include exercise therapy and physical measures as: ultrasound application, electrotherapy etc (7). Numerous studies have demonstrated the efficacy and usefulness of electric therapies in the treatment of gonarthrosis. Electrotherapy is considered as a branch of physical therapy which uses electrical current for therapeutic purposes.

Horizontal Therapy is a generation of electrotherapy used in the treatment of osteoarthritis due to its ability to stimulate both deep-down and surface joint tissues, simultaneously obtaining both bioelectrical effects and biochemical effects (8).

The aim of the study: To study the effectiveness of electrotherapy: Interferential Horizontal Therapy (TIF) combined with NSAID in the treatment of primary gonarthrosis, compared with NSAID treatment. To evaluate the effects of physical therapy in the pain level, the range of motion (ROM) and return to activities of daily life in patients with primary gonarthrosis.

Material and methods

Patients with gonarthrosis were recruited from the Rheumatology Clinic in the University Hospital Centre ''Mother Teresa'' in Tirana. Prospective randomized study, approved by national ethical committee. It has been compared the effects of various therapies for the treatment of gonarthrosis in the pain level and amplitude of articulation. The study was conducted in the period April 2011-March 2012.

Inclusion criteria: Patients diagnosed with primary gonarthrosis, through radiographic examination of the genu articulation when there is the presence of osteofit and narrowing of the articular space; diagnosis of bilateral knee osteoarthrosis according to the American College of Rheumatology criteria (9).

Exclusion criteria: Excluded from the study all cases with secondary gonarthrosis.

Severity of knee pain was assessed using a Visual Analogue Scale of pain (VAS). The VAS consists of a 10-cm line, with the left extreme indicating "no pain" or zero and the right extreme indicating "unbearable pain" or 10. The participants were asked to use the scale to indicate their current level of pain. Higher values suggest more intense pain. The values (in centimeters) were recorded for the statistical analysis.

Ranges of motion (ROM), Knee flexion ROM in degrees were measured bilaterally in a supine position according to Norkin and White using a goniometer (10).

The protocol of treatment: Group I, 100 patients had been followed by maximal attention for the scale of pain and range of articular motion (ROM- articular). In this plan of treatment patients were treated only with NSAID **(**Non-Steroid Anti-Inflammatory Drugs): 57 patients treated with Pyroxicam 20 mg/day in the morning for 10 days; 43 patients treated with Diclofenac 25 mg/day for 10 days. The treatment with only NSAID for the scale of pain and ROM-articular in this group of patients for 10 day was conducted in the Department of Rheumatology.

Group II. The 100 cases were followed by maximal attention for the scale of pain and range of articular motion (ROM- articular). This group was treated with NSAIDs and horizontal therapy, that was applied one cycle per diem for 10 days. In this group (Group II) we observed the scale of pain before the treatment, 3 months later and 6 months later.

At the end, it was studied the result of treatment with NSAID and electrotherapy, immediately after treatment, 3 months after treatment, and 6 months after treatment by evaluating the scale of pain and ROM-articular.

In the study is used treatment with ''Interferential Horizontal Therapy "(TIF). It was applied the frequency of 4000 - 4010 Hz to four electrodes placed perpendicular of each other, where the point of meeting of their currents produces low frequency of 10 Hz acting on knee articulation.

Statistical analysis: Statistical analysis of the study was conducted by SPSS 15.0 (statistical package for social sciences, version 15.0 Chicago, IL). Data are presented as the mean for numerical variables, number (n) or percentage (%) for categorical variables. Relative risk (RR) is used to compare risk for relieving pain and articular amplitude after treatment, 3 months after treatment, and 6 months after treatment. The value of $p < 0.0001$ was accepted statistically significant.

Results

We collected data from 245 patients: 170 males and 75 females. 100 patients with primary gonarthrosis, average age was 62.5 years old (range 45-80 years old). 10 men and 15 women discontinued treatment with electrotherapy before ending it. They were removed from statistical analysis. Also 15 men and 5 women discontinued treatment and were excluded from the statistical analysis because they manifested side effects of NSAID preparations: Arterial hypertension, gastritis, etc.

The radiological findings were the narrowing of the articular space and the presence of osteofit in 100% of cases and osteoporosis near the articular surface in 45% of cases.

The intensity of pain on a scale VAS before treatment with NSAIDs were (see Table 1): 55% of patients had (8-10) pain degree by rate of VAS; 35% of patients had (6-8) pain degree by rate of VAS and 10% of patients had (3-5) pain degree by rate of VAS.

The intensity of pain on a scale VAS after treatment with NSAIDs were (see Table 1): 26% of patients had (8-10) pain degree by rate of VAS; 54% of patients had (6-8) pain degree by rate of VAS and 20% of patients had (3-5) pain degree by rate of VAS.

The intensity of pain on a scale VAS after 3 months treatment with NSAIDs were (see Table 1): 35% of patients had (8-10) pain degree by rate of VAS; 45% of patients had (6-8) pain degree by rate of VAS; 20% of patients had (3-5) pain degree by rate of VAS;

The intensity of pain on a scale VAS after 6 months treatment with NSAIDs were (see Table 2): 35% of patients had (8-10) pain degree by rate of VAS; 50% of patients had (6-8) pain degree by rate of VAS; 15% of patients had (3-5) pain degree by rate of VAS;

The intensity of pain on a scale VAS before treatment with NSAIDs + Electrotherapy were (see Table 1): 0% of patients had (8-10) pain degree by rate of VAS; 51% of patients had (6-8) pain degree by rate of VAS and 19% of patients had (3-5) pain degree by rate of VAS. The intensity of pain on a scale VAS after treatment with NSAIDs + Electrotherapy were: 0% of patients had (8-10) pain degree by rate of VAS; 10% of patients had (6-8) pain degree by rate of VAS; 23% of patients had (3-5) pain degree by rate of VAS and 67% of patients had (0-2) pain degree by rate of VAS.

The intensity of pain on a scale VAS after 3 months of treatment with NSAIDs + Electrotherapy were: 0% of patients had (8-10) pain degree by rate of VAS; 0% of patients had (6-8) pain degree by rate of VAS; 58% of patients had (3-5) pain degree by rate of VAS and 42% of patients had (0-2) pain degree by rate of VAS.

The intensity of pain on a scale VAS after 6 months of treatment with NSAIDs + Electrotherapy were: 4% of patients had (8-10) pain degree by rate of VAS; 7% of patients had (6-8) pain degree by rate of VAS; 47% of patients had (3-5) pain degree by rate of VAS and 42% of patients had (0-2) pain degree by rate of VAS.

Patients of treatment with NSAIDs + Electrotherapy have decreased level of pain compared patients to treatment only with NSAIDs.

The ROM was increased in a higher degree from time 0, after 3 months and 6 months after treatment with NSAID and electrotherapy, compared to the ROM in patients with only treated with NSAID (Pyroxicam and Diclofenac) in Rheumatology.

The ROM in degrees before treatment with NSAIDs were (see Table 2): 40% of patients had ROM in degrees in flexion (71-90); 20% of patients had ROM in degrees in flexion (51-70); 23% of patients had ROM in degrees in flexion (31-50); 17% of patients had ROM in degrees in flexion (0-30);

The ROM in degrees after treatment with NSAIDs were: 50% of patients had ROM in degrees in flexion (71-90); 12% of patients had ROM in degrees in flexion (51-70); 23% of patients had ROM in degrees in flexion (31-50); 15% of patients had ROM in degrees in flexion (0-30);

The ROM in degrees 3months after treatment with NSAIDs were(see Table 2): 50% of patients had ROM in degrees in flexion (71-90); 14% of patients had ROM in degrees in flexion (51-70); 22% of patients had ROM in degrees in flexion (31-50); 14% of patients had ROM in degrees in flexion (0-30);

Table 1. The level of pain of patients at the time 0, after 3 months, and 6 months after the treatment

Pain VAS score	Group I (NSAIDS)				Group II (NSAIDS+ Electrotherapy)			
	Before treatment	After treatment	After 3 months	After 6 months	Before treatment	After treatment	After 3 months	After 6 months
0-2	0	0	0	0	0	67	42	42
3-5	10	20	20	15	19	23	58	47
6-8	35	54	45	50	51	10	0	7
> 8	55	26	35	35	30	0	0	4
10	0	0	0	0	0	0	0	0

The ROM in degrees 6 months after treatment with NSAIDs were: 47% of patients had ROM in degrees in flexion (71-90); 15% of patients had ROM in degrees in flexion (51-70); 25% of patients had ROM in degrees in flexion (31-50); 13% of patients had ROM in degrees in flexion (0-30);

The ROM in degrees before treatment with NSAIDs and electrotherapy were(see Table 2): 6% of patients had ROM in degrees in flexion (71-90); 45% of patients had ROM in degrees in flexion (51-70); 30% of patients had ROM in degrees in flexion (31-50); 19% of patients had ROM in degrees in flexion (0-30);

The ROM in degrees after treatment with NSAIDs and electrotherapy were: 3% of patients had ROM in degrees in flexion > 90; 57% of patients had ROM in degrees in flexion (71-90); 10% of patients had ROM in degrees in flexion (51-70); 18% of patients had ROM in degrees in flexion (31-50); 12% of patients had ROM in degrees in flexion (0-30);

The ROM in degrees after 3mouths treatment with NSAIDs and electrotherapy were: 5% of patients had ROM in degrees in flexion > 90; 55% of patients had ROM in degrees in flexion (71-90); 20% of patients had ROM in degrees in flexion (51-70); 15% of patients had ROM in degrees in flexion (31-50); 5% of patients had ROM in degrees in flexion (0-30);

The ROM in degrees after 6 months treatment with NSAIDs and electrotherapy were: 15% of patients had ROM in degrees in flexion > 90; 68% of patients had ROM in degrees in flexion (71-90); 12% of patients had ROM in degrees in flexion (51-70); 5% of patients had ROM in degrees in flexion (31-50); 0% of patients had ROM in degrees in flexion (0-30);

The ROM was increased in a higher degree from time 0, after 3 months and 6 months after treatment with NSAID and electrotherapy, compared to the ROM in patients the NSAID therapy. So electrotherapy treatment reduces the risk that those patients to have the amplitude of ROM from 0-50 (RR= 0: 52, 95% CI: 0.33-0.83, P=0.006). Electrotherapy treatment can increase the possibility that those patients 3 months after treatment to have ROM from 50 to 100 degrees, compared with that one before treatment with electrotherapy. (RR=1.29, 95% CI: 1.07- 1.54, P =0.006).

Electrotherapy treatment reduced the risk of having the amplitude of ROM from 0-50 (RR = 0.13, 95% CI: 0.05- 0.32, P < 0.0001).

Electrotherapy treatment increased the possibility of having a better ROM, ranging from 50 to 100 degrees compared with ROM before treatment with electrotherapy (RR = 1.53, 95% CI: 1.30-1.79, P < 0.0001).

Based on the questionnaire that addressed the perception of pain in patients after treatment with only NSAID and NSAID + electrotherapy we noted (see Chart 1) that: 88.5% of patients felt better after NSAID+ electrotherapy; 57.7% of patients felt better after drug treatment.

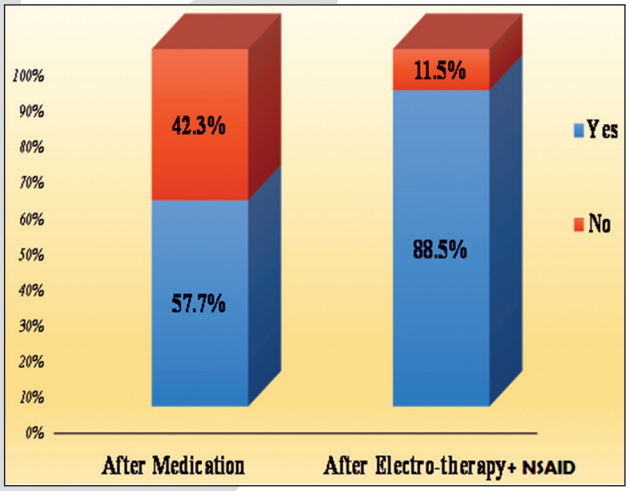

Chart 1. The comparison between the perception of pain after drug treatment and electrotherapy.

Table 2. ROM in time 0, after 3 months and 6 months after treatment

ROM (in degrees) In flexion	Group I (NSAIDS)				Group II (NSAIDs+ Electrotherapy)			
	Before treatment	After treatment	After 3 months	After 6 months	Before treatment	After treatment	After 3 months	After 6 months
0-30	17	15	14	13	19	12	5	0
31-50	23	23	22	25	30	18	15	5
51-70	20	12	14	15	45	10	20	12
71-90	40	50	50	47	6	57	55	68
> 90	0	0	0	0	0	3	5	15

The comparison of amplitude of genu articulation right after the treatment with NSAID + electrotherapy, after 3 months and 6 months. It is noted (see Chart 2)that articulation amplitude of movement (ROM) is improved according to the following schedule: right after drug treatment + electrotherapy, after 3 months and 6 months after the combined treatment. It is noticed that the articular amplitude is significantly increased from 0-30 degrees at the beginning until 70-90 degrees or >90 degrees after 6 months.

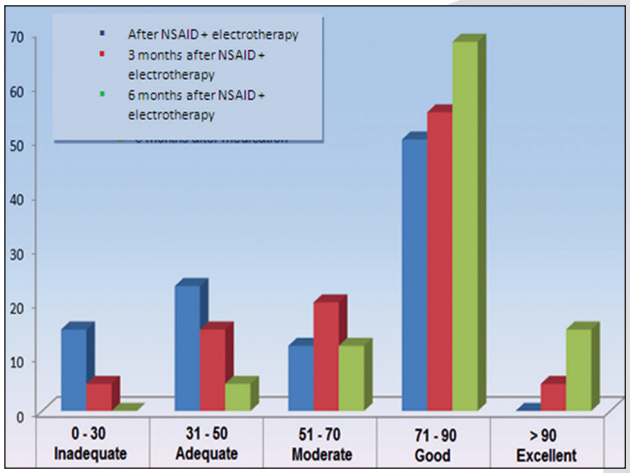

Chart 2. The comparison of ROM right after drug + electrotherapy treatment after 3, 6 months

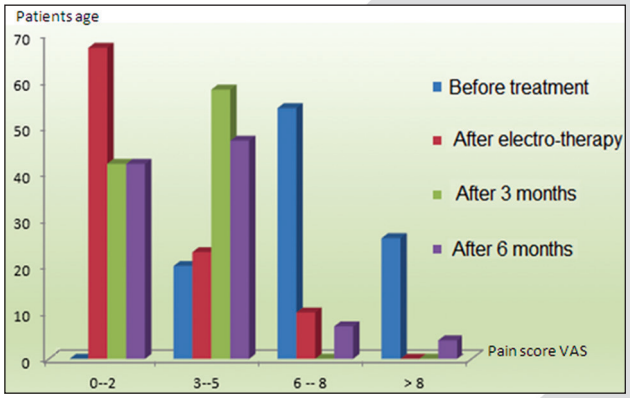

Chart 3. The comparison of Pain score

Comparison of the degree of pain (VAS), before treatment with electrotherapy + NSAID and after treatment with electrotherapy, 3 months, and 6 months after treatment. After treatment with electrotherapy, the largest number of patients have pain scale of 0-2 and 3-5, a small number of 6-8 degrees of pain, no patient has pain over 8 degrees. So by comparing the number of patients for each level of pain before treatment with electrotherapy, it is seen that treatment with electrotherapy had significantly reduced pain.

Discussion

Knee osteoarthritis is expected to be the fourth highest cause of disability in women and is responsible for the deterioration of quality of life and functional capacity (11). Few studies have investigated the effects of different types of nonpharmacological treatments on the pain and the range of motion. In a systematic Cochrane review Rutjes et al found little evidence of a significant effect for electrostimulation compared to sham or no intervention on pain in gonarthrosis (12). Another study contradict this systematic review, because Mascarin et al, found an improvement in the pain index after Kinesiotherapy, transcutaneous electrical nerve stimulation (TENS) and Ultrasound (13). NG et al studied 24 patients and showed that electroacupuncture treatment or TENS are effective in pain reduction (14). There are some published studies on the non-pharmacological treatment of knee osteoarthritis, in 6 trials were shown pain relief and improved mobility after electrostimulation (15).

In our study we evaluated the effect of treatment on pain using the VAS and we found that the Horizontal Therapy improved the pain. The Horizontal Therapy effect favors diffusion and thus distribution of pain mediators and is particularly important for patients with osteoarthritis, who due to pain are forced to control and reduce their joint movement. Through higher intensities, well tolerated by the joints, a further effect is added which blocks the fibers transmitting pain (8). The present study found an improvement in pain after electrotherapy, and this supports the results of the study conducted in 200 subjects (8). The study done by Saggini et al (8) showed that the treatment with Horizontal Therapy is effective in a statistically significant way in the short and medium term in the reduction of pain.

Range of motion was another variable evaluated in the present study. Pollard et al. showed that manual therapy reduces pain and improves function significantly, in comparison to a control group (16). An analysis of 17 randomized controlled trials showed that pain could be relieved, and function improved, by either individualized or group

therapy (17,18). As in the present study, a recent multicenter study observed improved knee articularity in patients, with a considerable and significant reduction in the use of corticosteroids and NSAID type drugs.

Conclusion

We came into the conclusion that combined treatment with electrotherapy and NSAID is more efficient than the treatment only with NSAID. Combined treatment with electrotheraphy and NSAID is more efficient in management of pain in patients with gonarthrosis, and is more effective in increasing the amplitude of articular in patients with gonarthrosis compared to monotherapy with NSAID.

Combined treatment with electrotherapy and NSAID has better economical effects because it prevents deformation, which is an indication for surgery- arthroplastique. This study was necessary because there were very few studies for gonarthrosis treatment with physiotherapy in our country. These results will effect in a better management of patients with gonathrosis.

Based on this study we can say that is very important to combine drug therapy with physiotherapy instead of only drug therapy in treatment of gonarthrosis.

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Isolation and Molecular identification of free-living amoeba of Acanthamoeba in Tehran hospitals in Iran

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Abstract

Background: Acanthamoeba spp. Is free-living amoeba which is opportunist in immunocompromised patients, and one of major etiology for keratitis in contact lenses wearers. Regarding the increasing number of acanthamoebiasis in recent decades, investigating the environmental pollution is now a focus of more attention. Surface stagnant waters are one of the important sources for human infections.

Objective: The aim of the present study was isolation and molecular identification of Acanthamoeba in Tehran hospitals in Iran.

Methods: A total of 80 samples of surface stagnant in Tehran hospitals were collected. The samples were initially filtered using nitrocellulose filters and later the residual components on filters cultured on non-nutrient agar. The cultures were examined microscopically for trophozoites and cysts of free-living amoeba. Positive cultures for amoeba were examined by PCR method using specific primers for genus of Acanthamoeba. All the positive PCR samples were sequenced to determine the species and genotypes of the isolates.

Results: Free-living amoeba were identified in 32 (40%) of samples by culture method. In addition, Acanthamoeba were identified in 43.8% (14/32) of positive cultures showing a nearly 500bp bands. 8(60%) Acanthamoeba sp, 3 (20%) Acanthamoeba castellani, 3(20%) Acanthamoeba polyphaga, were recognized by sequencing method. By using Choromas software and obtained data analysis, 60%, 20% and 20% of sequencing samples were respectively, Acanthamoeba genus, A.castellani and A.polyphaga. The comparison of the findings and data base available on world gen Bank showed that 80% and 20% of identified genotypes were respectively T_4 and T_2.

Conclusion: According to the data obtained in the present study, the genus Acanthamoeba is a common free-living amoeba in surface stagnant in Tehran hospitals; T_4 genotype is the most dominant genotype in this study. Therefore, more attention by the regional clinicians and health practitioners regarding the potential role of such waters in transmission of infection and the amoeba-associated disease should be paid.

Key words: Acanthamoeba, Hospitals, Isolation, PCR, Molecular identification.

Introduction

Acanthamoeba is a free living amebae which as a global distribution. However, these amebae can act as opportunistic pathogen, ampizoic amebae and facultative parasite.

Some of amebae has the ability not only to live as a free-living in nature but also to get into the body of host and live as a parasite. (1)

These symbionts are one of the important factors of infection in central nervous system in human and animals which are fatal in most cases. (2)

Researchers showed that Acanthamoeba can be found in different media including swimming pools, Jacuzzi, bottled water, dust, ear and lung secretion and mammalian cell cultures. (3, 4)

Besides, amebae has been found in dialysis, dental treatment and air conditioning units, hydrotherapy pools, ventilators and plumbing system of hospitals.(5,6)

Moreover, hot water pipes and physiotherapy pools of hospitals can be suitable atmosphere for heat resistant amebae to grow. (7)

On the other sides, there is evidence that shows the biofilm formed in wetted areas of sanitation facilities can lead to diseases caused by Acanthamoeba. (8)

A biofilm is any group of microorganisms in which cells stick to each other on a surface and they are also found in venous catheters and contact lenses.(9)

In fact wide distribution of amebae in environment would increase the possibility of getting infected to Acanthamoba in people who are at high risk. (10, 11)

Despite, all the mentioned characteristics for Acanthamoeba, it is defined as a transmitter of harmful and pathogenic bacteria which plays a very important role in healthcare facilities. (12, 13)

Besides, it is worthy to take the followings into consideration: lack of information in patients and staff, incorrect and incomplete disinfection program, chillers dust and also formed biofilms in toilet which is a suitable habitat for amebae in hospitals. (14, 15)

Patients with autoimmune disease and those subject to eye trauma such as eye surgery and corneal abrasion are at high risk of getting Acanthamoeba infection. (16)

Prevalence of Acanthamoeba genotypes is linked to increases of diseases such as HIV, diabetes, etc. which Show the importance of pathogenic free-living amebae in environment. (17, 18)

Since, there has been carried out limited studies on detection of Acanthamoeba genotypes from hospital sources in Iran and that of only on dust, therefore; the aim of this study is to isolate and identify Acanthamoeba genotypes of dust and biofilms from different section of selected hospital in Tehran by using 18 sr DNA gen, PCR and sequencing which are defined as specific method to detect Acanthamoeba.

Not having any information on free-living amebae in University hospitals caused that the present study has been carried out in university hospitals in order to separate and identify Acanthamoeba molecularly.

Materials & Methods

In this descriptive study, samples were collected from 80 different sections of hospitals from available sources such as dust and biofilm between 2012 and 2013.

Dust samples were collected from air chillers, fan coil unit, emergency unit and flowers for hospital patients and similarly biofilms samples were collected from bathrooms and toilet used by patients, showers head and sink by using filters and swabs filtered after dissolving in sterile water or by using 0.45 micron filters and then cultured by using non-nutrient agar (1.5%). Samples have been done microscopic analysis after culturing in above mentioned plate. Then positive samples (Acanthamoeba positive) cloned and after submerging Acanthamoeba trophozoite and cyst in sterile PBS solution, they transferred to a micro tube and the centrifugation was carried out for 5 minutes at 4000_{rpm} subsequently enough amount of sedimentation obtained.

Extraction of DNA was performed using DNG-plus kit (Cinagen, Iran) according to the protocol the concentration of extracted DNA was measured using a nanodrop ND-100 at 260nm by ng /µl (Termo Fisher Scientific,USA). Schuster, et al (5, 6) used partial nucleotide (gen) sequences of small-subunit rrna to transcript Acanthamoeba by the use of primers. Oligonucleotides JDP_1 and JDP_2 with the sequences of (5′GGCCCAGATCGTTTACCGTGAA) and (5′TCTCACAAGCTGCTAGGGGAGTCA) used as forward and reverse primers. The PCR reaction mixtures ($25_{µl}$ of total volume) consisted of 1.25 units of taq DNA Polymerase, 20_{ng} of DNA sample, 1.5mm Mg cl_2 , 300 µm dntp and 0.2 µm of each primer which was performed by using Veriti Thermal Cycler (Applied Biosystems, USA).

The PCR conditions (32 cycles) were as follows: 1 cycle denaturing at 94°C for 5 minutes, denaturing at 94°C for 30 seconds, annealing at 60°C for 30 seconds, final extending at 72 °C for 5 minutes.

The PCR products were electrophoresed on a 1.5% agarose gel containing ethidium bromide. The fragments were visualized by using Gel-documentation (Uvitec, Cambridge, UK).

The PCR analyzed by using positive and negative controls using Choromas software.

Results

Out of the 80 studied samples 32(40%) Acanthamoeba samples were identified by free-living amebae by using culture. However by PCR, out of 32 positive samples only 14 of those (43.7%) were identified by Acanthamoeba. (Table 1)

Table 1. Frequency distribution of free-living amebae by using culture technique

Sampling location	Culture-negative		Culture-Positive		Total	%
	No.	%	No.	%		
Dust and biofilm of different sections of hospitals in Tehran	48	60	32	40	80	100

After removing amebae from culture and extracting DNA in order to identify Acanthamoeba, precisely, PCR used by specific primer (JDP_1, JDP_2) and subsequently, the fragments sizes were confirmed with bands of a DNA length 500_{bp}. (Figure 1)

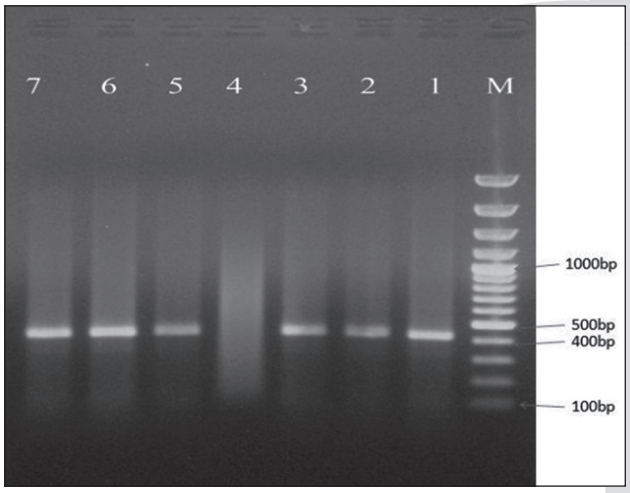

Figure 1. The PCR-products electrophoresis of culture-positive Acanthamoeba carried out in non-nutrient agar
Column 1: PCR positive control
Column 4: Negative Control
Column M: Marker
Column 3, 2, 5, 6, 7: Positive Samples

Discussion

This study showed that about 1/5 of hospital samples confirmed Acanthamoeba positive by PCR which approves potential risk of Acanthamoebiasis among groups who are exposed to it, particularly vulnerable people. This is now recognized that the wearing of contact lenses is the leading risk factor for amebic keratits and optical abrasions due to significant observation of Acanthamoeba among those who wear the contact lenses. In Iran, also, AK cases are increasing particularly among those wearing the contact lenses. (12, 16)

In a present study, the frequency of positive free living amebae (in culture) was 40% which is higher compare with the same study done in Tehran. Nevertheless, the Acanthamoeba frequency in present study by using PCR compare with another study in Tehran is almost the same. (Respectively 44% & 46%)

In a study done by Bagheri et al, out of 94 tap water samples, only 45 samples (48%) in 13 hospitals of different cities in Iran were identified by Acanthamoeba. (19) whereas in a present study, out of 80 samples, only 40% were identified by Acanthamoeba in hospitals.

In Porto Alegre, Carlesso, et al in a study done by using 135 samples from water resources on different sections of governmental hospitals showed that 47 samples (35%) were infected by free-living amebae.(20)

As sampling locations in both studies, the result of the recent study was almost the same as present study in percentage of infection to free-living amebae.

In a study done in 2006, out of 80 collected samples from water, soil and dental units 46.35% of those were infected to Acanthamoeba. Considering to sampling location of present study in both studies, the level of infection is almost the same. (21)

Studies done on 18 samples in 2009 showed that 6 dust samples were taken from hospital, 4 samples from tree, one sample from fertilizer and 2 samples were taken from laboratory which shows T_4 genotypes is a dominant among resources.(22)

In present study, the obtained result and available data in global gen bank showed that 80% of identified genotypes were respectively T_4 and T_2.

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Inclusion of molecular diagnosis of hearing loss in newborn hearing screening

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Abstract

The aim of this work is to elucidate the importance of the inclusion of genetic tests for hearing loss in newborn hearing screening protocol, through a review of mutations in the connexin genes and their implications in hereditary deafness. Thus, scientific articles published in the last seventeen years (1996-2013) were searched in the databases of *PubMed*, *and Scielo*, by using the descriptors: *"newborn hearing screening", "newborn genetic screening", "hearing loss", "connexin gene", and "deafness"*. Deafness can be caused by genetic and/or environmental factors, it can be manifested later in childhood and it cannot be detected by otoacoustic emissions equipment used in neonatal hearing screening (NHS). The molecular diagnosis is essential to complete the NHS. Currently, simple and low cost molecular tests are carried out through polymerase chain reaction (PCR) and they allow the identification of a group of genes associated with deafness. Half of the cases of non-syndromic genetic hearing loss are associated with mutations in the connexin gene, a protein involved in the communication between the cells responsible for conduction of sound stimuli. The identification of homozygous and heterozygous individuals for these mutations early in life involves the diagnosis and early deafness treatment. The inclusion of genetic testing on newborn hearing screening is extremely important to identify individuals with mutations in connexin gene, which will result in an accurate diagnosis and early treatment.

Key words: Hearing Loss, Genetic Tests, Newborn Screaning, Intercellular Junction.

Introduction

The hearing is essential for a perfect language acquisition. The peripheral auditory system of the fetus is already formed in the fifth month of pregnancy, allowing him to listen to the heartbeat and the mother's voice. Thus, the sound stimuli are among the first to be captured by the newborn (NB). From these stimuli, the NB begins to understand the environment around him by learning to interpret the sounds. Then he proceeds to develop responses through the spoken language or actions. It is through this *feedback* mechanism that the child optimizes his communication system, allowing him to aggregate intellectual and communitarian content, introducing himself in the scholar and social environment. The first two years of life are considered essential for the development of hearing and language skills. A good hearing is important to ensure the psychological, academic and lingual development of the child, as well as his inclusion and participation in society[1].

Epidemiology of deafness

The World Health Organization (WHO) in 2003 indicated that 250 million people have disabling hearing loss, representing 4.2% of the world's population[2]. These data have increased in the last estimate of the WHO, in 2012, when more than 360 million people worldwide have disabling hearing loss, equivalent to 5.3 percent of the world's population[3]. In Brazil, according to the Brazilian Institute of Geography and Statistics (IBGE), 7,574,145 feature some kind of hearing loss (2010 Census). The largest number of people with disabling hearing loss is between the ages from 20 to 34-year-olds[5]. Hearing loss is one of the most common congenital diseases, with approximately 1/1000 newborns affected by moderate, severe or profound permanent congenital hearing loss in a bilateral way[1,4].

In this context, the Neonatal hearing screening (NHS) is configured as an alternative to early identification of hearing loss. This screening consists mainly in conducting examinations, through

the use of otoacoustic emissions, to evaluate the sensitivity and ability hearing of NB. Such examinations are carried out in 24 to 48 hours after birth, and the NB should be evaluated before the hospital discharge[6].

In children, the prevalence of bilateral, sensorineural, profound and congenital hearing loss, equal to or greater than 80 dBNA is 1: 1000 per live births and children with risk indicators with moderate severe or profound hearing loss is 6: 1000[7]. By considering partial sensorineural loss, the incidence in normal live births reaches 6 to 8: 1000. Comparing with other universal screening diseases such as phenylketonuria (0,07/1000), congenital hypothyroidism (0,17/1000), sickle cell anemia (0,20/1000) or congenital adrenal hyperplasia (0,14/1000), hearing loss is significantly more frequent and therefore must be part of the universal screening protocol[8]. From this observation, in 2010 came into force in Brazil, the Federal Law No. 12,303/2010, which requires all hospitals and maternity hospitals of the Brazilian territory to perform hearing screening in all NBs.

Types of hearing loss

The deafness is defined as a decreased hearing acuity in which there is a detour or change of structures or of the hearing function, standing outside the bounds of normality. To understand the need of deafness neonatal diagnosis, it is necessary to know its different levels. According to the anatomical segment affected, hearing loss is classified into: sensorineural, conductive, central or mixed. The lesions of the external and/or middle ears (eardrum, ossicles, round or oval windows, and Eustachian tube), which hinder the capture of sound waves from the inner ear to be classified as conductive hearing loss. In cases of changes of cochlea and cochlear nerve, it is called sensorineural heraing loss[9.10]. If a problem occurs in the central hearing, it expresses the central hearing loss. There is also the mixed hearing loss, which affects the conductive and sensorineural components in the same ear[9].

Considering the manifestation period of disabilities there are: congenital hearing loss when it occurs since birth and the acquired hearing loss in postnatal life. Among the congenital hearing losses, we highlight those of genetic character. Genetic factors account for about 60% of registered cases of deafness, while environmental factors account for 30%, and 10% have idiopathic causes[11]. Among the losses of genetic causes, in developed countries, 30% correspond to syndromic forms, while 70% for non-syndromic forms[12]. In the literature there are more than 100 genes associated with non-syndromic hearing loss[13].

This article presents a review of the pathophysiology of deafness, the genetic hearing loss due to mutations in the connexin genes and the role of these gap junction proteins in the mechanism of hearing. All this prior knowledge is a base to discuss the importance of the inclusion of genetic deafness tests in newborn hearing screening protocol.

Methods

It was adopted a literature review in which were searched the scientific articles published in the last seventeen years (1996-2013) in *PubMed*, *Scielo e BVS databases*, by using the descriptors: *"newborn hearing screening", "newborn genetic screening", "hearing loss", "connexin gene", "deafness"*. The articles included should address not only the diagnosis of neonatal hearing loss, but also of the molecular and genetic aspects of that loss.

Results and discussion

The result of this work is exposed in a way that the reader can understand the importance of inclusion of molecular diagnosis of neonatal deafness, from basic concepts. Thus, this part of the article defines the molecules involved in the hearing, their mutations, and the types and ways to identify the mutant genes on hearing impairment.

Connexin, connexin 26, and communicating junctions (GAP type)

In the physiology of hearing, gap junctions are present in cochlear cells. They have an essential role in maintaining the ionic balance of the cochlear, perilymph and endolymph fluids. During the depolarization of the hair cells of the cochlea, there is a potassium output from endolymph to perilymph through potassium channels. After the passage of the potential receptor, the potassium ions spread should return to endolymph to allow new

depolarization and signal transduction (mechanical-electrical). The gap junctions, at the end of depolarization, open themselves and allow the reflow of K^+ ions to the endolymph, restoring the balance of the cochlear fluids and making them available to new stimuli[14]. Thus, it is understood that disturbances in the genesis of connexin affect the formation of gap junctions. Consequently, they interfere constitutively in the ionic balance of perilymph and endolymph, causing a hearing loss[15].

The connexins (Cx) are proteins that constitute the gap junctions, one of the most important ways for intercellular communication, by balancing ionic and metabolic interactions between adjacent cells[16]. 21 types of connexins have been identified in humans. The Cx26, Cx30, Cx31, Cx32 and Cx43, are associated to mutations that are responsible for sensorineural hearing loss, in which Cx26 is the most affected[17].

The Cx26 is a transmembrane protein which is a subunit of gap junction semi channels. Six units of connexin are required, which oligomerizes in the Golgi apparatus or in the endoplasmic reticulum to form a semichannel or connexon. It will join other semichannel in a neighboring cell membrane, constituting the set of gap junction or communicant. This association contributes to cell adhesion and communication between cytoplasm of adjacent cells, allowing the transit of ions, small molecules and metabolites up to 1kDa[18]. When a semichannel is composed of more than one type of connexin, it is called heteromeric; if a semichannel is homogeneous for a type of connexin, and its complement at the junction is formed by another type, they are called heterotypics, thus different combinations of connexin must generate channels with differentiated regulatory and functional properties[19].

The connexins 26 and 30 have approximately 77% identical amino acids from each other, and join together to form heteromeric and heterotypic channels[20]. In models of hearing impaired animals, it was proved that, in the absence of Cx30, an overexpression of Cx26 may prevent death and recover the sensitivity of the hair cells of the cochlea[21].

In that context, research strategies aim to identify the types of mutations in the genes of the connexins to understand the molecular mechanisms involved in these changes and seek alternative forms of treatments for hearing loss.

Mutations in the connexin genes

Connexin genes are implicated in several hereditary human disorders like cataracts, the Charcot-Marie-Tooth disease, oculodentodigital dysplasia, and inherited syndromic and non-syndromic hearing loss[22].

In terms of frequency in the human population, the hearing loss is the most important of the diseases linked to connexins[23,24]. Approximately 50% of all hearing impairments are due to mutations in one of the connexin genes: the GJB2 (*Gap Junction Beta-2*) encodes the Cx26; the GJB6 gene encodes the Cx30; the GJB3 gene encodes the Cx31; the GJB1 gene encodes the Cx32 and the GJA1 gene (*Gap Junction Alpha*-1) encodes the Cx43[23, 25, 26]. Patients with mutations in GJB2 gene showed statistically significant hearing loss when compared to those with no mutations[27].

In relation to the mutations of Cx26 associated to hearing loss, are classified into four types: (a) mutations that affect the transport of semichannels to the the plasma membrane or the meeting of gap junction channels*;* (b) the mutations that produce gap junctions with non-functional channels; (c) the mutations that produce channels of non-functional gap junctions that have aberrant opening or altered permeability; and (d) the mutations that produce functional semichannels in the plasma membrane that can open in physiological conditions, affecting the ionic equilibrium or homeostasis of metabolites, which decreases cell viability[19].

Inheritance patterns vary among: autosomal dominants (AD), autosomal recessive (AR), linked to X (LX) and mitochondrial[9, 10]. The mutation in Cx26 in GJB2 gene which is located on chromosome 13q11-12 is associated to an autosomal recessive disorder characterized by congenital non-progressive hearing loss known as DFNB1 (OMIM 220290)[10, 28, 29, 30, 31]. The DFNB1 is responsible for 20% of all deaf children and can be found in a carrier frequency of 2.8% in the USA[32]. In samples of 53 to 560 individuals (from newborns to adults), the prevalence of 35delG mutation carriers ranged from 0% (USA, African-Americans, England, France, Egypt) to 4.4% (Estonia)[33]. Among families with non-syndromic hearing loss in a study in the Mediterranean, 49% of cases with AR pattern had mutations in GJB2

gene[31]. In a study in the Brazilian State of Espírito Santo, it was found the occurrence of 3.9% for the same mutation in homozygous[34]. Still in Brazil was done a study with 1,856 newborns of ten different cities to verify if the ethnic composition of the various regions causes variation in the frequency of 35delG mutation. The same was found in 25 neonates (1/74), with a frequency of 1/47 in the North, 1/124 in the Northeast, de 1/64 1/64 in the Southeast and of 1/85 in the South[35]. In a study in patients who received cochlear implants, but which the cause of the deafness was determined as idiopathic, it was detected after molecular study that 31% had 35delG mutation[36].

The 35delG mutation occurs due to a deletion of a guanine at position 35 of the GJB2 gene, it is located on the long arm of chromosome 13 (13q11-12)[37], it forms a stop codon causing the formation of a truncated protein, with only 12 amino acids, which the normal amount is 226 amino acids[34]. Mutations in GJB2 gene, as the 35delG, are responsible for 80% of deafness cases in an AR pattern[38].

Due to AR pattern, the 35delG mutation, alone, does not cause deafness in heterozygosis, because the non-mutant allele of the GJB2 gene on homologous chromosome may still be able to encode normal Cx26. Thus, the heterozygosis for this mutation is not the cause for hearing loss. However, some heterozygous present auditory deficit (10 to 42% of cases), further studies are needed in the area[37]. In several European countries around 2 to 4% of the population with normal hearing possessed a mutant allele for 35delG[34]. However, it was reported a new point mutation in the GJB2 gene, the pL76P which in heterozygosis with the 35delG mutation, caused a recessive non-syndromic deafness in a Brazilian family[39].

Other mutations in GJB2 gene, which encodes the Cx26, have been associated with non-syndromic hearing loss, such as 167delT, 235delG, R143W, M34T, W24X, W77R and E47X[25, 31, 40, 41, 42, 43, 44].

The difference in prevalence is associated with ethnic diversity. The 167delT mutation is associated mainly to the Jewish population; the 235delC mutation to the East Asian population; the R143W to the population of Ghana[45]; the W77R to the Pakistani and Indian families. *Loss* of *function* mutations are the most common types in the Cx26[19].

The important role of the Cx26 gene on pathology of the dysacusia emphasizes the need for a better understanding of genotype-phenotype relationships of individuals affected. This would impact both the clinical practice as genetic counseling for dysacusia. In addition, it is important to extend this relationship to the Group of carriers (heterozygotes) of 35delG mutation in order to investigate possible differences between carriers and non-carriers individuals.

Molecular diagnosis

The polymerase chain reaction (PCR) is a process of small quantities of DNA replication. For the detection of mutations in the Cx26 genes, it is used a sample of DNA extracted from the blood, primers containing the sequence of the genetic fragment to be amplified, an enzyme to break the tape of DNA (Taq polymerase) and deoxyribonucleotide. The result follows after an electrophoresis to compare the bands formed by that and by a normal DNA. Another type of Multiplex-PCR – allows the identification of pathology, mutation, or different manifestations of the same mutation (homozygous dominant or recessive and heterozygosis) with the use of more than one pair of primers, this can also be useful in the diagnosis of mutations of Cx26 genes. Other types of PCR are also used in the detection of mutations, such as real-time PCR, asymmetric PCR, assembly PCR, PCR in Situ (ISH) and reverse transcription PCR.

In General, the PCR is not one of the most complex and costly procedure; it is a fact the need for implementation in more molecular diagnostic centers in the country, making possible the diagnosis of genetic dysacusia.

The importance of genetic testing for hearing loss in newborn hearing screening

The prior detection of hearing impairments is extremely important, especially in the first year of life; it is proved that it enables more effective results for the habilitation of children [46]. Thus, early diagnosis enables a more effective intervention, by decreasing the damage caused to the child's development and improving their prognosis, which includes school performance, psychological well-

being and social production. This intervention must occur at all levels: in **primary prevention**, with the use of awareness programs about the consequences of dysacusia, and genetic counseling; in **secondary prevention**, early diagnosis of auditory deficit; and in the **tertiary prevention**, by involving rehabilitation and treatment of conditions associated with deafness, using a multidisciplinary team, with professionals in pediatry, otolaryngology, surgery, phonoaudiology, psychology and genetics.

The Neonatal hearing screening (NHS) allows the identification of hearing loss shortly after birth, through otoacustic examinations. The *Joint Committee on Infant Hearing* defends the screening earlier than three months old, to enable the intervention before the six months [47]. The NHS can be divided into two types: behavioral and electrophysiological. Behavioral screening evaluates clinical aspects of neonate through basic tests, as: the cochlear palpebral reflex (CPR), that evaluates the eyelid movement in response to an intense sound stimuli; the *Crib-O-Gram*, in which motion-sensitive transducers are coupled to the cradle of child to detect motor responses to intense noise and the *Auditory Response Cradle*, other equipment, installed in the cradle, allows capturing various behavioral/physiological responses of the baby to sound stimuli, like scares, head movements and breathing [48].

However, the behavioral screening is little clear in the identification of dysacusias, especially in patients with no risk factors. It is estimated that if the hearing screening were performed only in children with risk factors, 50% of cases of deafness would pass unnoticed [49].

To identify with greater accuracy the hearing impairments it is used the electrophysiological screening methods, such as: Brainstem Auditory Evoked Potentials (BAEPs) or Brainstem Evoked Response Audiometry (BERA) and Transient Evoked Otoacoustic Emissions (TEOAEs) [50]. The first two works under similar mechanisms: preferably during the physiological sleep of RN, are coupled electrodes on his head, which evaluate the functional integrity of the auditory pathways from the cochlear nerve until the brainstem, estimating the sensitivity limit of way. These processes are fast, non-invasive and effective; they show low rates of false positives and false-negatives [51]. The BAEPs, however, is more complex than the TEOAEs, It may require the use of sedatives to their completion and the equipment has a higher cost [49].

The TEOAEs constitute a procedure simpler for analysis of the pre-neural peripheral auditory system. They are a register of a type of sound energy emitted by the hair cells of the cochlea during its function. These energy waves propagate from the inner ear to ear (outer ear), where they are captured by probes [52].

The viability, the efficiency of cost, and the benefits of TEOAEs were supported by several studies [53, 54]. However, the TEOAEs may suffer 3 types of limitations. First, since the target condition for most TEOAEs is permanent hearing loss > 35 dBHL, children with mild hearing loss will not be identified [55]. Second, children with onset or progressive hearing loss cannot be identified by TEOAEs, because their hearing is normal or almost normal at birth [56]. Third, even in countries where the NHS with TEOAEs was established, it is difficult to approach specific subgroups of infants, such as those who born outside of hospitals [57]. The molecular analyses should monitor NHS, by enabling early identification of dysacusias and causes of auditory deficits, their chance of recurrence in the same family and suggesting to those responsible for the child a genetic counseling, justifying the presence of the geneticist in the neonatal team [58]. Thus, the genetic tests should be carried out as a complement to the NHS and consists of o amplify a DNA sample taken from the baby's blood, which has been obtained by heel puncture, as in neonatal heel prick. And in the case of multiplex PCR multiplex allows the identification of homozygous and heterozygous for mutations in demand.

Conclusions

The Cx26 has an important role in the physiology of the human hearing, and mutations in its encoding gene compromise hearing. Thus, it is important to study this molecule in order to identify possible changes in the structure of its gene. It is aimed the availability of NHS, by the Unified Health System – SUS, for all newborns in Brazil, including, the molecular analyses for the diagnosis of non-syndromic genetic hearing loss. On the

prospects of this work, it will be encouraged the adoption of genetic testing programs in medical centers in Brazil.

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Neglected Prognosis Factors in Patients with Pulmonary Arterial Hypertension

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Abstract

Objective: Evaluation of depression and social status in pulmonary arterial hypertension patients and corelation with other prognosis factors.

Methods: The adult PAH patients' evolution included in the local registry was monitored for 6 years of specific vasodilator therapy (Bosentan / Ambrisentan / Sildenafil). Besides the commonly monitored parameters, depression (by Beck Depression Index), marital status, family support, work integration and average income were also evaluated.

Results: 52 adult patients with PAH (53.84% female; average age 48,86±15,69 years) were included, the majority from an urban area (69,23%) and with severe forms (71,15%), NYHA Class III (55,1%). Only 17 patients work (32,69%), 29 have an income below 150 euro/month; 57,69% are or were married as 7 are divorced. Moderate and severe depression is present in 71,15% with maximal values in scleroderma patients. 13 patients died (25%), 7 of these began to be noncompliant to treatment/diet/medical exams. Only 9 patients (18,36%) received a psychiatric consultation and were under antidepressive treatment for a while Increased depression and precarious social status have been identified as aggravant factor, present to 68.23% of registered deceases.

Conclusions: Life expectancy is growing, but significant decrease in ability to work, and therefore income, loss of family support and severe depression often lead to noncompliancy. Psychological assesment and social and material support become mandatory.

Key words: pulmonary hypertension, depression, social status, prognosis

Introduction

Up until the year 2000, we knew that Pulmonary Hypertension (PH) and particulary Pulmonary Arterial Hypertension (PAH) was a serious, rare, unknown illness for which not many therapeutical possibilities existed. According to Fuster V the median interval from diagnosis to death was 1.9 years, and more than three-fourths of the deaths occurred within the first 5 years after diagnosis.[1]

The apparition of numerous clinical studies and articles on the etiology, diagnosis and treatment[2-8] of this multi-etiological syndrome has triggered an alarm signal in our current practice. Hence, as of 2005 we have participated in the initiation of a national work group for diagnosing and treating PAH patients, having, at the time, two patients (both diagnosed with Idiophatic PAH).

Following the proceedings of five large university centers in our country (our clinic being one of these) the National Program (NP) of PAH patients was approved in October 2008. Consequently we had access for the first time to treatment with Sildenafil (cost of approximately €8000/ year) and Bosentan (cost of approximately €28.000/year). Initially, we treated seven patients with this program. Eventually, the number of patients increased constantly from one year to the other, reaching a total of fifty-two patients included until the end of 2013.

As of 2012, we also had Ambrisentan at our disposal. Therefore, for nine years (2005-1013) we have accumulated a great deal of experience and a rich database comprising patients with different forms of pulmonary hypertension (PH), and particularly PAH. We constantly monitored the evolution[9] of the patients in this NP treatment, applying all the tools of evaluation recommended by international guidelines (the European Society of Cardiology and the European Respiratory Society).[10]

We resorted to examinations every 3 to 6 months (or as needed in case of aggravation) with the evaluation of the clinical status and framing within the NYHA functional class, the 6-minute walking test, echocardiography, spirometry, computer to-

mography/thoracic x-ray, biological samples.[11,12] A constant connection with the patients and close members of their family was maintained (where family support existed, patients would often come accompanied). All the deaths and circumstances of death were recorded. We mention that we are a centre exclusively destined to adult patients.

We found that the evolution of patients under specific vasodilator treatment was broadly good, with improved functional class, increased exercise tolerance, and longer survival duration. The estimation tools of patient prognostic stipulated by clinical guides[10,11,12] were found to have a good predictive value, in our case too, although we also noticed the appearance of disruptive factors that radically modified the evolution of the cases.

Objective: Evaluation of depression and social status in PAH patients and corelation with other prognosis factors and deaths.

Methods: We made a retrsospective study, the adult PAH patients' evolution included in the local registry was monitored for 6 years (2008 - 2013) of specific vasodilator therapy (Bosentan/Ambrisentan/Sildenafil).

According to etiology, severity and possibility of addressing within the clinic, controls from 3 to 6 months were realised, with the monitoring of usual parameters (clinical, biological, echocardiographic, 6-minute walking test, spirometry, as well as dynamic imaging evaluations). When including every patient in the program, we noted the marital status (married/ single/ divorced/ widowed), family support (whether they have close relatives able to tend to the patient), level of education, origin (urban/rural), distance from the clinic, work integration and average income. In addition, a depression questionnaire was applied that is the Beck Depression Index, the version (Beck &Steer 1993) with 21 groups of four statements relating to symptoms of depressive disorder. Respondents report how they are filling at the moment of the evaluation . Responses in each cluster are scored numerically with a 0 to 3 representing level of severity (range for measure is 0-63). Recommended cut-offs: none to minimal depression < 10, mild to moderate 10-18, moderate to severe19-29 and severe depression 30-63. Usually takes 5-10 minutes to complete. We try to monitor daily physical activities through pedometry (Canyon pedometers), but we have not received results from all patients. We have not applied similar standards to all patients from the very beginnig, so we could not have a just analysis of the results.

Every visit we discussed with the patients and their attendants, if necessary, about the treatment compliance and new issues, if any. After periodical visit, each patient received a list with recommendations regarding its treatment, physical activity and the diet. Afterwards the contact with the patients was done by telephone monthly or every time the patients needed and requested. The nurses have questioned the patients about their adherence to each chart, and encouraged them to continue their diet, physical training and treatment as recommended. Throughout surveillance, modifications occured in the situation of patients with psychosocial status indicators were registered. All the deaths and aggravating circumstances leading to them were also registered.

Results

During six years, 52 patients were enrolled (figure 1), 28 of which were females (53.84%), and 24 male (46.15%), with an average age of 48,86 ± 15,69, the majority from an urban area (36 cases, 69.23%), and 37 patients with severe forms (71.15%), most of them with NYHA Class III (55,1%).

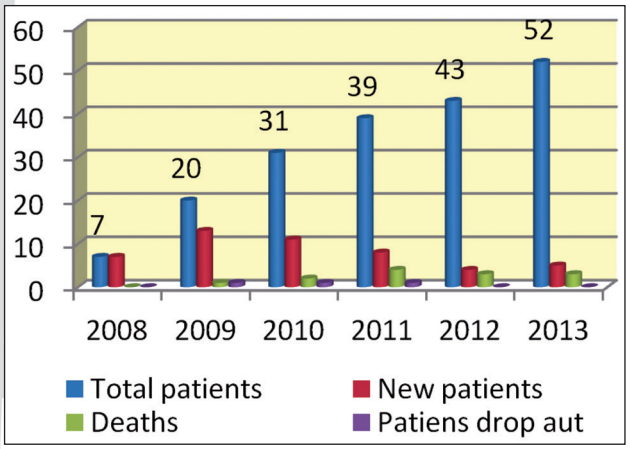

Figure 1. Dynamic of patients enrolled in the local PAH Registry Treatment Program

Etiologically speaking, 16 of them (30.76%) were idiopathic, and 36 withs associated/secondary forms. Among the IPAH, the average age was 46.93 ± 6.2 and females were predominant (9, 56.26%). Within the majority of secondary/associated forms the etiolology was congenital cardiac malformations (19 cases, 52.77%),), 6 collagenoses (16.66%),

5 with chronic pulmonary thromboembolism, and other 7 cases (HIV infection, Down syndrome, histiocytosis X, COPD associated (table 1).

Table 1. Etiology of PAH forms treated through the local registry between 2008 - 2013

Etiology	Patients / Gender	Deaths
Idiophatic PAH	16 patients (30.76%) 9 ♀ / 7 ♂	3 2♀/1♂
Associated / secondary forms of PAH/PH	36 patients (69.24%) 19 ♀ / 17 ♂	10 3♀/7♂
	19 cardiac malformations 6 collagenoses 5 chronic pulmonary thromboembolism 3 forms COPD associated 1 case HIV infection 1 case Down syndrome 1 case histiocytosis X	

Only 17 of the patients work (32.69%). 29 patients have a low income (below €150/month), 18 have average incomes and only 5 have sufficient income. 57.69% are or were married, and 7 are divorced. At last evaluation only 15 patients (28.84%) had no significant elements of depression (absent or mild), the remaining 37 patients presented moderate forms (21 patients, 40.38%) and severe (16 patients, 30.76%), with maximal values in scleroderma patients. 13 patients died (25%, the average age 56.6 years), 7 of these began to be noncompliant to treatment/diet/medical exams. Only 9 patients (18,36%) received a psychiatric consultation and were under antidepressive treatment for a while. Increased depression and precarious social status have been identifies as strong aggravating factors present to 69.23% out of registered deaths (figure 2).

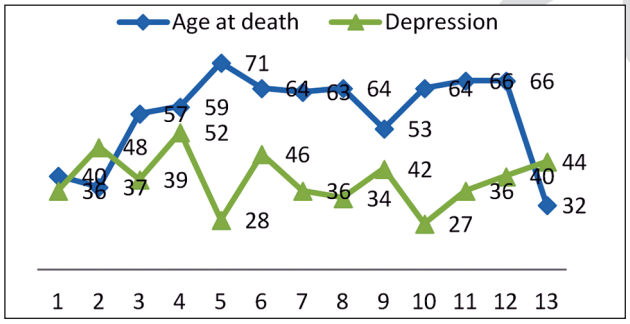

Figure 2. The last depression status in dead patients

A great etiologic variety was remarked, but in particular the high number of cardiac malformations (19 patients), the majority of which were discovered late, thus inoperable (this demonstrates serious deficiencies in diagnosing these disorders). As expected, the female sex is predominant, particularly due to idiopathic and collagenous forms. We ascertained an increase of the annual age average throughout the 6 years of monitoring, with an average rate of 1.32 / years, and, implicitly, of survival. At the same time, we observed the loss/ decrease of family support by the high divorce or death rate of the supporting members of the family (parents, husbands/ wives). Founding and maintaining a family was difficult, so only 30 (57.69 %) are/were married, and 7 have divorced. Dealing exclusively with adult patients, we distinguished the low percentage of 32.69% of those who work or have worked at some point. Being unable to work, most of them are medically retired or have the status of disabled person, and, implicitly, the scarce income that greatly limit their living possibilities of these patients (29 bordering poverty).

Being a chronic disease, it needs multiple monthly investigations (liver enzymes, complete blood count, INR, etc.), some of them costly, hardly accessible (ecography, CT, right catheterization), expensive and complex therapies, and a frustrating lifestyle (low-salt diet, oxygen dependence). In time, all these elements inevitably affect the psyche. The greater the distance is to the clinic, laboratory or family doctor, the lower the number of examinations and adherence to treatment. Many patients have accused major difficulties in moving both related to the disease (dyspnea, fatigue, oxygen dependence) and to economic matters (overbudged costs).

The analysis of all registered deaths revealed the constant association of psychosocial factors that undoubtedly contributed to their occurrence. All these influence the quality of life and the level of adherence to diet and recommended treatment. Among these, we particularly mention the degree of psychical alteration. Depression, which we identified in medium and severe forms in 71.15% of the patients (directly linked to severity of illness and age of onset, as well as social condition), was reported by several other studies.[13-17] If major depressive disorder is estimated to have a prevalence in the general population of approximately

5%-6% (Kessler RC et all)[16], the prevalence of depressive symptoms in outpatients with left-sided cardiac failure is estimated to be approximately 30%, and in this population, depressive symptoms have a significant impact on functional status and quality of life.[17] Among patients with PAH, the REVEAL Registry found that 25% of patients report a history of depression[18]

The image of these patients is of tired, ill facies (cyanotic), sad, poor and hopeless young adults. They gradually isolate, significantly reducing their current social relationships and daily activities (proven with pedometer, that is achieving the average of the entire group of only 4426,12±2568.34 steps/day).

Consequently, it lowers the level of adherence to the lifestyle and recommended treatment, going as far as deliberate suicide by abandoning all treatment and diet (two such cases were recorded by us, being only 15.38% of all deaths). The analysis of all death cases throughout the 6 years, revealed the constant association of these psychosocial factors, which have undoubtedly contributed to their occurrence (identified in 9 deaths out of 13).

A study published in 2013 by *Wen-Hu*[19] also shows that the a lower socioeconomic status is strongly associated with a higher risk of death in idiopathic PAH. Moreover, the authors believe that this association was independent of clinical characteristics, hemodynamics, and treatment.

We believe that for a correct prognostic evaluation of PH patients, with given parameters[11,12] new criteria must be defined to quantify precisely these aspects (depression, compliance to treatment and diet, daily activity, income and social support). We suggest to every visit the completion of a brief questionnaire on these issues and monitor their current physical activity by pedometer. Any worsening of the physical or social status requires psychological counselling, possible hospitalization or temporary institutionalization.

Conclusions

The altered psychological and social status has a determining role in the prognosis of PAH patients. In addition to specific pharmacological treatment, prompt and efficient intervention is also needed for psychological and social support.

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Comparison of celiac disease prevalence in patients with type 1 diabetes and normal population considering tissue-transglutaminase antibody and anti-endomysial antibody

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Abstract

Background: Considering genetic and autoimmune connections between Celiac Disease (CD) and Type 1 Diabetes (T1D), we aimed to compare CD prevalence in patients with T1D and normal population considering tissue-transglutaminase antibody (IgA tTG-Ab) and anti-endomysial antibody (IgA EMA).

Method: Current analytical cross-sectional study was conducted on 128 diabetic patients, using convenience sampling. They referred to Tehran Rasoul Akram Hospital and Ali Asghar Children's Hospital between years 2002 to 2011. Levels of IgA tTG-Ab, IgA EMA, and total IgA were measured by ELISA method in all diabetic patients' serum. Only patients with their IgA reported as "sufficient" were included. Data was compared to whom obtained from a methodologically powerful study of Tehran University of Medical Sciences which aimed to determine the prevalence of CD in Iranian population using IgA tTG-Ab and IgA EMA. The data was analyzed in SPSS version 13.

Results: The IgA tTG-Ab was positive in seven diabetic patients (7: 128), whereas the ratio was 29: 2799 in normal Iranian individuals according to mentioned study. All seven IgA tTG-Ab positive patients were EMA positive in current study, whereas only five were simultaneously positive for EMA in aforesaid study. So considering compatible IgA tTG-EMA-based diagnosis, there is a significant difference in CD prevalence between type 1 diabetic patients and normal Iranian population (OR 32.3273, 95% CI 10.1139- 103.3283, P-value < 0.0001).

Conclusion: It is suggested that in Iranian populations, prevalence of CD in Type 1 Diabetic patients is significantly higher than its prevalence in normal individuals considering seropositivity.

Key words: Celiac Disease, prevalence, Type 1 Diabetes, IgA anti Endomysial antibody, IgA anti-tissue transglutaminase antibody

Introduction

Celiac Disease (CD) is an autoimmune enteropathy that occurs in genetically susceptible individuals. It would be triggered by an inappropriate T-cell-mediated immune response to the ingestion of specified dietary grain proteins. If untreated, it can lead to intestinal villous atrophy, causing symptoms like diarrhea, malabsorption, failure to thrive, weight loss, and also extra intestinal symptoms (e.g. iron deficiency, anemia, osteoporosis, neurological deficit, and depression) (1).

Over last few decades, development in serological tests with higher sensitivity and specificity has changed previous diagnostic criteria for CD, which required endoscopy with small bowel biopsy(2).

Previous studies have shown that when the IgA tTG-Ab titer were changed to >100 and <20 U and IgA levels is verified, the sensitivity and specificity stands very high. Patients with mid-range TTG values (20 –100 U) or values of <20 U with negative IgA status should continue to undergo biopsies for diagnosis of CD (3). Kalle Kurppa's study demonstrated that irrespective of the initial serum titers or clinical presentation, EMA positivity as such is a very strong predictor of a subsequent CD

diagnosis (4); and Akbari et al. have shown that the sensitivity and specificity of the human-recombinant IgA tTG-Ab assay were 100 and 99%, respectively, whereas the results for IgA EMA were 19 and 100%, respectively. They also have been suggested that IgA EMA was positive in cases with advanced mucosal lesions of the small bowel (5). Consequently current study's diagnosis of CD was based on compatible positive serology for IgA tTG-Ab and IgA EMA.

It has been shown that CD is associated with HLA-DQ2 and HLA-DQ8 genetically(6). CD and other autoimmune (e.g. T1D) coherence is suspected. Additionally it seems T1D also would associate with HLA-DQ2. About one third homozygote diabetic patients, suffer from CD. The ratio for patients without the gene is only 2%.(7)

We aimed to determine CD prevalence in type 1 diabetic patients and to compare the prevalence with CD prevalence in a normal population, considering compatible IgA tTG-EMA-based diagnosis.

Method and material

We conducted a analytical cross-sectional study in which the data was compared to a methodologically powerful study conducted by the Tehran University of Medical Sciences. One-hundred twenty eight type 1 diabetic children, who were hospitalized in Rasoul Akram Hospital and Ali Asghar Children's Hospital from 2001 to 2010, were recruited. All patients with sufficient level of IgA which was measured at least one-year after diagnosis of their T1D were entered our study. In clinical follow-up, the serum levels of IgA tTG-Ab, IgA EMA, and total IgA was measured by ELISA method in all diabetic patients.

Assay kits were as followed:

Serum concentration of IgA EMA and IgA tTG-Ab was assayed by ELISA kit (Inc. AESKO) with diagnostic accuracy of 15 U/cc and ELISA kit (Inc. Euroimmun) with diagnostic accuracy of 20U/cc, respectively.

The recordings were compared to measurements obtained from mentioned methodologically powerful study. Mentioned study was conducted by Tehran University of Medical Sciences Digestive Disease Research Centre with a great collaboration of Kerman University of Medical Sciences and Mazandaran University of Medical Sciences. Using a stratified random sampling method, a total of 2799 individuals (1438 from Sari and 1361 from Kerman) were enrolled the study to determine the prevalence of CD in Iran. IgA tTG and IgA EMA were determined in the serum of all subjects. (5)

Information about age, height, weight, years after diabetes diagnosis, Fasting Blood Sugar (FBS), hemoglobin A1C (HbA1C), and celiac auto-antibodies was gained reviewing their hospitalization and clinical recordings. Data about years after diabetes diagnosis, whether diagnosis based on Diabetic Keto-Acidosis (DKA) for the 1st time, family history of type one diabetes, drug history before diagnosis, and digestive symptoms (e.g. abdominal pain, diarrhea, and constipation) were also collected.

The study complies with the Declaration of Helsinki and unwritten informed consent was obtained from every patient.

The data was analyzed by SPSS version 13. For qualitative variables, absolute and relative frequency was used; rather quantitative variables were reported as mean± SD. To compare quantitative variables among diabetic patients and normal Iranian population, we used a Non-parametric Chi-square test and Mann-Whitney U test. The association between CD and T1D, also IgA tTG-Ab and IgA EMA was determined using Odds Ratio (OR), together with 95% Confidence Interval (CI).

Findings

We included 128 type 1 diabetic patients, with mean age of 9.17 (SD=2.86). Data on patients' height, weight, years after diabetes diagnosis, Fasting Blood Sugar, HbA1C are mentioned in table 1. Celiac IgA tTG-Ab and IgA EMA were positive in seven enrolled patients (5%). Among these, mean serum levels of IgA tTG-Ab and IgA EMA were 25 U/cc (SD= 6.07) and 41 U/cc (SD= 6.08) respectively.

The IgA tTG-Ab was positive in seven diabetic patients (7: 128), whereas the ratio was 29: 2799 in normal Iranian individuals according to mentioned study. So IgA tTG-Ab positivity has yielded a significant difference in CD prevalence between type 1 diabetic patients and normal Iranian population (OR 5.5258, 95% CI 2.3731 to 12.8668, P-value< 0.0٠01).

Table 1. Demographic data

	Mean	SD	Minimum	Maximum
Age	9.17	2.86	1	16
Height(cm)	123.7	15.62	74	167
Weight(kg)	26.4	7.2	7.5	43
Years after diagnosis	2.27	1.41	1	6
Fasting Blood Sugar(mgr/dl)	131.85	20.06	82	176
Hemoglobin A1C	7 %	0.4	6.5	8.4

Table 2. Celiac auto-antibody prevalence

Celiac Disease Auto-antibody	Type one diabetic patients	Normal Iranian Population	Odds ratio	Confidence interval	P-value
IgA tTG-Ab	7: 128	29: 2799	5.5258	2.3731- 12.8668	< 0.0001
IgA EMA	7: 128	5: 2799	32.3273	10.1139- 103.3283	< 0.0001
Compatible IgA tTG-Ab with IgA EMA	7: 128	5: 2799	32.3273	10.1139- 103.3283	< 0.0001

In current study, all seven seropositive patients for IgA tTG-Ab were EMA positive, whereas only five (5: 29) were simultaneously positive for EMA in Tehran University of Medical Sciences' study. Multivariate analysis revealed a strong significant association between IgA tTG-Ab and IgA EMA in type 1 diabetic patients compared to normal population (OR 66.8182, 95% CI 3.2987- 1353.4485, P-value = 0.0062).

So considering compatible IgA tTG-EMA-based diagnosis, there is a significant difference in CD prevalence between type 1 diabetic patients and normal Iranian population (OR 32.3273, 95% CI 10.1139- 103.3283, P-value < 0.0001).

In diabetic patients with positive serology for CD, mean FBS and HbA1C was 130.00 (SD= 18.11) and 7.2 (SD=0.45), mentioned values were 131.96 (SD= 20.29) and 7.23 (SD= 0.44) in sero-negative patients, respectively. None of them have significant difference across two sero-positive and sero-negative groups, using Mann-Whitney U test (P-value= 0.816 for FBS and P-value= 0.767 for HbA1c).

Diabetic diagnosis was based on DKA for the 1st time in five out seven sero-positive patients (71.4%); while the ratio for sero-negative patients was 54 out 121 (44.6%). This gave an OR 3.1019 with 95% CI 0.5789- 16.6194.

So FBS level, HbA1C levels, and DKA incidence as the 1st manifestation didn't show a significant difference between serologically positive and negative type 1 diabetic patients.

Among all the 128 type 1 diabetic patients, 12 have a family history of T1D among their first-degree relatives, two of which (16%) diagnosis were made after DKA occurrence as the 1st manifestation. Diabetes diagnosis was based on DKA occurrence in 59 (46%) patients, among which two have positive family history of T1D and 57 ones doesn't. So positive family history of T1D is significantly associated with DKA-onset T1D (OR 0.2070, 95% CI 0.0434- 0.9864, P-value= 0.0480)

Considering these 59 DKA-onset diabetic patients, 39 (66%) cases reported their previous referral for their diabetic symptoms, but misdiagnosed and wrong treatment (Antibiotics in 16 cases, anti-emetic drops in 35 cases, and acetaminophen in 37 ones) was administered.

Considering clinical documentations, 51 out 128 cases (39%) had experienced gastrointestinal symptoms such as abdominal pain, constipation, and diarrhea.

Disscusion

Considering sero-positivity, prevalence of CD in Type 1 Diabetic patients is significantly higher than its prevalence in normal individuals. Those with T1D had more than a 32-fold increase in the odds of CD prevalence.

As the people aged, the incidence of celiac disease rose. Echoing the findings of other studies, a 2008 Finnish study in Digestive and Liver Disease found that the prevalence of CD in the elderly is

nearly two and a half times higher than the general population (8-10). Considering a significant age difference (P-value <0.001) between our patients (9.17) and mentioned study's (35.4), the effect size would be greater than it has been shown here. So the importance of CD screening among diabetic children would be higher than what has been demonstrated. Since most cases were undiagnosed, active case finding by serologic screening is encouraged. Increased awareness of the disease and extensive availability of accurate serological tests can also lead to improved diagnosis of this disorder, both in children and adults.

Celiac prevalence in type 1 diabetic patients was studied in many countries, where it is 4.1% in western countries (11, 12), 2.8% in Cuba (13), 5.48% in Egypt (14), and 2.4% in Brazil (15). The age of the patient and duration of disease can affect the prevalence, and more studies should be done to determine the effects of ethnic, genetic and environmental factors such as diet to identify the reasons for these differences. Our study showed that the prevalence of CD in diabetes mellitus type 1 children in Iran is 5.47% similar to that observed in Egypt; but considering our small sample size would simply confound our descriptive data as Iran CD prevalence, make it invalid.

Findings have shown that a positive family history for T1D significantly can decrease the risk of DKA as the 1st manifestation of T1D. An Italian study reveals that about 13% of diabetic children with positive family history for T1D diagnosed after DKA occurrence, while the ratio was 37.4% for non-diabetic children (p-value< 0.001) (16). A Finnish study has also demonstrated above percentages as 7.4% vs. 20.5% (p-value<0.001) (17)

DKA, not as single-stage syndrome, ranged from mild and non-specific symptoms (e.g. weakness and fatigue) to more severe ones (such as coma). So being familiar to diabetes symptoms is necessity for children's parents and would potentially lead to early referral to medical centers before DKA severe symptoms occurrence.

Considering the effect of DKA severity and duration on its complications, and a growing need to prevent late diagnosis, physicians and health policy makers have to focus their most endeavors on "diabetes symptoms education". These findings would emphasize the importance of T1D and DKA symptoms education. Such an appropriate education will lead to early diagnosis and DKA complications prevention.

Delayed diagnosis and coma occurrence would increase the chance to which irreversible injuries will occur. These also may emphasis the importance of medical staff awareness about early and non-specific symptoms (e.g. weakness, fatigue, weight loss, polyuria, and polydipsia).

Here we focused on some other limitations existed:

Having a small sample size may be among our descriptive study limitations, but because of a significant difference yielded in CD prevalence between two populations it is not amongst our limitations in analytical comparisons.

Lacking age-matched control group were also amongst.

There is a probability of hypoglycemia and reduced need for insulin in diabetic patients with celiac, which has not been detected in our study. We did not investigate hypoglycemia in a month before or after. Additionally similar HbA1C in sero-positive and sero-negative groups couldn't rule out the blood glucose fluctuations in sero-positive group.

Conclusion

It is suggested that in Iranian populations, prevalence of CD in Type 1 Diabetic patients is significantly higher than its prevalence in normal individuals considering seropositivity, so it might be beneficial to screen celiac auto-antibodies in diabetic patients.

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All authors have participated sufficiently in the intellectual content, conception and design of the present study. Arash Balouch did data acquisition. He also collaborated in data analysis/interpretation together with Faeze Gohari. All authors have participated in drafting the manuscript, critical revision of the manuscript and approval of the article.

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Intima media thickness of big vessels in COPD patients and the relation of this situation with pulmonary hipertension

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Abstract

Introduction: The aim of the present study was to investigate and compare the carotid and brachial intima media thicknesses in chronic obstructive pulmonary disease (COPD) patients with and without pulmonary hypertension (PHT).

Material and Methods: A total of patients separated in three groups were involved in the study. Group 1 consisted of 47 COPD patients with PHT, Group 2 was composed of 71 COPD patients without PHT, and Group 3 was made up of 37 healthy controls. Demographic features, biochemical markers, and carotid and brachial arterial intima media thicknesses (IMT) were comparatively assessed in these 3 groups.

Results: The mean ages for Groups 1, 2 and 3 were 59.7±9.0, 55.0±10.2 and 57.6±9.7, respectively. Age, gender and smoking habit was detected equal in three groups.Prevalences of diabetes mellitus (p=0.06) and hypertension (p=0.11) were similar between groups. Carotid IMT, brachial IMT, hemoglobin, hematocrit, serum levels of triglycerides, cholesterol, LDL, oxygen saturation, CRP, and HDL exhibited statistically significant difference between controls and COPD patients. When Groups 1 and 2 are compared; only the right carotid arterial IMT was found to be thicker in Group 1 (p=0.006). The other parameters studied were found to be similar between COPD patients with and without PHT.

Conclusion: Our results have shown that COPD and PHT may result in significant changes in IMTs of carotid and brachial arteries. While there is an obvious difference between intima media thickness of control and COPD groups, no important difference was detected amongst patients who have pulmonary hipertension and those who don't have in COPD group. Further prospective, randomized, double-blinded trials are required to unveil the actual potential of IMT in the diagnosis and follow-up.

Key words: Carotid artery; brachial artery; intima media thickness; chronic obstructive pulmonary disease; pulmonary hypertension.

Introduction

Chronic obstructive pulmonary disease (COPD) has a prevalence of 10% in adults and is not only a major cause of mortality and morbidity worldwide but it also constitutes a challenge in terms of prevention, treatment, and cost. Pulmonary hypertension (PHT) is defined as a resting mean pulmonary artery pressure ≥ 25 mm Hg and is confined to World Health Organization (WHO) classification group III in case it is associated with COPD [1,2]. Pulmonary hypertension in patients with COPD can cause reduced functional capacity and cor pulmonale. In this circumstance, mortality and morbidity will increased and more health-care resources will be used. Significant effort has been spent to treat PHT in COPD patients to improve the clinical outcomes, but only limited success could be achieved. However, the entire pathophysiological mechanism and its potential influences of PHT in COPD currently still remain vague. There is renewed interest in understanding the mechanisms contributing to PHT in COPD as the basis for exploring new therapeutic strategies [2-5] .

The pathogenesis of PHT in COPD is complex and multifaceted. Mechanisms that contribute to the pathophysiology are hypoxia, acidemia, dynamic pulmonary hyperinflation, inflammation,

pulmonary vascular remodeling and endothelial dysfunction [1-4]. Intima media thickness (IMT) is a quantitative index of atherosclerosis and has been linked to coronary heart disease [6]. In healthy adults, IMT ranges from 0.25 to 1.5 mm, and values >1.0 mm are mostly accepted as abnormal [7]. Ultrasonographic diagnosis of increased IMT in an individual under risk of atherosclerosis might aid in stratification of the risk factor and better justification of the decision to treat and to monitor the efficacy of preventive therapy. Carotid and brachial arterial IMTs can be used for prediction and evaluation of the course of atherosclerosis and for foreseeing the subsequent clinical complications. Intime media thickness of carotid and brachial arteries were measured in our study because they are the big vesels of the body which are thought to reflect atherosclerosis.

Early detection of these changes may help to slow the progression of the atherosclerotic disease and enhance the treatment of the underlying illness [6,7]. Therefore, the screening and detection of the risk factors for IMT are quite important before symptoms or disease really exist.

Carotid IMT, which is an indirect measure of coronary artery disease, had been reported to be increased in COPD patients [8]. However, to our knowledge, the impact of pulmonary hypertension on intimal hyperplasia has not been investigated up to now. In this study, we aimed to compare the IMTs of carotid and brachial arteries in COPD patients with and without pulmonary HT and to investigate any correlation with demographic and biochemical parameters. The difference of our study from other studies is that we evaluated brachial arteries and also compared the results of the COPD patients who have pulmonary hipertension and those who have no pulmonary hipertension.

Patients and methods

Study Design: This study was approved by the local Institutional Review Board and was performed between January 2013 and May 2013 in accordance with the principles of the Helsinki Declaration. Written informed consent was obtained from all patients prior to involvement in the study. Forty-seven COPD patients with PHT (pulmonary arterial pressure ≥25 mmHg at rest) and 71 COPD cases without PHT (pulmonary arterial pressure <25 mmHg at rest) that admitted to the chest diseases department of our tertiary center constituted Groups 1 and 2 respectively, whereas Group 3 serving as the control group was composed of 37 healthy volunteers.

The patients had been diagnosed with COPD and PHT at different periods. The clinical history was closely investigated, and physical examination together with chest X ray, electrocardiography, echocardiography, ambulatory blood pressure monitoring, and ultrasonographic examination of the carotid and brachial arteries were conducted in all cases. All patients included in the study were with severe or very severe COPD. COPD severity was defined according to the GOLD criteria: severe if FEV1/forced vital capacity (FVC) <70% and FEV1 30–50% predicted (GOLD Class III) band very severe if FEV1/FVC <70% and FEV1 <30% predicted (GOLD Class IV) [9].

Exclusion criteria were acute coronary syndrome, ischemic heart disease, systolic blood pressure ≥220 mmHg, pulmonary restrictive disease, stroke, malignancy, renal insufficiency, liver disease and uncontrolled diabetes mellitus.

The controls had no systemic or cardiovascular diseases with completely normal physical examination, chest X ray, electrocardiogram, and Doppler echocardiogram results. Blood pressure measurements were made to the nearest 5 mmHg with a standard mercury column sphygmomanometer on the right arm of subjects sitting after a 5-minute rest. Hypertension was described as the systolic BP of >140 mmHg and/or a diastolic BP of >90 mmHg calculated as the mean of three measurements in at least three visits at 1-week intervals or under antihypertensive treatment [10]. Smoking was defined as current smoking or having a history of habitual smoking.

After overnight fasting, levels of blood glucose, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, CRP and D-dimer were evaluated from blood samples drawn by venipuncture. Enzymatic colourimetric method by clinical chemistry auto-analyzer (Aeroset, Abbott Laboratory, Abbott Park, IL, USA) was used in this purpose.

Outcome parameters: In addition to C-IMT and B-IMT measurements, age, gender, pulmonary artery pressures, co-existing systemic disea-

ses such as diabetes mellitus, hypertension, smoking habit, oxygen saturations and ejection fractions were recorded. Serum levels of hemoglobin, hematocrit, cholesterol, triglycerides, low density lipoproteins (LDL), high density lipoproteins (HDL), C-reactive protein (CRP) and D-dimer were assessed and compared between groups.

Ultrasound measurements: All patients were evaluated by high-resolution ultrasound via IMT measurement was performed via B-mode ultrasonography (Applio Ultrasound, Toshiba Medical Systems, Tokyo, Japan) with a sectorial probe of 7.5 MHz with axial and lateral resolution of 0.15 mm. The transducer was manipulated having the near and far walls of the common carotid artery (CCA) parallel to the transducer footprint, and the lumen diameter was kept as maximum in the longitudinal plane. The point which is 1 cm proximal to the carotid bifurcation was identified, and the IMT of the far wall was measured in the distance between the lumen–intima interface and the media–adventitia interface [11].

The IMT measurements made on 4 consecutive sites at intervals of 1-mm, and the average of the four measurements was used for analyses. The average of sequential to the measurements taken from both right and left CCAs was calculated. All measurements were made manually on images obtained during the ultrasonographic scanning.

Subjects were maintained in supine position and the images were obtained bilaterally of the proximal CCA to distal CCA, including bifurcation, internal carotid artery (ICA) and external carotid artery (ECA). For having greater precision and reproducibility, each subject had IMT measured on the far wall of the distal CCA. A single experienced examiner who was blinded to the data performed all the measurements.

Statistical Analyses: Data were analyzed using the Statistical Package for Social Sciences 19.0 for Windows (SPSS Inc., Chicago, IL). A normal distribution of the quantitative data was checked using Kolmogorov-Smirnov and Shapiro-Wilk tests. Parametric tests were applied to data of normal distribution and non-parametric tests were applied to data of questionably normal distribution. Independent-samples t-test was used to compare independent groups. Paired t test was used to compare groups of independent continuous variables. The distribution of categorical variables in both groups was compared using Pearson chi-square test. Data are expressed as mean±SD or median (interquartile range), as appropriate. All differences associated with a p value <0.05 were considered as statistically significant.

Results

The mean ages for Groups 1, 2 and 3 are 59.7±9.0, 55.0±10.2 and 57.6±9.7. Age, gender and smoking habit was detected equal in three groups.Prevalences of diabetes mellitus (p=0.060) and hypertension (p=0.110) were similar between groups. Carotid and brachial arterial IMTs, biochemical, respiratory and cardiovascular parameters are shown in Table 1. Hemoglobin, hematocrit, LDL, triglycerides, cholesterol and oxygen saturation values are expressed in mean±standard deviation, while HDL, CRP and D-dimer levels are referred as median±interquartile range. As it can be seen obviously, carotid IMT, brachial IMT, hemoglobin, hematocrit, serum levels of triglycerides, cholesterol, LDL, oxygen saturation, CRP, and HDL exhibited statistically significant difference between 3 groups.

When Groups 1 and 2 are compared; right carotid arterial IMT was found to be thicker in Group 1 (p=0.006). Other than this, the other parameters were found to be similar between COPD patients with and without PHT. Compared to the control group, COPD patients (with / without PHT) had significantly diminished oxygen saturations (p<0.001), elevated CRP levels (p<0.001).

Discussion

Chronic obstructive pulmonary disease (COPD) is a major international health burden and is responsible for substantial morbidity and mortality [12-14]. It may be complicated by the development of pulmonary hypertension PHT and although the severity of PHT in COPD patients is usually mild, the presence of PHT in COPD is associated with increased mortality, shorter survival, worse clinical evolution, increased hospitalizations and reduced exercise function [2,5,7]. The prevalence of PHT in moderate / severe COPD ranges from 23% to 91%, depending on selection of patients and diagnostic criteria [4]. In COPD,

Table 1. Results of IMT measurements, laboratory and respiratory data of the three groups.

	Group 1	Group 2	Group 3	p Value
Right C-IMT (mm)	0.77±0.26	0.63±0.18	0.39±0.11	<0.001*
Left C-IMT (mm)	0.79±0.28	0.70±0.19	0.45±0.11	<0.001*
Right B-IMT (mm)	0.42±0.13	0.39±0.12	0.18±0.10	<0.001*
Left B-IMT (mm)	0.40±0.12	0.37 ±0.11	0.16±0.10	<0.001*
Hb (g/dl)	15.67±2.47	16.02±2.33	14.89±1.59	0.045*
Hct (%)	47.97±8.01	48.45±7.18	44.89±5.03	0.039*
LDL (mg/ml)	102.40±42.36	120.44±36.84	111.54±31.58	0.040*
Cholesterol (mg/ml)	173.11±49.99	194.58±46.69	180.03±39.56	0.040*
TG (mg/ml)	138.11±62.77	196.11±162.72	133.67±109.62	0.015*
Oxygen saturation (%)	82.11±7.10	86.75±3.85	97.08±1.11	<0.001*
HDL (mg/ml)	42.00±11.00	38.00±14.00	45.00±17.00	0.015*
CRP (mg/ml)	0.97±1.03	0.67±0.61	0.40±0.41	<0.001*
D-dimer (mg/ml)	167.00±108.00	137.00±91.00	110.00±77.00	0.071

*(**Abbreviations:** C-IMT= carotid artery intima media thickness; B-IMT= brachial artery intima media thickness; Hb= hemoglobin; Hct= hematocrit; LDL= low density lipoproteins; HDL= high density lipoproteins; TG= triglycerides; CRP= C-reactive protein; EF= ejection fraction; min= minutes)*

pulmonary hypertension tends to be of moderate severity and progresses slowly. The development of PHT in COPD is an important prognostic indicator [1-3]. There is renewed interest in understanding the mechanisms underlying PHT in COPD to determine new therapeutic strategies.

Many factors may contribute to the development and maintenance of PHT in COPD. The most significant of which are the remodelling of pulmonary vessels and hypoxic pulmonary vasoconstriction [1,2,13]. Despite extensive investigations performed in recent years, the etiopathogenic mechanisms responsible for pulmonary vascular abnormalities in COPD are not well understood.

No single mechanism is supposed to be responsible for PHT in COPD cases. Hypoxia clearly plays a pivotal role in the development of PHT via two mechanisms. First, alveolar hypoxia results in acute pulmonary vasoconstriction of the small muscular pulmonary arteries. This process may subsequently increase pulmonary vascular resistance (PVR). Second, chronic hypoxia causes pulmonary vascular remodeling, leading to intimal thickening and neo-muscularization of the small pulmonary arterioles, which also raises PVR. We thought that the intimal thickening mentioned above may exist in carotid and berachial arteries and determination of this finding may be of use in cases with COPD and PHT [3,5]. In this aspect, our study is original and unique since we came across no articles dealing with carotid and brachial artery IMTs in COPD patients with PHT in the literature (PubMed). Even though brachial artery IMT is less sensitive to changes secondary to atherosclerosis compared to carotid artery IMT, it may serve as a co-indicator for assessment of arterial IMTs. In addition, bilateral assessment of carotid arteries helps to overcome any misinterpretations that may ensource from asymmetrical involvement.

Since we could not detect any difference in terms of IMT between COPD patients with and without PHT, our results indicate that PHT seems not to constitute an additional risk for atherosclerosis. Regarding the biochemical, respiratory and cardiac parameters, COPD patients had higher CRP levels and lower oxygen saturation than the control group. CRP may be considered as a marker of inflammation and in consequence, inflammatory process underlying the pathophysiology may contribute to the respiratory and cardiac hazards of COPD. Chronic obstructive pulmonary disease (COPD) is characterized by chronic and progressive airway destruction leading to irreversible airflow obstruction. Its cardiac manifestations are numerous including coronary artery disease, right ventricular dysfunction, pulmonary hypertension and arrythmias. Pulmonary hypertension (PHT) shares common pathophysiological basis with koroner arter disease (CAD) such as systemic inflammation and endothelial dysfunction. In this study we sought

to determine whether there is a relationship between pulmonary hypertension and CAD and whether pulmonary hypertension is an additional risk factor for the presence and extent of CAD in COPD patients.These findings need to be investigated in clinical trials conducted on larger series.

Recognition of pulmonary hypertension in COPD is usually difficult [15,16]. Symptoms such as dyspnea or fatigue, are hard to distinguish from the clinical presentation of COPD. Most of the symptoms are not specific and the physical signs occur lately at an advanced stage of the disease far after the development of PHT [15-17]. Furthermore, the identification of some clinical signs may be hindered by chest hyperinflation or the flactuations in intrathoracic pressure. Cardiac sounds may be disturbed by the presence of bronchial rales or overinflated lungs. The the typical auscultatory findings such as ejection click, increased pulmonary component of the second heart sound and pansystolic murmur of tricuspid regurgitation encountered in PHT are uncommon in COPD patients [2-5].

The sensitivity of the electrocardiogram for the diagnosis of PHT is poor (20–40%) and a normal ECG does not exclude the presence of PHT in COPD patients. The radiological prediction of PHT is even more problematic since radiological signs lack both sensitivity and specificity [13-15]. Magnetic resonance imaging is useful for the measurement of right ventricular mass, right ventricular ejection fraction and the diameter of the pulmonary artery. Its role in the diagnostic algortihm of PHT in COPD is not well established [15-17]. Doppler echocardiography is a good and noninvasive method and the pulmonary artery diastolic pressure in cases of pulmonary regurgitation can be estimated with continuous wave Doppler echocardiography.

Right heart catheterization continues to be the gold standard for diagnosis of PHT, but the main drawback is its invasiveness [18-21]. The procedure carries some risks and it can not be performed on a large scale in COPD patients [4,5]. Furthermore, there is no evidence-based study demonstrating its clinical value in advanced COPD and its routine use is not advocated [5,18]. Therefore, cheaper and more practical modalities will be useful at least to select the cases to undergo right heart catheterization [3-5]. We think that sonographic IMT measurement may be an important measure in this future. In case IMT gains validity and popularity for diagnosis or follow-up of PHT in COPD, both some silent cases can be diagnosed earlier and unnecessary invasive procedures can be avoided resulting in improved life quality and decreased healthcare cost.

Established diagnostic potential of IMT for PHT in COPD may pioneer further studies on the role of endothelial dysfunction and vascular process in the underlying physiopathology.

In conclusion we found a high prevelance of CAD in patients with COPD. But despite similar operating pathophysiological mechanisms and resultant inflammatory cascade no correlation between the presence and severity of CAD and PHT was detected.Our results have shown that COPD and PHT may result in significant changes in IMTs of carotid and brachial arteries. However, no specific sonographic changes regarding IMT could be detected for PHT in COPD cases. Further prospective, randomized, double-blinded trials are required to unveil the actual potential of IMT in the diagnosis and follow-up.

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Self-reported hypertension and cardiovascular risk factors in Brazilians aged 80 years and over

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Abstract

Objective: To investigate the association between SRH and CRFs, either isolated or clustered, in subjects aged 80 years or over.

Methods: 113 elderly subjects of both sexes, aged 80 to 95 years. The studied variables were: **dependent**–SRH, and **explanatory**–sex, age, waist circumference (WC), body mass index (BMI), percentage of body fat (%BF), glucose, total cholesterol and triglycerides. Logistic regression analysis was used to investigate the association between hypertension and CRFs.

Results: A positive association between SRH and WC ($p \leq 0.001$), BMI ($p \leq 0.001$), %BF ($p \leq 0.001$), glucose ($p=0.046$), total cholesterol ($p \leq 0.001$) and triglycerides ($p \leq 0.001$. The presence of two or more CRFs (OR=4.29, CI 1.03 to 1.31) and a BMI $\geq 28 kg/m^2$ (1.18, CI 1.82 to 10.11) demonstrated a higher risk of SRH.

Conclusion: Self-reporting is positively associated with WC, BMI, %BF, glucose, total cholesterol and triglycerides and inversely associated with being aged 86 or over.

Key words: Aged, 80 and over, Brazil, Diseases, Elderly, Hypertension

Introduction

Life expectancy of the population is growing worldwide. From 1980 to 2025, the number of elderly people aged 60 and over in Latin America and the Caribbean will, on average, double and, in some countries, triple[(1)].

Although in 2000, the population aged over 80 accounted for only 17% of the elderly population, it is projected that in 2050 these individuals will represent about 28% of this population[(2)].

It has been observed that the development of several chronic non-communicable diseases, including hypertension, which is one of the most prevalent[(3)], is associated with the aging process. This factor is considered an alarming public health problem, affecting 22-44% of the Brazilian population[(4)]. It is a major cause of morbidity and mortality, and one of the most prevalent risk factors for the development of various diseases, such as strokes and peripheral, coronary, renal and cardiac diseases[(5)]. The association between hypertension and other cardiovascular risk factors (CRFs), such as hyperglycemia, obesity[(6)] and dyslipidemia[(7)] increases the possibility of cardiovascular complications[(8)].

The relevance of this study is that these chronic diseases are responsible for more than half the deaths worldwide and more than 60% of those in Brazil[(9)]. Research that involves the association of self-reported hypertension (SRH) and CRFs in populations aged 80 years or over is scarce, especially in developing countries. Thus, the objective of this study was to investigate the association between self-reported hypertension and cardiovascular risk factors, either isolated or clustered, in a Brazilian sample of individuals aged 80 years or over.

Materials and methods

Sampling

A cross-sectional study was conducted from October 2009 to May 2010, in the city of Presidente Prudente, São Paulo state - Brazil.

Presidente Prudente is a city in southeastern Brazil (~ 200,000 habitants) with a human development index of 0.806, being the 14th largest city in São Paulo state[10].

According to the Brazilian Institute of Geography and Statistics (IBGE), the projection for the number of Brazilians aged 80 years or over for the year 2009 was 2,653,060 subjects, representing 1.1% of the total Brazilian population. Conforming to this proportion, Presidente Prudente currently has approximately 2,100 people in this age group. For the sample composition of the present study, a margin of error of 3% and an adherence of 60% were used. Thus, the total sample consisted of 226 individuals aged 80 years or over.

The President Prudente Public Health Service provided all the information on the target population including the names, addresses and telephone numbers of individuals living in the city. In order to have a sample from all regions of the city, 226 individuals were randomly invited by phone to participate in the study.

Individuals who were unable to walk (n=48), rural residents (n=11), institutionalized patients (n=25), those with pacemakers (n=7) and subjects with incomplete data (n=22) were not included or excluded from the sample. Thus, the study sample consisted of 113 individuals, aged 80 years or over, of both sexes. Individuals who agreed to participate in this study were informed about the objectives and methodology, and only those who signed the consent form were included in the sample. All protocols were reviewed and approved by the Ethical Committee of the Paulista State University (nº. 26/2009).

Self-Reported Hypertension

In order to characterize the participants as hypertensive or normotensive, the subjects answered the following question which had been translated into Portuguese and adapted for NHANES III[11]: Has a doctor or nurse ever told you that you have high blood pressure?

Information on the use of antihypertensive medication was obtained by questionnaire, and the answers were used in order to classify the subjects according to their hypertension status.

Body Composition

Body mass was measured with an electronic scale (precision 0.1 kg; Filizzola PL 150, Filizzola Ltda), and height with a wall-mounted stadiometer (precision 0.1 cm; Sanny, Sao Paulo, Brazil). Body mass and height values were used to calculate the body mass index (BMI). All participants were measured barefoot and wearing light clothing.

The elderly were categorized into normal weight (BMI < 28 kg/m^2) and overweight/obese (BMI ≥ 28 kg/m^2) to verify the association between hypertension and high BMI [12].

Waist circumference was measured at the lowest circumference between the superior border of the iliac crest and below the lowest rib with an inelastic tape (precision 0.1 cm; Sanny, Sao Paulo, Brazil), with the participants in a standing position, breathing normally, and arms relaxed beside the trunk. The measurement was recorded at the end of a normal expiration. The cutoff values of ≥88 cm for women and ≥102 cm for men were used as CRFs[13].

All anthropometric measurements were performed by the same researcher, according to standardized techniques[14].

For the assessment of total body fat, Dual Energy X-ray Absorptiometry (DXA) was used, with Lunar DPX-NT (Lunar/GE Corp, Madison, Wisconsin) equipment. The evaluation followed the manufacturer's recommendation, with the participant stationary in the supine position, their arms relaxed alongside the trunk, palms facing the thigh, throughout the examination. The results were transmitted to a computer connected to the device for later analysis. From the percentage of body fat obtained, the participants were classified as either eutrophic or having excess body fat, according to the classifications of Morrow et al[15] (men above 25% and women above 33%).

Blood Sample Analysis

Blood collection was performed after 12-hr of fasting, in a private laboratory located in the city of Presidente Prudente. Samples were collected in vacuum tubes containing gel with anticoagulant; after collection, blood was centrifuged for 10 min at 3,000 rpm, for analysis of total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and very low-density

lipoprotein cholesterol, triglycerides, and fasting blood glucose, using an enzymatic colorimetric kit processed in an Autohumalyzer A5[16]. The reference values adopted for characterization of hyperglycemia, hypertriglyceridemia and hypercholesterolemia were >100 mg/dl, >150 mg/dl, and >200 mg/dl, respectively[17].

Information on the use of antidiabetic and lipid-lowering medications was obtained by questionnaire and the answers were used in order to classify the subjects according to the risk factor.

Considering the studied variables hyperglycemia, hypertriglyceridemia, hypercholesterolemia (measured by blood sample), total obesity (measured by DXA) and central obesity (measured by WC) and their potential as CRFs, the individuals were categorized into two groups: **no risk**, in the presence of just one or no risk factors, and **at risk**, in the presence of two or more CRFs.

Statistical Analysis

The Kolmogorov-Smirnov test was used to verify the normality of the numerical data, and where the data did not show normal distribution, nonparametric analysis was applied. The quantitative variables were presented as mean and standard deviation. These variables were distributed and the comparison of risk and no risk groups was performed using the Mann-Whitney test.

The magnitude of association between the dependent and explanatory variables was made using univariate and multiple analysis logistic regression. Statistical analysis was performed using SPSS (SPSS inc. Chicago. IL), version 20.0, and the p value was set at 5%.

Results

Table 1 presents the mean values and standard deviations of the quantitative variables according to the clusters of CRF. The comparisons between those who presented zero or one CRF and those with a cluster of two or more CRFs, showed statistical differences in weight (P<0.001), BMI (P<0.001), WC (P<0.001), glucose (P=0.046), triglycerides (P<0.001), total cholesterol (P<0.001) and body fat percentage (P<0.001). When the results were compared according to sex, higher values for height (p<0.001), weight (p< 0.001), WC (p<0.001), total cholesterol (p=0.005) and body fat percentage (p< 0.001), were found in male subjects.

The prevalence of hypertension according to the number of CRFs can be observed in Figure 1. In the group of subjects that showed no CRFs, 75% did not have SRH (p< 0.001). While in the subjects with two, three or four or more CRFs, the prevalence of hypertension ranged from 71.4% to 81.5%, and these values were significantly higher when compared with non-hypertensive groups (p< 0.001).

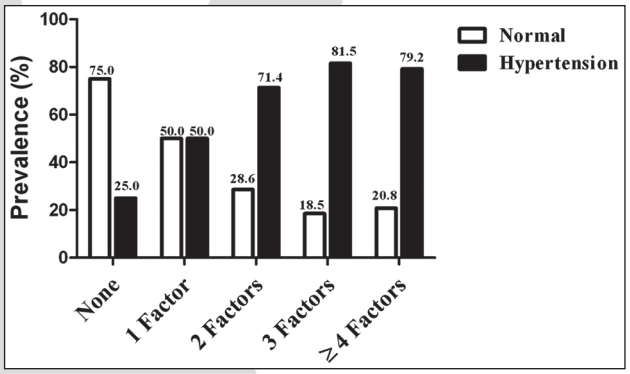

Figure 1. The prevalence of SRH according to the number of CRFs

Table 1. Mean, standard deviation and comparisons of variables according to the number of cardiovascular risk factors in Brazilian subjects aged 80 or over.

Explanatory variables	Number of CRFs		P
	< 2 factors (n=34)	≥ 2 factors (n=79)	
	Mean (SD)	Mean (SD)	
Age (years)	83.66 (3.18)	83.15 (2.60)	0.369
BMI (kg/m^2)	22.82 (2.98)	27.73 (3.91)	**≤ 0.001**
WC (cm)	81.53 (9.40)	95.82 (11.64)	**≤ 0.001**
Glucose (mg/dL)	92.76 (20.19)	103.73 (27.24)	0.046
Triglycerides (mg/dL)	92.32 (21.16)	152.73 (70.60)	**≤ 0.001**
Total cholesterol (mg/dL)	175.91 (33.27)	209.96 (39.40)	**≤ 0.001**
% Body fat	29.09 (8.84)	40.22 (7.43)	**≤ 0.001**

SD= Standard deviations; BMI= Body mass index; WC= Waist circumference

Table 2. Association between self-reported hypertension and cardiovascular risk factors, either isolated or clustered, in Brazilian subjects aged 80 or older

Variables	Self-Reported Hypertension			
	Odds ratio	CI	P	r^2
Number of factors				
< 2	1.00		**0.001**	0.08
≥ 2	4.29	1.82 – 10.11		
BMI (kg/m²)				
< 28	1.00		**0.002**	0.07
≥ 28	1.18	1.06 – 1.31		
Sex				
Male	1.00		0.513	0.00
Female	1.31	0.58 – 2.95		
Age (Years)				
< 86	1.00		**0.036**	0.03
≥ 86	0.32	0.11 – 0.93		
Final model				
Risk Factors (≥2)	2.66	0.92 – 7.69	**0.002**	0.12
BMI (≥28kg/m²)	1.09	0.96 – 1.25		
Sex (Female)	1.27	0.51 – 3.20		
Age Group (≥86 years)	0.42	0.13 – 1.34		

CI= Confidence Interval; BMI= Body Mass Index

In Table 2, with the exception of sex, statistically positive associations can be observed between SRH, the presence of two or more CRFs ($p<0.001$) and a BMI greater than or equal to 28 kg/m²($p<0.002$), whereas aged ≥ 86 years was considered a protective factor ($p=0.036$) for CRFs. The univariate analysis showed that the cluster variables explained up to 8% of hypertension.

The variables which were significant in the univariate analysis were entered into the multivariable model. In the final model, which included two or more risk factors, BMI≥28 kg/m², sex (female) and age group (≤86y), were significantly associated with hypertension, with a high explanatory power of 12%.

Of all the individuals included, 19.0% had hyperglycemia and 5.0% were smokers.

Discussion

The present study found an association between SRH and CRFs, either isolated or clustered with hyperglycemia, hypertriglyceridemia, hypercholesterolemia, total obesity and central obesity, in Brazilian subjects aged 80 or over.

In the present study, we found that individuals aged 80 years or over, with two or more CRFs are 4.29 times more likely to present hypertension. Pereira et al.[18] investigated 3,142 individuals aged 60 or over who had two or more CRFs, and found that they were 1.6 times more likely to present ischemic heart disease, which is associated with hypertension[18,19]. The effect of clustered CRFs on hypertension can increase the number of admissions up to 350% compared to those aged 75 years or over[20] without CRFs. Many of the variations observed in the CRFs, in different populations, may be understood by the clustering of these factors as they tend to act synergistically, producing an effect which is greater than the sum of their individual effects[21].

A BMI ≥28 kg/m² was associated with SRH, being 1.18 times more likely (CI=1.06 to 1.31) when compared to those with a BMI <28 kg/m². Similar results were found in another investigation composed of 426 Brazilians of both sexes, aged 60 years or over (OR=1.65, CI=1.23 to 2.20)[22]. Concerns about obesity are justified because it is associated with diabetes[23], dyslipidemia, and SRH[24].

Abdominal body fat is associated with elevated levels of glucose, total cholesterol, triglycerides and hypertension, and consequently a higher risk of atherosclerotic disease[17]. This fact was supported by the results found in the present study, since subjects with two or more CRFs presented higher WCs than those with only one or no CRFs ($p<0.001$).

Several studies have reported an increased risk of hypertension in women over 60 years[22,25-27]. However, in the present study, we found no association (OR=1.31, CI= 0.58 to 2.95), confirming the results of a study by McDonald et al.[28], which evaluated 3,810 US individuals aged 65 or over, where women presented no additional risk of hypertension, compared to men (OR = 0.82, CI = 0.62 - 1.09).

It is well documented in the literature[5] that age is a CRF for hypertension. However, in the present study, individuals aged 86 years or older presented a protection factor for SRH, compared to those under this age. This result needs to be further investigated since few studies have examined risk factors for hypertension in a sample of Brazilians of advanced age (80 years or over). Age stratifications are commonly made with individuals of 70 years or over[29], with few studies stratifying age groups above 80 years.

The study by Pereira et al.[18] may also explain this protection for CRFs in subjects of more advanced ages. These authors found, in a population consisting of the Brazilian elderly, that with increasing age, the clustering of diseases decreases, including hypertension, and that this may be explained by the early mortality of younger people exposed to these factors or because of changes in risk behavior after the illness.

In terms of public health, the present study demonstrated some important evidence to be applied in the protection against CRFs related to SRH in the Brazilian elderly population, but some limitations must be reported. Our results are from a sample from just one specific Brazilian geographic location. It should also be mentioned that the information on hypertension was self-reported.

Morbidity information enables identification of individuals who have had at least one diagnosis made in their life, but omits those who are unaware of the condition of being hypertensive and may lead to an underestimation of the prevalence of this chronic condition. However, Vargas et al.[30], based on data from the National Health and Nutrition Examination Survey III, and Lima-Costa et al.[31], based on data from Brazilian elderly, found that SRH, reported by interview, was valid for estimating the prevalence and determinant factors of hypertension in the population.

Conclusion

In conclusion, body fat and clustering of two or more CRFs increases the chance of people aged 80 years or older, presenting hypertension. These results suggest that preventive public health should be used to control these variables, in addition to preventive work in younger populations. Further studies should be conducted involving a larger number of subjects and including other CRFs that influence the occurrence of cardiovascular disease.

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Views of University Students Regarding Social Gender Roles

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Abstract

Objective: This study was conducted to determine the views of students regarding social gender roles in terms of business life, social life, married and family life.

Method: This is a descriptive study. 110 third-year students, who received education at the Faculty of Health Sciences in the academic year of 2012-2013 and accepted to participate in the study, were included in the study. A three-stage (agree, disagree, undecided) questionnaire form of socio-demographic features, which was generated by the researcher upon literature reviews to determine the views of students regarding social gender roles and involved 15 statements and 9 questions, was used as the data collection instrument. Percentage distributions and Chi-square were used in the evaluation of the data.

Results: It was determined that the age average of students who participated in the study was 21.36±1.87 and while 79.1% were female students, 20.9% were male students. Examining the views of students regarding social gender roles about business life, social life, married and family life, it was found out that there was a statistically significant difference ($p<0.05$) between genders in a great majority of statements.

Conclusion and recommendations: In the study, it was determined that while male students had more traditional views regarding business life and married life, male and female students had equalitarian views regarding social life and family life in their statements. The fact that there have been still students with traditional views regarding the social gender view in the university education shows that the university education, which targets to train intellectual individuals, has simply failed to do so and there is a necessity to raise sensitivity in students in terms of both basic professional knowledge and social gender equality.

Key words: Social gender; gender roles; university students.

Introduction

According to the universal declaration of human rights; "all women and men have equal rights to life, health, education and employment without discrimination". However, considering from past to present; many areas of social life have had an inequality model that appreciates men more than women. This inequality stands out more especially in areas such as social life, married and domestic life/roles, business life, educational status, politics and decision mechanism and availing of health services (1-7). The necessity of preventing the inequalities in these areas from negatively affecting women's social status was discussed for the first time during the 4th World Conference on Women that was held in Peking in 1995. This conference revealed the necessity of adapting the social gender view into all programs and politics in order to provide the equality of women and men (8).

While gender is a concept related with genetic, physiological and biological properties of an individual as woman or man; social gender is a concept related with the roles, duties and responsibilities attributed by the society, as well as how the society regards the individual and the perceived expectations (9,10). One of the concepts which the social gender incorporates is the social gender roles. Social gender roles traditionally express roles that are accepted to be related with both women and men. Social gender roles culturally involve personality traits and behaviors (roles) that are attributed to women and men. They place different burdens on both genders. Another truth accepted is that gender more affected by inequality resulting from social gender is woman (10).

Social gender roles show distinct differences in roles of women and men especially in business

life, social life, married and family life. Women who are exposed to social gender discrimination are also exposed to inequalities in having political, social, legal and economic rights, using these rights and having resources such as land and capital (9). Examining the reflections of social gender roles on the business life; it is observed that women are deemed worthy of working in unrecorded sectors with statutes such as casual, time, part-time jobs that pay less and receiving the permission of their husbands. Social life includes a number of judgements that disable women to go out alone at nights and live alone. Considering the family life; women are expected to hide the violence of their husbands if any and take charge in houseworks like childcare and cleaning. In married life, on the other hand, women are attributed some roles such as avoiding sexual intercourse before marriage and increasing their status by giving birth to boys. Totally opposite roles are attributed to men in these areas (10-12). As a result of this, while employment in the public sphere and politics are naturally adopted and accepted as a man thing; special areas related to houseworks and family are adopted and accepted as a woman thing (3).

Status of individuals is determined by factors such as social gender, educational background, having a regular income-generating job and equal participation in the political life (9). The aforementioned discriminations regarding business, family, married life and social life areas adversely affect the social status of women. Thus, women have failed to reach the required status and catch up with men in many areas of the society and an inequality has appeared between genders. However, traditional roles of women and men have started to change in favor of women in societies, where the educational level of women has increased and women have entered into the business life today (13).

The increase of educational level, especially the university level, brings a modern view in individuals' social gender roles and becomes a determinant for social gender equality and equity in favor of women. In addition, it is very important to raise awareness and sensitivity in society regarding social gender roles in order to provide the equality between women and men in social life and increase the social status of women. Thus, it is primarily required to determine the views of society regarding social gender roles. It is thought to be very important to investigate the meaning of roles, which are attributed to women and men especially regarding the business, family, married life and social life areas in our society, which has a traditional structure in general, in terms of university students. Furthermore, the views of the next generation regarding social gender roles could be shaped in an equalitarian way through determining the views of the young regarding social gender roles.

The study was conducted to determine the views of third-year students of Atatürk University Faculty of Health Sciences Department of Nursing regarding social gender roles concerning business life, social life, married and family life and make relevant recommendations for educational life of university.

Research Question

1-Are views of university students regarding social gender roles equalitarian or traditional?

2-Are there differences between the views of female students and male students regarding social gender roles?

Method

Type of the Study

This is a descriptive study.

Sample Group of the Study

Population of the study consisted of a total of 120 third-year students, who received education at Atatürk University Faculty of Health Sciences Department of Nursing in the academic year of 2012-2013. Since some students could not be reached on the day and hour when the study was conducted, the sample group of the study consisted of a total of 110 students.

Data Collection Instruments

Being formed by the researcher, they consist of;

1 - Questionnaire Form of Socio-Demographic Features,

2 - Three-stage (agree, disagree, undecided) 15 statements aimed at determining the views of students regarding social gender roles. These statements involve business life (four statements), social life (five statements), married life (three statements) and family life (three statements).

Data collection instruments were prepared by the researcher through using the relevant researches and literature knowledge. Besides, participating students were informed about the objective of this study before filling the questionnaire and voluntary participation and their verbal permissions were obtained. The prepared questionnaire forms were distributed and students were enabled to fill them individually.

Assessment of the Data

The SPSS 18.0 software program was used to assess the data. Descriptive statistics were calculated and comparisons were made with the chi-square test for views of students regarding the statements related to social gender roles according to their genders.

Results

Examining the socio-demographic characteristics of students who participated in the study; it was determined that students had an average age of 21.36±1.87 (aged between 19-35 years), 79.1% were female and 20.9% were male. 75.5% of students were from the city center, 38.2% stayed at state dormitories, 70.9% had nuclear family and 69.1% had more than 3 siblings. Educational level of mothers of 53.6% and educational level of fathers of 42.7% was at the primary school level; mothers of 98.2% were housewives and fathers of 64.5% were employed.

Table 1 involves views of students who participated in the study regarding the statements related to business life and social life according to their genders. While 48.3% of female students disagreed with the statement "A woman should not work without her husband's permission", 52.2% of male students agreed. While 72.4% of female students disagreed with the statement "There is no necessity for a woman to work if her husband is rich", 39.1% of male students agreed. While 80.5% of female students disagreed with the statement "Regarding women and men working under the same status in the business life, it is normal when men are given priority in promotions", 69.6% of male students, which is a great rate, agreed. While 63.2% of female students disagreed with the statement "Poli-

Table 1. Distribution of Views of Students regarding the Statements related to "Business Life" and "Social Life" according to Gender

Statements related to "Business Life"	Gender	Agree		Disagree		Undecided		Total		p
		n	%	n	%	n	%	n	%	
A woman should not work without her husband's permission.	Female	29	33.3	42	48.3	16	18.4	87	100.0	,143
	Male	12	52.2	6	26.1	5	21.7	23	100.0	
There is no necessity for a woman to work if her husband is rich.	Female	12	13.8	63	72.4	12	13.8	87	100.0	,003
	Male	9	39.1	8	34.8	6	26.1	23	100.0	
Regarding women and men working under the same status in the business life, it is normal when men are given priority in promotions.	Female	11	12.6	70	80.5	6	6.9	87	100.0	,000
	Male	16	69.6	5	21.7	2	8.7	23	100.0	
Politics is usually a man thing.	Female	19	21.8	55	63.2	13	14.9	87	100.0	,000
	Male	15	65.2	7	30.4	1	4.3	23	100.0	
Statements related to "Social Life"										
If the family has a low economic condition, only boys should be sent to school.	Female	5	5.7	77	88.5	5	5.7	87	100.0	,406
	Male	2	8.7	18	78.3	3	13.0	23	100.0	
It is not accurate for widow, divorced women or those who have lost their husbands to live alone.	Female	15	17.2	62	71.3	10	11.5	87	100.0	,006
	Male	11	47.8	9	39.1	3	13.0	23	100.0	
It is not accurate for women to go out alone at nights.	Female	27	31.0	49	56.3	11	12.6	87	100.0	,013
	Male	13	56.5	5	21.7	5	21.7	23	100.0	
Contraception should basically be the responsibility of women.	Female	13	14.9	69	79.3	5	5.7	87	100.0	,032
	Male	8	34.8	12	52.2	3	13.0	23	100.0	
Female patients should not be examined by male doctors.	Female	8	9.2	73	83.9	6	6.9	87	100.0	,005
	Male	6	26.1	12	52.2	5	21.7	23	100.0	

tics is usually a man thing", 65.2% of male students agreed. The fact that majority of male students who participated in the study agreed with all statements related to business life is an important finding.

Female and male students generally disagreed with the statement "If the family has a low economic condition, only boys should be sent to school". The fact that 17.2% of female students and 47.8% of male students agreed with the statement "It is not accurate for widow, divorced women or those who have lost their husbands to live alone" is an important finding. Besides, 31% of female students and 56.5% of male students agreed with the statement "It is not accurate for women to go out alone at nights". 14.9% of female students and 34.8% of male students agreed with the statement "Contraception should basically be the responsibility of women". Furthermore, it was determined that 9.2% of female students and 26.1% of male students agreed with the statement "Female patients should not be examined by male doctors". The difference between genders was found to be statistically significant ($p<0.05$) in other statements of students who participated in the study regarding gender, except for first statements that were related to business life and social life.

Table 2 involves the distribution of views of students who participated in the study regarding the statements related to married life and family life according to their genders. While 42.5% of female students agreed with the statement "Men should not be shorter than women in marriages", 65.2% of male students disagreed. This finding is thought to be important in terms of statements related to married life regarding the social gender. A great majority of both genders disagreed with the statement "It is normal for a married man to cheat on his wife". The fact that 9.2% of female students and 8.7% of male students agreed with this statement is an important finding. It was determined that 34.8% of male students, which is a great rate, agreed with the statement "A man should definitely marry with a virgin woman". No statistically significant difference ($p>0.05$) was found between female and male students who participated in the study regarding their statements related to married life, in terms of social gender.

Majority of female and male students disagreed (female: 86.2%, male:73.9%) with the statement "Family inheritance should only be used by boys". 21.7% of male students agreed with the statement "A woman could be committed violence by her husband if she deserves it". Majority of female (88.5%) and male (60.9%) students disagreed with the statement "If a woman is violated by her husband, she should hide this from other people". A statistically significant difference ($p<0.05$) was found between all statements of female and male students who participated in the study related to family life, except for the statement "Family inheritance should only be used by boys" regarding social gender.

Table 2. Distribution of Views of Students regarding the Statements related to "Married Life" and "Family Life" according to Gender

Statements related to "Married Life"	Gender	Agree		Disagree		Undecided		Total		p
		n	%	n	%	n	%	n	%	
Men should not be shorter than women in marriages.	Female	37	42.5	42	48.3	8	9.2	87	100.0	,321
	Male	6	26.1	15	65.2	2	8.7	23	100.0	
It is normal for a married man to cheat on his wife.	Female	8	9.2	75	86.2	4	4.6	87	100.0	,744
	Male	2	8.7	19	82.6	2	8.7	23	100.0	
A man should definitely marry with a virgin woman.	Female	21	24.1	54	62.1	12	13.8	87	100.0	,127
	Male	8	34.8	9	39.1	6	26.1	23	100.0	
Statements related to "Family Life"										
Family inheritance should only be used by boys.	Female	7	8.0	75	86.2	5	5.7	87	100.0	,187
	Male	2	8.7	17	73.9	4	17.4	23	100.0	
A woman could be committed violence by her husband if she deserves it.	Female	8	9.2	72	82.8	7	8.0	87	100.0	,028
	Male	5	21.7	13	56.5	5	21.7	23	100.0	
If a woman is violated by her husband, she should hide this from other people.	Female	5	5.7	77	88.5	5	5.7	87	100.0	,002
	Male	2	8.7	14	60.9	7	30.4	23	100.0	

Discussion

According to literature, there are distinct differences between women and men especially in business life, social life, married and family life in terms of social gender roles. Women are expected to avoid having sexual intercourse before marriage, living alone before marriage, going out alone at nights, select jobs such as teaching and nursing that are convenient for their traditional roles, hide the violence of their husbands from the environment, avoid visiting friends including healthcare organizations without the permission of family elders and increase their status by giving birth to boys. A woman who partially or completely rejects the social role that is attributed to her could be punished in many ways including exclusion (14).

In the study, the views of students regarding social gender roles were examined in four areas as business life, social life, married and family life. Considering the distribution of the views of students who participated in the study regarding the statements related to business life and social life according to their genders, a statistically significant difference ($p<0.05$) was found between the views of female and male students in all statements, except for statements "A woman should not work without her husband's permission." and "If the family has a low economic condition, only boys should be sent to school". Regarding the statements related to business life, it is remarkable that views of male students regarding the involvement of women in business life simply support gender discrimination (Table 1). Considering the general characteristics of female employment in Turkey, the participation of women in labor force is at low level. According to the data of the Republic of Turkey, Prime Ministry, State Planning Organization (SPO) in 2008, women's rate of participation in labor force in Turkey is 22%. This rate is considerably lower compared to European Union countries (15). In a study that was conducted by Çıtak (2008), it was determined that female participants had more positive attitudes towards female employment than men, single women living in metropolis displayed more positive attitudes and women had more positive attitudes towards female employment than men in terms of different age groups (16). In the study of Gönüllü and İçli (2001), women indicated teaching and public service as the most convenient jobs for girls and as engineering, attorneyship, medicine for boys, which would require more physical force, intelligence or longer working hours (17). How these roles that are attributed to women and men are explained in terms of their meaning and perceived by university students, who will generate the enlightened group of the future, is also important. In a study that was conducted by Yılmaz et al. in 2009; it was determined that men adopted more traditional roles in areas related to business life (1). In a similar study that was conducted by Vefikuluçay et al. (2007); it was specified that male students had more traditional views regarding the business life (18). These reasons show a similarity with results of the study. The reason for men to have traditional social gender roles might be associated with the fact that these judgments are on their behalf and this condition is supported by the society.

Another area where gender-related inequalities are intensely experienced is the social life. Considering the distribution of the views of students who participated in the study regarding the statements related to social life according to their genders; it was determined that male students had more equalitarian views in statements related to social gender roles aimed at women in the society. The rate of students who disagreed with the statement "If the family has a low economic condition, only boys should be sent to school" is very high (Table 1). In the study of Yılmaz et al. (2009), it was determined that female and male students had equalitarian views in statements related to social life (1). In a similar study that was conducted by Vefikuluçay et al. (2007), majority of students stated that they disagreed with the statement related to social life (18). In both studies, a great majority of students thought that female and male students had to have equal rights to education.

In the study, it was specified that male students had a traditional view regarding the statement "It is not accurate for widow, divorced women or those who have lost their husbands to live alone". The fact that 56.3% of male students agreed with the statement "It is not accurate for women to go out alone at nights" is a remarkable finding (Table 1). In the study of Yılmaz et al. (2009), it was determined that female and male students had equalitarian views regarding the statement "It is

not accurate for widow, divorced women or those who have lost their husbands to live alone". However, the fact that almost one in every three male students agreed with the statement "It is not accurate for women to go out alone at nights" shows a similarity with result of the study (1). In the study of Vefikuluçay et al. (2007), it was determined that male students had traditional views regarding the same statements (18).

The fact that a great majority of female and male students disagreed with the statement "Contraception should basically be the responsibility of women" shows that they have the awareness of taking an equalitarian role in using family planning methods. It was determined that female and male students had equalitarian views regarding the statement "Female patients should not be examined by male doctors" (Table 1). In the study of Yılmaz et al. (2009), it was specified that female and male students had equalitarian views regarding the same statements (1). The most important area where the social gender discrimination is observed regarding women's health is the reproductive health services (2,3,5,19-21). Today, our women may still remain incapable about using reproductive health services in terms of some subjects such as safe motherhood, gynecological problems, infertility, family planning etc. Due to their positions in the family, women have difficulties in making independent decisions about receiving health services, experience problems in going to a healthcare organization, face obstacles in transportation and consequently, fall behind with receiving health services (5). In the study of Yangın (2004), 69.2% of pregnant women stated that they preferred being examined by a female doctor. In the same study, 7.6% of pregnant women stated that they had to go to a female doctor due to the insistence of their husbands, which shows the effect of men's sanction power on these views of women (22). Even though women are in tendency to be examined by female doctors due to reasons such as their religious views, privacy and shame in the Turkish society, the fact that majority of both male and female students stated that female patients could be examined by male doctors in this study has been evaluated as a positive result.

Female sexuality and tight control of women are encountered as a distinctive property of patriarchal societies just like in the Turkish society (23). While men are expected to take an active role in order to protect his and his family's honor, women are expected to protect their chastity (virginity) and look after their children very well (17).

Examining the views of students who participated in the study regarding the statements related to married life according to their genders; no statistically significant difference ($p>0.05$) was found between the views of female and male students in all statements. It was determined that male students had traditional views regarding the statement "A man should definitely marry with a virgin woman" (Table 2). In studies of Yılmaz et al. (2009), and Vefikuluçay et al. (2007), findings regarding the same statement show a parallelism, as well (1,18). In the study of Civil and Yıldız (2010), it was determined that almost all of the students were single, 60.5% considered virginity very important and 31% stated that it was not possible for women-men to be equal in terms of sexuality even though they still had an active sexual life and that virginity was important in terms of women (24). According to the moral structure and value judgments of the society, sexual intercourse before marriage is an unacceptable behavior for women (17). Women are expected to protect their chastity until marriage. In societies that never accept sexual intercourse before marriage for women, men have the freedom of sexuality. Public statements like "it's a washable dirt for men" or "real men cheat on their wives" are the indicators of social acceptance. By this way, chastity and honor of women are encountered as an element that is controlled and inspected by men and determines the social position of men (25). When training girls and boys, it is important to consider chastity equal with sexuality, perceive and accept it as a concept of women. As a consequence, it is possible to say that male students are unable to go beyond ideationally social norms even though they are well aware of social taboos. The existence of students with traditional views regarding social gender at universities that aim to train enlightened individuals has been very discouraging. This condition reveals the necessity of raising sensitivity in students during the university education, in terms of both basic professional knowledge and social gender equality.

Examining the views of students who participated in the study regarding statements of family life according to their genders; a statistically significant difference ($p<0.05$) was found between female and male students in all statements, except for "Family inheritance should only be used by boys". In the study, the fact that 21.7% of male students agreed with the statement "A woman could be committed violence by her husband if she deserves it", which is very challenging and discouraging finding. It was determined that female and male students had equalitarian views regarding the statement "If a woman is violated by her husband, she should hide this from other people" (Table 2). In their study, Yılmaz et al. (2009) determined that 13.2% of male students thought that women could be violated by their husbands (1). In a study that was conducted by Günay et al. (2006) in İzmir, almost one-third of women indicated that violence was caused by themselves, the three out of four kept silent against violence and only 1.6% applied to official authorities (26). One of the primary facts caused by social gender inequality in Turkey is violence against women. Violence against women could be encountered as domestic physical, psychological, economic, sexual violence, as well as rape, sexual slavery, constraint for pregnancy, prevention of women's participation in political life, mobbing, honor-chastity crimes, examination of hymen, constraint for marriage, women suicides, sexual abuse in workplaces/streets, adolescent pregnancies, termination of pregnancies with girls and negligence of girls (27). The perception that accepts the fact that men are stronger and more respectable than women forms a basis for aggressive behaviors of men and violence against women. When social roles that are attributed to men and women are accepted by women as well, this causes women to justify violence and keep silent against violence (2). It could be asserted that answers given to statements related to family life reflect the properties of the Turkish society.

Conclusion and recommendations

As a consequence; it is remarkable that male students have more traditional views regarding statements related to business and married life compared to female students; on the other hand, female and male students have equalitarian views regarding statements related to social life and family life. The existence of female and male students with traditional views regarding social gender at universities is challenging and discouraging in terms of showing that the university education can not precisely fulfill this objective. Considering results of the study; it is recommended to provide lessons aimed at social gender equality at universities, establish clubs or student communities and support the participation of male students in such activities, enable students to discuss about the subject at symposiums and panels on social gender and realize the traditional views shaped by society, and conduct extensive studies in order to determine the relevant regional differences across the country.

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Impact of using appointment system on patients' satisfaction

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Abstract

Analyzing the use of modern systems in every organization is highly important. The important point involved in using such system is analysis of the results which are obtained as a result of using this system. This study is aimed at measurement of the effect of using appointment system on patients' satisfaction referring to clinics of Sina hospital affiliated to Tehran University of Medical Science.

This study was conducted by intervention method in the time period from November 2012 to May 2013. The study population was selected by convenience sampling method, of which 600 patients were selected, and were assigned to two pre-intervention and post-intervention groups. Data collection was conducted by researcher made questionnaire. Data analysis was conducted using t-tests on two cases.

The results showed that except for factors of "admission to doctor's visit interval" and "timely attendance of doctor in clinic", all factors results in increased patients' satisfaction after implementation of appointment system. The highest satisfaction related to factors of "patient's satisfaction with clinic's physical condition", followed by "patient's entrance to clinic to admission time interval", and "knowledge that the clinic is on duty".

Since the use of such systems imposes high costs for an organization, reporting the results obtained from it can significantly help managers in decision making.

Key words: patients' satisfaction, appointment system, clinic

Introduction

To increase quality of health care, there requires to be feedback system for both service provides and recipients(1). To improve its quality, each system requires knowledge and application of opinions of its clients and customers(2). Therefore, it is not right for the hospitals to provide their services without regard for requirements and demands of clients, merely focusing on their interests. Satisfaction factor is important in raising the quality in healthcare organizations, because in the competitive world today, customer is extraordinarily important for providers of healthcare services. Under such circumstances, attention is definitely focused on behaviors, interests, and sensitivities of clients, so that service providers organize their orientations based on them(3).

Customer satisfaction is a concept which is especially important in health and medical care today, and is among the main criteria in evaluation of medical centers(4). Satisfaction means meeting the expectations of individuals of high quality services(5). According to Thomas and Bond, the only way in which patients may be involved in healthcare is to research on their satisfaction. Patient satisfaction is a major part of quality guaranty(6). If heath and healthcare professionals want to have a successful career, they must ultimately attract customer satisfaction(7).

The results of researches showed that such factors as notification of patients, skill and knowledge of staffs, patients waiting time, and proper communication are among factors affecting patients' satisfaction(8). Patients' dissatisfaction with healthcare services has bad consequences. Dissatisfaction of people results in their disconnection from health system, or at least, staffs' sense of incompetence, and consequently reduced efficiency of health system(9).

Accordingly, managers of hospitals deem meeting patient's requirements, and recovery of patient to be their main pre-requisite, and design the objective of hospital in line with of patient's objective(10).

The clinic of each hospital functions as its window(11, 12) and one of the first points with which patients encounter upon referring to hospital. The manner in which services are provided in this place has an important role in overall perception of patients of healthcare services of hospital(13). In clinic, patients encounter with different problem such as overcrowding, delayed consultation and doctor's visit, lack of provision of proper guidance, etc., which result in dissatisfaction of patient(14, 15). Since outpatients have more choice in terms choosing health service provider, it is very important to know how patients decide on choice and use of health service given optimized use of public resources and services and importance of this type of care(16). Satisfaction of patient with clinic is not only affected by perceived quality of received medical services, but experience of taking a number also plays a very important role in patient's satisfaction . Managers of clinics seek high patients' satisfaction in the surveys because in this way they can attract new and more patients(17). Evaluation of satisfaction of outpatients and identification of problems leads to making necessary provisions and taking required actions for solution of existing problems, enabling ongoing improvement of care level. On this basis, and given use of appointment system in Sina Hospital, affiliated with Tehran University of Medical Science, this study aims to study the impact of the use of appointment system on patients' satisfaction referring to clinic.

Material and Method

The present study is of interventional type, and falls within category of quasi-experimental study. The studies population included all patients who referred to the clinic of Sina educational hospital, affiliated with Tehran University of Medical Sciences. In this study, a sample comprising two groups of patients was selected. The first group included patients who used traditional system of admission and appointment. In other words, satisfaction of this group was measured before intervention (i.e. before use of smart appointment system). The second group included patients whose satisfaction was measured after intervention and use of appointment system in clinic. To determine the sample size, the following formula was used[1]. (T-test)

$$n_i = \frac{\left(z_{\frac{\alpha}{2}} + z_{\beta}\right)^2 \sigma^2}{2(\mu_1 - \mu_2)^2}$$

Therefore, with power of 80%, and confidence of 95%, and maximum standard deviation of 0. 5, about 400 patients are required to be included in the sample. However, 200 patients will be required to be included in each group. Given sampling error is possible, and increased confidence about the results, about 266 patients were studied in the first group (pre-intervention group), and 300 patients were studied in the second group (post-intervention group). Simple randomized sampling was used and convenience samples were selected. Researcher-made questionnaire was used to determine the patients' satisfaction. This questionnaire had two sections. The first section includes items on background details of patients, and the second section includes 18 items measuring patients' satisfaction. Cronbach's alpha coefficient was used to measure reliability of question, which was estimated to be 0.7. Having been designed, the used questionnaire was evaluated by a number of experts of the hospital, and their opinion about validity of questionnaire was collected, and applied, so that the final desired validity of data collection instrument is insured. Having administered and collected questionnaires, raw data were analyzed using SPSS 18 Software on two levels of descriptive and analytic statistics. Two-sample t-test was used as the basic test to determine if there was significant difference between two groups of patients in terms of satisfaction before and after intervention. In all inferential tests, confidence level was considered as 0.05.

Findings

Of patients referring to clinic of hospital, 44% were male, and 54% were female. The patients were

1 Chow, Shao and Wang, *Sample Size Calculations In Clinical Research*, Taylor& Francis, NY. (2003) Pages 56-57.

Table 1. Distribution of patient's demographic variables in Sina hospital's clinic

Demographic variables	Group	Frequency			Percentage of Frequency		
		Before	After	Total	Before	After	Total
Sex	Man	119	140	259	45.2	46.7	46
	Woman	144	160	304	54.8	53.3	54
Living place	Tehran	167	208	375	63.3	69.3	66.5
	Other cities	97	92	189	36.7	30.7	33.5
Age	10-20	20	14	34	7.6	4.7	6
	20-30	50	43	93	18.9	14.3	16.5
	30-40	64	65	129	24.2	21.7	22.9
	40-50	59	55	114	22.3	18.3	20.2
	50≥	71	123	194	26.9	41	34.4
Marital Status	Single	83	54	137	31.2	18	24.2
	Married	183	246	429	68.8	82	75.8
Number of referral	Once	72	144	216	27.3	48.2	38.4
	Twice	192	155	347	72.7	51.8	61.6
	Morning	173	232	405	85.2	77.3	80.5
	Evening	30	68	98	14.8	22.7	19.5

Table 2. Mean and SD of Patient Satisfaction Factors before and after appointment system

Factors	Time	Number	Mean	SD
Convenience of taking an appointment	Before	259	2.75	0.612
	After	300	2.99	0.115
Entrance to clinic to admission time interval	Before	265	1.58	0.777
	After	299	2.89	1.206
Admission to doctor's visit time interval	Before	263	1.49	0.73
	After	278	1.44	0.756
Knowledge that the clinic is on duty	Before	266	1.73	0.871
	After	300	3	0.00
Clinic's physical condition	Before	263	1.44	0.712
	After	211	2.98	0.137
Behavior of doctor toward patient	Before	241	2.93	0.321
	After	211	2.98	0.137
Behavior of admission staff and cashier toward patient	Before	261	2.85	0.423
	After	299	2.97	0.18
Behavior of admission stories secretary toward patient	Before	265	2.86	0.429
	After	293	2.98	0.13
Keeping order of turns by secretaries	Before	260	2.86	0.447
	After	270	2.98	0.135
Keeping order of turns by patients	Before	253	2.72	0.569
	After	232	2.9	0.305
Overcrowding of patients and their relatives	Before	266	1.64	0.831
	After	293	1.81	0.914
Convenient finding of the place of take-a-turn and admission place	Before	264	2.91	0.348
	After	296	2.98	0.141
Convenient finding of clinic (doctor's office)	Before	261	2.94	0.27
	After	284	2.99	0.118
Timely attendance of doctor at clinic	Before	261	2.3	0.955
	After	293	2.45	0.893
Your commutation between wards and stories	Before	261	2.3	0.882
	After	297	2.84	0.51
Second-time choice of Sina clinic	Before	256	2.6	0.707
	After	259	2.93	0.248
Recommending the hospital to others	Before	251	2.67	0.656
	After	254	2.93	0.264
Overall patients' satisfaction	Before	266	2.38	0.195
	After	300	2.76	0.165

Table 3. The means differences between pre-and post-intervention

Factors	t	Degree of freedom	P value	Mean difference	Range limits at confidence level of 95%	
					Low	High
Convenience of taking an appointment	-6.326	273.9	≤ 0.001	-0.24	-0.32	-0.16
Entrance to clinic to admission time interval	-15.51	514.9	≤ 0.001	-1.31	-1.47	-1.14
Admission to doctor's visit time interval	0.748	539	0.455	0.05	-0.07	0.17
Knowledge that the clinic is on duty	-23.868	265	≤ 0.001	-1.27	-1.38	-1.16
Clinic's physical condition	-34.395	285.9	≤ 0.001	-1.54	-1.63	-1.45
Behavior of doctor toward patient	-2.456	333.6	0.015	-0.06	-0.1	-0.01
Behavior of admission staff and cashier toward patient	-3.982	341.4	≤ 0.001	-0.11	-0.16	-0.05
Behavior of admission stories secretary toward patient	-4.609	307.6	≤ 0.001	-0.13	-0.18	-0.07
Keeping order of turns by secretaries	-4.282	304.3	≤ 0.001	-0.12	-0.18	-0.06
Keeping order of turns by patients	-4.419	392.9	≤ 0.001	-0.18	-0.26	-0.10
Overcrowding of patients and their relatives	-2.203	557	0.028	-0.16	-0.30	-0.02
Convenient finding of the admission place	-3.081	339.4	0.002	-0.07	-0.11	-0.02
Convenient finding of clinic (doctor's office)	-2.602	349.2	0.01	-0.05	-0.08	-0.01
Timely attendance of doctor at clinic	-1.919	534.1	0.056	-0.15	-0.30	0.004
Your commutation between wards and stories	-8.696	404.4	≤ 0.001	-0.54	-0.66	-0.42
Second-time choice of Sina clinic	-7.192	316.2	≤ 0.001	-0.34	-0.42	-0.24
Recommending the hospital to others	-5.739	327.9	≤ 0.001	-0.26	-0.34	-0.17
Overall patients' satisfaction	-25.06	564	≤ 0.001	-0.38	-0.41	-0.35

mostly aged over 50, who constituted 34.4% of sample. Table 1 shows demographic details of patients.

Table 2 shows mean score of each factor of patient's satisfaction before and after use of appointment system.

Before use of smart appointment system, overcrowding of patients and their relatives, clinic's physical condition, knowledge that the clinic is on duty, admission to doctor's visit interval and patient's entrance to clinic to admission time interval, having less-than-mean scores (less than 2) had the lowest effect, and finding the clinic and relevant doctor's office conveniently, behavior of doctor toward patient and finding place of appointment system and admission desk conveniently had the highest effect on satisfaction of clients, respectively. Overall patients' satisfaction was above average level (2.38).

The results from two-sample t-test showed that of 17 studied factors of patients' satisfaction, except for "admission to doctor's visit time interval" and "timely attendance of doctor in clinic", all factors led to increased patients' satisfaction after use of appointment system (table 3).

Table 3: Output of two-sample t-test for measurement of difference between means before and after intervention.

Findings showed that biggest changes related to factors of "satisfaction with clinic's physical condition", "entrance to clinic to admission time interval", and "knowledge that the clinic is on duty", respectively, with each increasing satisfaction at least by one unit. Also, mean patients' satisfaction scores before and after set-up and commissioning of appointment system were 3.8 and about 2.78, respectively. In other word, there is a significant difference between these two conditions (P_value≤0.001, CI: -0.35_-0.409).

Discussion and conclusion

Findings showed that use of appointment system has a positive effect on overall satisfaction , and highest changes related to "satisfaction with clinic's physical condition ", "entrance to clinic to admission time interval", and "knowledge that the clinic is on duty". In Chang's study, the most important predictor of patients' satisfaction were items which were related to clinic (planning for turns and clinic waiting time) and quality of interaction between doctor and patient(18). Among objectives of using appointment system was reduced waiting time for receiving service. Waiting time and access to care are the best known issues involved in provision of

outpatient services, which has a considerable effect on patient's satisfaction(19).

In 4-phase study by Levesque, which was conducted to measure the effect of reduced waiting time for receiving service in clinic on patients' satisfaction, the findings of study suggested that after waiting time was reduced, percentage of patients who described their satisfaction as high increased from phase 4 to phase 4 (from 14.6% in phase 3 to 31.1% in phase 4). Satisfaction mean scores were 3.3, 3.6 and 3.9 in phases 2, 3 and 4, respectively. In their study, difference between phase 3 and 4 of study in terms of satisfaction was significant(20). In our study, except for "admission to doctor's visit time interval" and "timely attendance of doctor at clinic" factors, all factors led to increased patients satisfaction after use of appointment system, and the highest satisfaction related to factors of "satisfaction with clinic's physical condition", "entrance to clinic to admission time interval" and "knowledge that the clinic is on duty". Findings of Nobile's study suggested that there is a relation between requesting for taking a number time to time set for doctor's visit interval, and also between time of patient's arrival at clinic to time of doctor's visit interval, so that as this time increased, patient's satisfaction decreases(21). Given patients had to refer to clinic early in the morning before use of appointment system, and they took number manually and in an unorganized manner to some extent, one the objectives of using this system was to reduce necessity patients' referral to clinic early in the morning, and to facilitate appointment process. Given no significant change occurred in patients' satisfaction with time interval between admission and doctor's visit, and time presence of doctor at clinic, and problems caused by overcrowding of patients and their relative have still remained, it seems that patients still refer to clinic early in the morning. Given number of doctor's visit in each clinic is limited, one the reason for the above mentioned problem may be that patients are worried that their queue line of their intended clinic may be filled up, which problem may be solved to some extent by providing training to patients. On the other hand, given satisfaction with presence of doctors in clinic has not changed significantly, it is clear that patients spend a relatively long time waiting for doctor's visit. However, given findings of the study, the other reason for prolongation of waiting time is disorders and occasionally delayed attendance of doctors at the clinic. In study by Roudpeyma et al, late attendance of doctors and lack of supervision by specialized doctor were two major factors of patients' dissatisfaction(22). Also, in the conducted studies, patients who attended the clinic later than the specified time caused overcrowding and prolongation of waiting time(17, 23). Finding of study by Hang suggested that it is generally the case that patients who attend clinic on-time wait patiently for 37 minutes, and patients who attend clinic late wait patiently for less than 63. Patients who are late for 15 minutes expect to be visited sooner(24). In study by Nasiripour, simultaneous referral of a large number of patients to clinic and not timely attendance of doctors are among the most important causes prolonged waiting time(25). It has been noted in different studies that the length of time patients have to wait before doctor's visit is the common source of dissatisfaction(26). Finding showed that in addition to planning for giving number to patients, there must be provisions taken for doctors to attend clinic timely. Evaluation of using modern systems in medical centers has high importance. The important point of using such systems to evaluate the results which are obtained from using such systems, because use of such systems has a high cost for organization, and reports of its results may significantly help managers in decision making, and if the effects of using this system is positive, use of system must be defended documentarily, and if the result is negative, the previous method and procedure must be used.

This report and study can be used as the basis of an important managerial decision with regard to use of a modern organization system for diagnostic and therapeutic affairs. The result of this report can have IT system managerial feedback.

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CPR-induced traumatic injury varies by resusciation team and patient age: A cadaver study

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Abstract

Objectives: This study aimed to investigate iatrogenic trauma following successful cardiopulmonary resuscitation (CPR) by examining associations between traumatic injury and resuscitation team, and patient age.

Methods: We retrospectively reviewed post-mortem reports for 702 patients who underwent successful CPR for non-traumatic cardiac arrest (CA) but who later died. Reports were obtained from the Republic of Turkey Ministry of Justice İstanbul Forensic Medicine Institution for patients between January 2010 and August 2012. Findings were analyzed according to the teams administering CPR [Ambulance Transport and Emergency Service Team (ATEST), consisting of an emergency medicine doctor, medical practitioner, nurse; Clinical Team (CT), specialist doctor, resident doctor, nurse; Intensive Care Unit Team (ICUT, ICU specialist doctor, resident doctor, nurse)] as well as patient age.

Results: Rib fractures were more common among patients receiving care from the ATEST group (66.2%) compared to the CT group (33.3%) or ICUT group (43.5%) (p=0.000). There were no differences between groups with respect to sternal fractures (p=0.314). Defibrillator marks were more common in patients receiving care from the ATEST group (53%) compared to the CT group (42.9%) or ICUT group (32.3%) (p=0.04); the patients receiving care from the CT group had more defibrillator paddle marks compared to the patients receiving care from the ICUT group (p=0.03). There were no differences between groups with respect to heart, tracheal or liver trauma, or food content in the trachea (p=0.227). Rib and sternal fractures were more common in patients over 65 (p=0.000); but, defibrillator paddle marks were lower (p=0.00). Pulmonary trauma lower in patients over 65 (p=0.001); but there were no differences between age groups with respect to incidence of heart, tracheal and liver trauma, or presence food contents in the trachea (p=0.962).

Conclusions: According to our data, chest compressions may be more traumatic, and more common usage of defibrillator in ATEST group. In patients over 65, chest compressions also may be traumatic, but less common usage of defibrillator.

Key words: cardiopulmonary resuscitation, iatrogenic trauma, recovery, autopsy

Introduction

Cardiopulmonary resuscitation (CPR) management following cardiac arrest (CA) should include prevention of secondary iatrogenic injury, as well as detection and treatment of these injuries when they occur [1]. Today, CPR-induced injuries spur both medical and legal questions. Post-mortem studies have been shown superior to imaging to detect CPR-induced injuries [2]. Therefore, autopsy studies, since the first publication by Baringer et al. in 1961 to report post-CPR iatrogenic injuries, are more appropriate than imaging studies [3].

The most frequently reported skeletal injuries following CPR and chest compressions (CCs) are rib and sternal fractures [4,5,6]. Injuries to the upper airway, pulmonary system, heart, major vasculature, gastrointestinal system, (e.g., liver, or splenic lacerations) and retroperitoneal hemorrhage occur with varying frequencies [7,8,9,10]. The incidence of post-CPR rib and sternal fractures varies widely [5,11,12] due to differences in detection methods and risk factors (e.g., advanced age, female sex, CPR duration, history of osteoporosis) [13]. Although CCs have been a fundamental component of CPR since its introduction [14], concern about

associated trauma and resultant complications has arisen in the published literature [3,15]. Some physicians believe that more rib fractures demonstrate more effective CPR. The 2010 European Resuscitation Council CPR guidelines emphasize that CCs can be applied by anyone during a CA [16]. Although the literature supports these suggestions, we believe that the negative impact of secondary injuries on prognosis should be clarified and that recommendations may change.

Successful CPR following CA has increased in recent years [17]. Intensive Care Unit (ICU) physicians frequently care for patients who have received successful CPR. In this study, we retrospectively examined post-mortem reports for patients who experienced non-traumatic CA, received successful CPR, but died later. We aimed to determine frequencies of iatrogenic CPR-induced trauma to the thorax, mediastinum and other body parts vis-à-vis resuscitation team and patient age.

Methods

After receiving study approval (no. 361, dated 06/21/2012, from the Republic of Turkey Ministry of Justice Istanbul Forensic Medicine Institution's permission committee), we obtained our sample from 9534 post-mortem reports for autopsies performed in the Republic of Turkey Ministry of Justice İstanbul Forensic Medicine Institution between January 2010 and August 2012. The autopsies were performed by pathologists, and included examination of the cranial, thoracic and abdominal cavities as well as post-mortem toxicology and histopathology. Radiography was not performed. We included post-mortem reports in which the examiner noted that "reanimation is possible." However, the reports did not include information on whether spontaneous circulation returned during CPR. We excluded patients who had CA due to: trauma, sharp object injury, gunshot wound, vaccination or aortic aneurysm rupture. We also excluded those who had thoracic surgical scars or cardiac rupture due to ischemic heart disease. Thus, post-mortem findings were reviewed for 702 eligible patients who experienced non-traumatic CA but later died.

We recorded age, sex, height, weight, pregnancy status and cause of death from post-mortem reports. The team providing CPR was classified as the ambulance transport and emergency service team (ATEST; consisting of an emergency medical specialist doctor, medical practitioner, nurse), the clinical team (CT; specialist doctor, resident doctor, nurse) or the ICU team (ICUT; ICU specialist doctor, resident doctor, nurse). Post-mortem notes regarding defibrillation marks, sternal, vertebral and rib injuries, intra-thoracic organ injuries, intra-abdominal findings, new tooth fractures, and neck and airway injuries were recorded. CPR duration was also noted when available. Defibrillation marks were classified as "present" or "not present." Rib fractures were classified by location: parasternal, mid-clavicular, front axillary, mid-axillary, mid-scapular, or paravertebral. Sternal fractures were classified by location: manubrium, corpus, or xiphoid. Macroscopic pulmonary trauma was classified as: petechial bleeding, hyperemia, congestion, stasis, or contusion. Needle puncture sites on the neck and thorax were recorded.

Incidences of traumatic findings were evaluated by group performing CPR and by patient age.

Statistical analysis: Descriptive frequencies, rates, means and standard deviations were obtained using SPSS 20.0 (Statistical Package for Social Sciences, IBM Corp., New York, NY). Chi-square tests were used to compare categorical data. When the sample size was too small for chi-square analysis, Fisher's exact test was used. We used a significance level of of $p<0.05$ for all analyses.

Results

Demographic and post-mortem characteristics are presented in Table 1.

The most frequent CPR-induced trauma was rib fracture (63.2%); the mean number of rib fractures for the 444 patients who experienced at least one rib fracture was 6.9, whereas the mean number of rib fractures overall was 4.4. Rib fractures occurred in: the left hemithorax in 125 cases (28.2%), the right hemithorax in 25 cases (5.6%), and bilaterally in 294 cases (66.2%). The most frequently broken ribs were the left 4th rib (in 52.1% of all cases with at least one rib fracture), left 3rd rib (51.7%), left 5th rib (47%), left 2nd rib (38.2%) and the right 3rd rib (36%). Rib fractures most frequently occurred at the mid-clavicular line (62.2%), followed by the front axillary line (20.6%) and the

Table 1. Demographic and post-mortem characteristics for 702 patients who underwent successful CPR but later died

Age (years)	46.3 ± 19.7 (1 month to 93 years)
Gender (M/F)	542/160
Pregnant females	4 (2.5%)
Body weight (kg)	74.5 ± 20.9
Body height (cm)	164.7 ± 17.8
BMI (kg/m^2)	26.9 ± 5.8
Resuscitation team	
ATEST	619 (88.3%)
ICUT	62 (8.7%)
CT	21 (3%)
CPR duration recorded in autopsy report	69 (9.8%)
Causes of death recorded in autopsy report	
Ischemic heart disease	375 (53.4%)
Suicide/Intoxication	70 (10%)
Drowning in water	32 (4.6%)
Pulmonary disease	32 (4.6%)
Cerebrovascular disease	28 (4%)
Electric shock	9 (3%)
Intra-abdominal event	7 (1%)
Cancer	6 (0.9%)
Metabolic disease	3 (0.4%)
Foreign body aspiration	1 (0.1%)
Anaphylaxis	1 (0.1%)

parasternal line (14.6%). Hemorrhage (identified as blood clots on the surface of the fracture) resulted from 65.1% of rib fractures. Sternal fractures occurred in 334 patients (47.6%), most commonly at the corpus (99.4%). Hemorrhagic fracture was detected in 46% of sternal fractures.

Table 2. CPR-induced rib fractures, by location

Rib fractures (n= 444)
Isolated left hemithorax: n= 125 (28.2%)
Isolated right hemithorax: n= 25 (5.6%)
Bilateral: n=294 (66.2%)
Most frequently broken ribs
Left 4th rib: 52.1%
Left 3rd rib: 51.7%
Left 5th rib: 47%
Left 2nd rib: 38.2%
Right 3rd rib: 36%
Rib fracture localization
Mid-clavicular line: 62.2%.
Front axillary line: 20.6%
Parasternal line: 14.6%.
Sternal fracture (n=334)
corpus: n=332 (99.4%)
manubrium: n=2 (0.6%)

Table 3. Macroscopic finding of pulmonary trauma after CPR

Macroscopic finding of pulmonary trauma after CPR: **n=403 (57.4%)**
Petechial bleeding (case): n=181 (44.9%)
Hyperemia (case): n=127 (31.5%)
Congestion (case): n=122 (30.2%)
Stasis (case): n=109 (27%)
Contusion (case): n=5 (1.2%)

Table 4. Organ trauma after CPR

Pulmonary trauma (case): n=403 (57.4%)
Tracheal trauma (case): n=70 (10%)
Cardiac trauma (case): n=30 (4.3%)
Liver trauma (case): n=10 (1.4%)

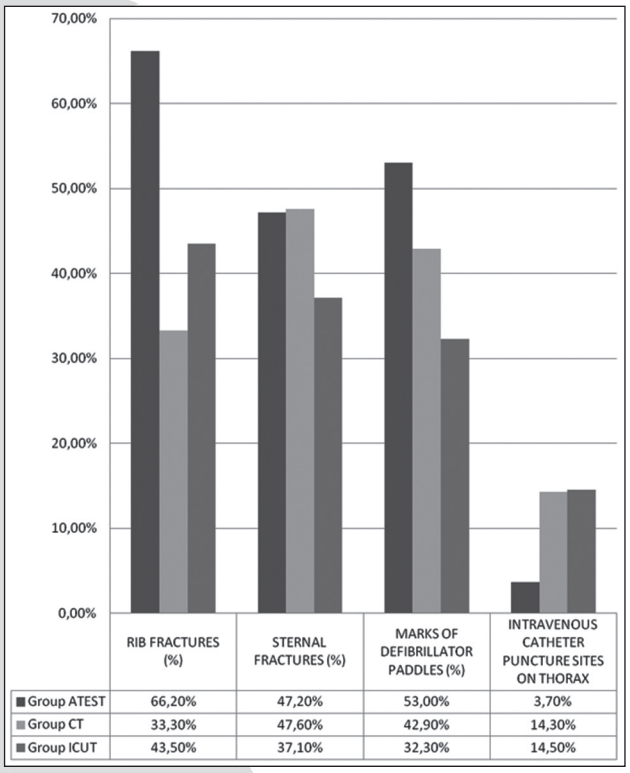
New CPR-induced tooth fractures were observed in 5 cases (0.7%).

Pulmonary trauma occurred in 403 cases (57.4%) and included: petechial bleeding in 181 cases, hyperemia in 127 cases, congestion in 122 cases, stasis in 109 cases, and contusion in 5 cases. Ten patients (1.4%) experienced liver trauma

(contusion, laceration, rupture, subcapsular bleeding), including 8 patients who experienced life-threatening intra-abdominal bleeding. Cardiac trauma (contusion, laceration, rupture) was noted in 30 cases (4.3%). Tracheal trauma (laceration, rupture) was noted in 70 cases (10%). Food contents were detected in the trachea in 28 cases (4%).

Differences between resuscitation teams with respect to rib and sternal fractures, defibrillator paddle marks, and needle puncture sites are as follows. Rib fractures occurred in 410 of 619 patients (66.2%) resuscitated by the ATEST team, in 7 of 21 patients (33.3%) resuscitated by the CT team, and in 27 of 62 patients (43.5%) resuscitated by the ICUT team. The difference between the ATEST group and each of the CT and ICUT groups was statistically significant for rib fractures (p=0.000). There was no difference between the CT and ICUT groups (p=0.19). Sternal fractures were present in 292 of 619 ATEST patients (47.2%), 10 of 21 CT patients (47.6%) and 23 of 62 ICUT patients (37.1%); the pair-wise differences were not significant (p=0.314). Defibrillator paddle marks were observed in 357 cases (50.9%), including 53% of the ATEST group, 42.9% of the CT group and 32.3% of the ICUT group. Patients in the ATEST group showed more defibrillator paddle marks compared to either the CT or ICUT groups ($p<0.05$ for both comparisons) and defibrillator paddle marks were also observed more frequently in the CT group compared to the ICUT group (p=0.03). There were no differences between groups performing CPR with respect to heart, tracheal or liver trauma, or food content distribution in the trachea (p=0.227). A total of 43 intravenous catheter puncture sites were noted on the neck and thorax of 35 patients (5%): 18 in the right jugular vein, 13 in the right subclavian vein, 7 in the left jugular vein, and 5 in the left subclavian vein. The proportion of needle puncture sites to the neck and thorax was lower in those receiving CPR from the ATEST group (3.7%) compared to the CT group (14.3%) and the ICUT group (14.5%). There was no difference between groups CT and ICUT with respect to number of intravenous catheter punctures (p=0.314).

Evaluation of CPR-induced trauma by age showed that rib and sternal fractures were more common in patients over 65 compared to patients aged 19 to 65 (p=0.000) and 18 and younger (p=0.000). Defibrillator paddle marks were lower among patients over 65 compared to patients aged 19 to 65 (p=0.000) and patients 18 and younger (p=0.000). There was no difference between the two younger patient groups with respect to defibrillator paddle marks (p=0.487). Pulmonary trauma was lower in patients over 65 compared to patients aged 19 to 65 (p=0.001) and patients 18 and younger (p=0.001). There were no differences between age groups with respect to incidence of heart, tracheal and liver trauma, or presence food contents in the trachea (p=0.962).

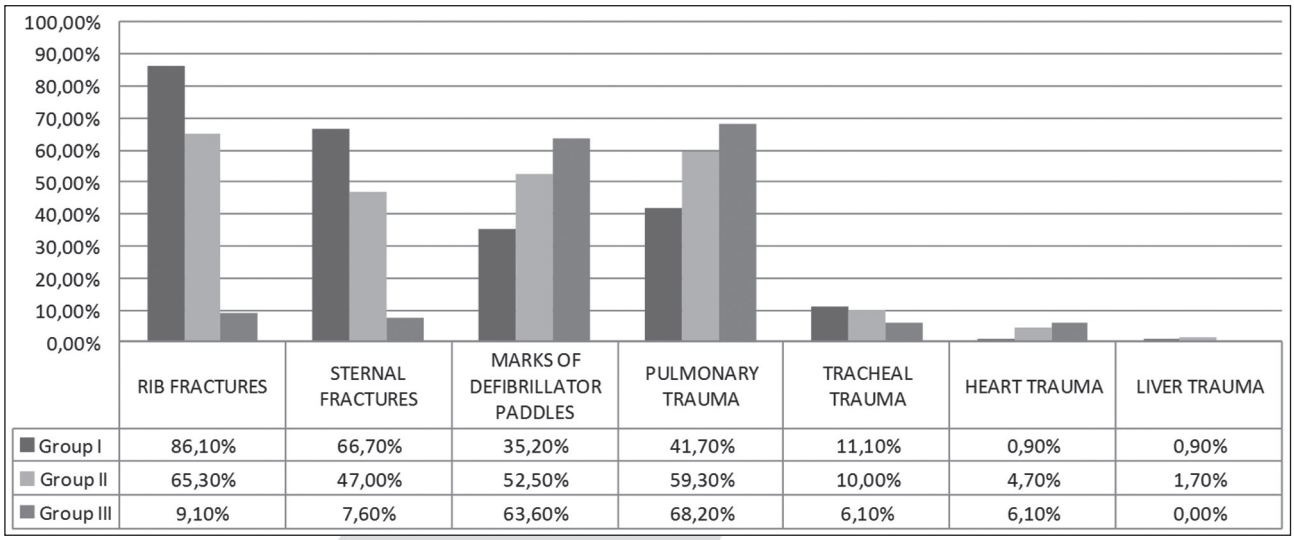


	RIB FRACTURES (%)	STERNAL FRACTURES (%)	MARKS OF DEFIBRILLATOR PADDLES (%)	INTRAVENOUS CATHETER PUNCTURE SITES ON THORAX
Group ATEST	66,20%	47,20%	53,00%	3,70%
Group CT	33,30%	47,60%	42,90%	14,30%
Group ICUT	43,50%	37,10%	32,30%	14,50%

Figure 1. CPR-induced trauma by team performing resuscitation
ATEST: Ambulance Transport and Emergency Service Team
CT: Clinical Team
ICUT: Intensive Care Unit Team

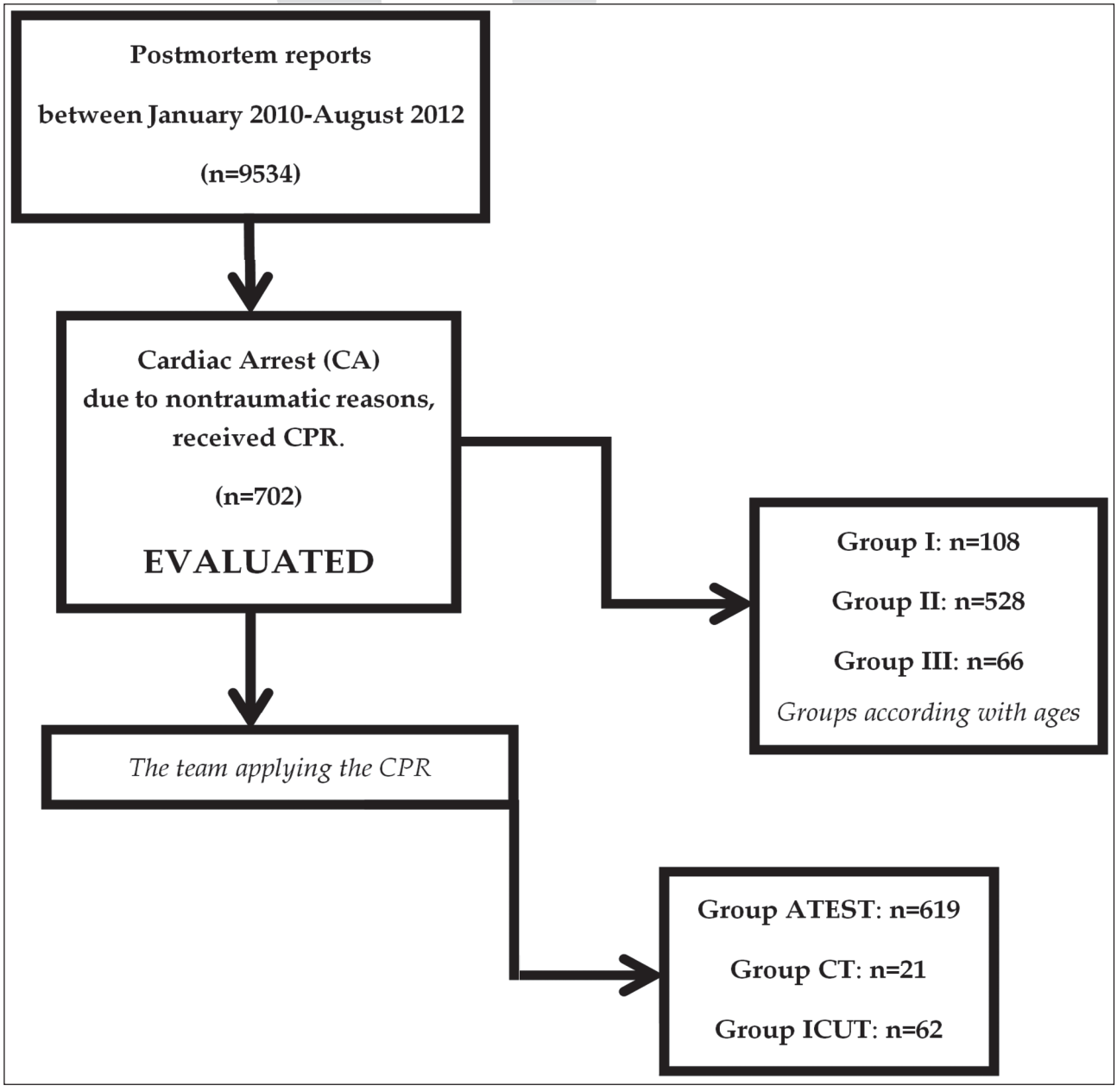
Discussion

We aimed to investigate iatrogenic trauma following successful CPR by examining associations between traumatic injury and resuscitation team, and patient age. We retrospectively reviewed post-mortem reports for 702 patients who underwent successful CPR for non-traumatic CA but who later died. Our principal findings are, patients who received CPR from ATEST personnel (i.e.,



	RIB FRACTURES	STERNAL FRACTURES	MARKS OF DEFIBRILLATOR PADDLES	PULMONARY TRAUMA	TRACHEAL TRAUMA	HEART TRAUMA	LIVER TRAUMA
Group I	86,10%	66,70%	35,20%	41,70%	11,10%	0,90%	0,90%
Group II	65,30%	47,00%	52,50%	59,30%	10,00%	4,70%	1,70%
Group III	9,10%	7,60%	63,60%	68,20%	6,10%	6,10%	0,00%

Figure 2. CPR-induced trauma by patient age



first responders) experienced higher rates of rib fractures and defibrillator paddle marks compared to patients who received CPR from hospital-based personnel, either CT or ICUT members. We found that patient age also was a risk factor for CPR-induced traumatic injury.

The rate of CC-induced rib fractures in adults in the literature ranges from 13% to 97% [1,18,19]. Hashimato et al. [20] detected rib fractures in 52% of 96 autopsy cases; 43% of these were localized in the right hemithorax, 48% in the left hemithorax, and 39% were bilateral. Our observed rib fracture rates are consistent with these published studies. Other studies report that only 10% to 14% of rib fractures found during autopsy were detected on chest radiographs [21]. We point out that, following successful CPR, chest radiography is unnecessary [13] and risky because of patients' unstable medical status.

In evaluating rib fractures by CPR provider, we found that CPR performed by ATEST members was more likely to result in rib fractures. It is not clear why this is the case, but perhaps it is related to the varied physical environments encountered by first responders in the field or the fewer resources they may have for treatment, so that they must rely on CCs for rapid stabilization. We found that defibrillator paddle marks are observed more frequently in patients receiving care by ATEST members, likely because CAs occurring at home are more frequently associated with ventricular fibrillation and ventricular tachycardia. The number of catheter punctures performed by the ATEST group was likely higher because they encounter persons at home who require vascular access; hospitalized patients already have vascular access.

Relationships are known to exist between the incidence of skeletal fractures, a common CPR-induced traumatic finding, and age, sex and CPR duration [1,2,4]. Because female gender is associated with osteoporosis, it is considered a risk factor for skeletal fracture during CPR [4]. Together with degenerative skeletal changes, advanced age is associated with higher fracture risk as well [2]. Although most trauma occurs during the first minutes of CPR, fracture incidence is also affected by CPR duration [1]. Although Smekal et al. [22] did not find an association between number of rib and sternal fractures and CPR duration, they did report a correlation between the number of rib and sternal fractures and age, sex, and person performing CPR. Hoke et al. [19] reported that rib fractures increase with age and Kim et al. [13] reported that sternal fractures were observed more frequently in females. Our finding, that older patients experienced more fractures and young patients experienced fewer fractures, is consistent with the published literature. Our finding of fewer defibrillator paddle marks on older patients suggests that they were defibrillated less often, possibly because their cardiac rhythms were less likely to respond to defibrillation.

In the end, we have some limitations about this study. First, retrospective nature of the study. It is very difficult to explain retrospectively determine a causal relationship between chest compressions and injury. Second, we have not any information about that when the patients died during CPR, or after 1 hour, after 24 hour or weeks later. Unfortunately, we also have not any information how many patients had a return of spontaneous circulation durin CPR.

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Security enhanced automated in-home patient monitoring system

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Abstract

In-home patient monitoring system plays an important role in early detection and prevention of diseases. This paper presents the design of wireless sensor network to monitor the patient in his/her home. Different body sensors are fitted on patient's body to collect the body parameters like temperature, blood pressure, ECG and pulse rate. Currently most of the monitoring systems use Personal Computer (PC) as local database to store patient's body parameters before sending them to the hospital. Here the need for a PC is eliminated by mobile phone. The body parameters collected by sensors are confidential and are forwarded to the hospital in a secure way. A variation of Ciphertext Policy Attribute Based Encryption (CP-ABE) with double encryption technique is used to achieve security. When a patient moves away from the home, outdoor monitoring is also supported by the mobile phone because the mobile phone is always carried by the patient. Hence the mobile phone is used as a local database, eliminates the need for a PC and supports outdoor monitoring. Finally a real time monitoring is implemented with the help of temperature sensor. The sensing circuit consists of temperature sensor, Analog-to Digital Converter (ADC), microcontroller, LCD and Bluetooth device. Laptop is designed as hospital server using mhotspot tool. Temperature readings are automatically forwarded to android mobile of the patient. Then it is forwarded to laptop using wi-fi communication and immediate response is given to patient's mobile phone.

1. Introduction

Chronic diseases are more common among elderly people and they affect the e-healthcare systems throughout the world [9], [10]. Recently waiting time in hospitals, emergency admissions etc., are very costlier and increases the workload of doctors and medical experts. Providing quality treatment, reducing the cost and caring for seniors are important issues in healthcare. These issues are solved by in-home patient monitoring or personal health systems [11].

Wireless Sensor networks (WSNs) have been increased in recent years because of the wireless communication technologies and advances in micro-electro-mechanical systems [12]. They support in-home patient monitoring also. It consists of different sensors fitted on patient's body and collects the body parameters continuously and stores them in a PC. There are some problems when using PC as a local database. Hence it is eliminated by GSM (Global System for Mobile Communications) enabled mobile phone [15], [17]. The stored parameters should be securely and correctly forwarded to hospital for preventing dangerous situations of the patient [14]. To achieve security, a variation of CP-ABE scheme is used here [2].

In some of the existing systems, patient can wear a monitoring device to collect the movement details of the patient. It collects and forwards them to the local database with the help of Access Points (AP) that were located in patient's home [16]. When a patient moves from one room to another, the monitoring device selects any one of the AP to send the details. But it does not support outdoor monitoring. That is when a patient moves away from the coverage area of an AP, movement patterns cannot be tracked. Hence the outdoor monitoring is supported in the proposed system by GSM enabled mobile phone.

2. Literature survey

2.1 Patient monitoring with body sensors

WSN for monitoring vital signs of multiple patients was proposed in[1]. It consists of group of sensors to monitor the physiological signals. ECG sensors were fitted on patient's body to monitor

heart activity, heart rate and so on. Multiple patients were monitored and they were considered as nodes of the WSN and hospital is considered as a central node or sink. SimpliciTI wireless communication protocol was used to setup a WSN. All the sensors transmit ECG signals to a wireless access point which is located in the patient's home. These nodes are connected to a central node which is installed in the hospital through an internet. Special software is installed at hospital server. It receives and saves the ECG signals in a database. Doctors can able to monitor their patients, detect the abnormalities and take necessary steps. Here the need for a PC to act as an access point was eliminated. Also an IP address is allocated for each user and the system is easy to configure. Most of the BSNs do not support long-term healthcare monitoring. A continuous acquisition of body parameters based on compressed sensing was described in [6]. It used a sparsification model to find the sparse representation of biomedical signals. These measurements are transmitted to a fusion center through BSN. A weighted group sparse reconstruction algorithm was proposed to reconstruct the signals accurately at the fusion center. It shows that this scheme was efficient, scalable and robust.

Infrared (IR) sensor based system was proposed in [18]. Different feature values of the patient like activity level, mobility level and non response level were collected by Support Vector Data Description (SVDD) method. Normal and abnormal behaviors were differentiated by this method. The behavior patterns Behavior patterns were classified by the classification algorithm. These schemes were expected to be suitable in home environment.

In [19], a distributed telemonitoring system based on Services laYers over Light PHysical devices (SYLPH) model was proposed. A service oriented architecture model was used here to distribute the resources among multiple WSN. It supports to connect different networks with varying wireless technologies.

2.2 Patient monitoring with security

A distributed data security concept was described in [2], [13]. Here the enforcement of access policies and policy updates were done by CP-ABE. Data owners define their access policies on set of user attributes. But it faces key escrow problem. That is Key Generation Center (KGC) is responsible for generating keys. It can decrypt the message to see the original data because it knows the keys of all users. Another problem is user revocation. The key escrow problem was solved by key issuing protocol which was constructed between key generation center and data storing center. Fine-grained user revocation could be supported by proxy encryption.

In [3], authors proposed healthnet mobile electronic health monitoring and data collection system. It consists of body sensor network which was embedded in clothes that wirelessly communicate with wearer's mobile phone. The mobile phone is used to collect, store and transfer the data. Security and privacy methods also described here. Patient's data may be forwarded to trusted parties like medical professionals, friends, etc. the patient has entire control on his data and decides who may access it. During data collection and data storage, confidentiality was achieved by AES-128 encryption and the trusted parties are identified by certificates of 2048 bit RSA keys.

Data security and privacy in Wireless Body Area Networks (WBAN) were described in [4]. Two data security issues were considered: Secure and dependable distributed data storage and fine grained distributed data access control for sensitive and private patient medical data. The authors analyzed different methods for secure distributed data storage but they concluded that these techniques incur high communication and storage overhead. For fine grained data access control two schemes were discussed: SKC (Symmetric Key Cryptography) based schemes and PKC (Public Key Cryptography) based schemes. In SKC based approach, fine grained access control was hard to realize, vulnerable to user collision and compromising node will expose the data. In PKC based schemes, CP-ABE was discussed. ABE based access control method is suitable to implement on local servers than other techniques. It also used for achieving all the security requirements.

To protect the patient's confidential information in point-of-care system, a wavelet based ECG steganography technique was proposed in [5]. The ECG signals and other physiological readings are collected by BSN and send it to the hospital. It is very essential to protect the patient's confidential data. The wavelet based steganography technique

combines encryption and scrambling technique for confidential data protection. ECG signal was used to hide other physiological information. The effectiveness of this scheme was evaluated by two metrics: Percentage Residual Difference (PRD) and Wavelet Weighted PRD (WWPRD). It shows that high security protection was achieved.

A new framework was introduced in [7] with four logical entities: sensor, server, database and matcher. It is used for analyzing security and privacy in biometric authentication systems. Different generic attacks were developed. Blackbox approaches were used to perform operations on biometric data and input/output behavior was analyzed. Different attack goals were considered and the requirements on data flows also analyzed. Sharing of Personal Health Records (PHRs) was described in [8]. It is based on attribute based encryption. Patients can control the access of their own PHRs. Before sharing PHRs with trusted parties, they were encrypted. To achieve privacy, scalability and flexibility a novel patient-centric framework was proposed here. The encryption is based on attribute based encryption technique. Key management complexity was reduced by multiple data owner scenario and the users were divided into multiple security domains. A high degree of privacy was achieved by multi-authority ABE. CP-ABE based on access policy was proposed in [20]. Generation of keys, encryption and decryption were supported by different algorithms. A fine-grained access control over sensor data and distributed data access control scheme were proposed in [21]. It uses a novel cryptographic primitive called attribute-based encryption (ABE) and recovers strong attacks such as sensor compromise and user colluding. Performance and security requirements were satisfied by this model.

3. Proposed work

In the proposed work, a WSN is designed with body sensors. The overall system architecture is shown in Figure 1. Different sensors are fitted on patient's body to enable continuous and accurate acquisition of body parameters like body temperature, blood pressure, ECG and pulse rate. The collected vital signs are forwarded to android mobile phone which is carried by the patient. The communication between sensors and mobile phone is done though short range Bluetooth communication. Here the support of PC is eliminated and the mobile phone itself is used to collect, store and forward the details to the data server which is located at hospital. The data server consists of KGC (Key Generation Center) and DSC (Data Storing Center). Both KGC and DSC generate keys for secure data communication. Finally the body parameters are forwarded to the doctors for diagnosis.

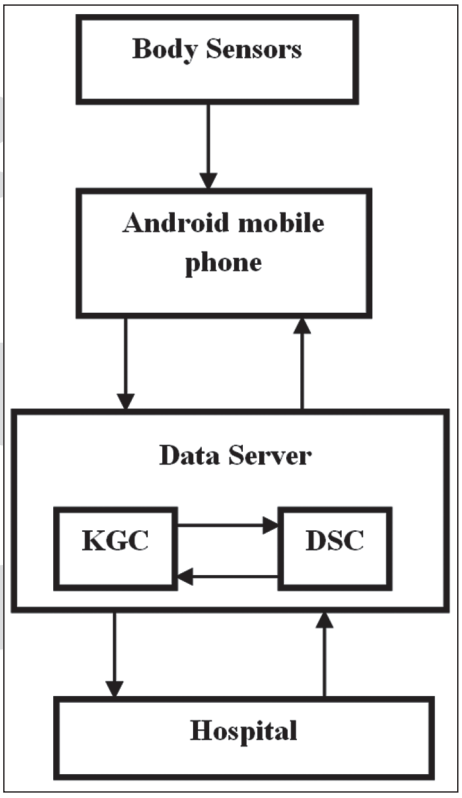

Figure 1. Proposed system architecture

Security is one of the essential features when the patient details are forwarded to the hospital. Here security is enabled in the patient monitoring based on modified CP-ABE technique. The patient (Data owner) has the entire control of his data and decides who can access it. Both KGC and DSC are responsible for generating keys. KGC performs authentication process. Initially all the authorized users have to register in DSC. The steps used in modified CP-ABE are given as follows:

1. KGC generates a private key KGCPr and public key KGCPu.

2. DSC generates a private key DSCPr and public key DSCPu.

3. Data owner encrypts its ID (UID) with KGCPu and send it to KGC for authentication.

4. KGC decrypts it by KGCPr and compares it with DB for authentication.

5. If it is authenticated, KGC generates a key (UK1) by applying KGCPr and UID and send it to the data owner.

6. DSC generates another key (UK2) by applying DSCPr and UID and send it to the data owner.

7. KGC and DSC communicate with each other to know about UK1 and UK2.

8. Using UK1 and UK2 data owner can derive the secret key set (DOPr, DOPu).

9. Data owner encrypts its data with its private key (DOPr) and gives to DSC.

10. Authenticated user has to register in DSC. They can only get encrypted data from DSC and decrypts it by DOPu.

Initially KGC generates a private and public key. Similarly DSC generates separate pair of private and public key. Public keys are known by data owner and user. Data owner encrypts its ID with KGC's public key. KGC receives it and decrypt it by its private key. Registered user names are present in the database. KGC verifies the decrypted ID with the database for authentication and gives OK message to data owner.

KGC generates a new key UK1 by its private key and user ID and DSC generates another key UK2 by its private key and user ID. Both UK1 and UK2 are given to data owner. KGC and DSC communicate with each other to know about UK1 and UK2. Using UK1 and UK2 data owner can derive a private, public key pair. Sensor data can be encrypted by data owner private key and given to DSC. Authenticated user has to register in DSC and they can only decrypt it by data owner's public key.

In CP-ABE, security is enhanced by double encryption. The first encryption is done by KGC during authentication process and it is depicted in Figure 2. The second encryption is done by the data owner during data encryption and it is applied for every patient data before sending them to the hospital. It is depicted in Figure 3.

The architecture of the proposed work is implemented in java and key generation process is done with the help of standard RSA algorithm. There are three stages in the implementation.

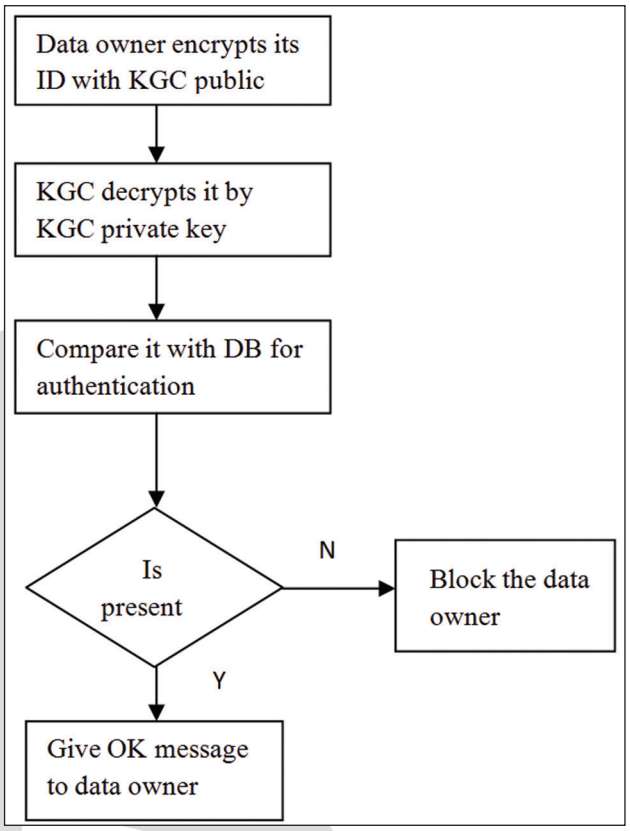

Figure 2. Authentication process by KGC

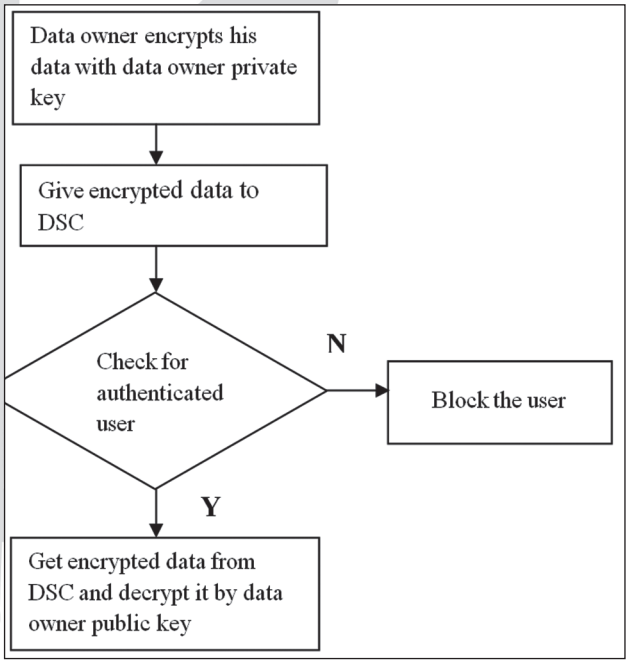

Figure 3. Data encryption by data owner

In the initial stage, the communication is established between client (laptop) and web server. A list of authorized user IDs are initially stored in a database. Different medical readings like body temperature, blood pressure, ECG and pulse rate are stored in separate files as inputs. The initial

step is login process for authentication. User name and password is given and it is verified with the database. If it matches with the database (authenticated), it shows that it is a valid user. KGC and DSC generate private and public keys. From these keys owner generates his own private and public keys. When an input file is selected and uploaded, a reply is sent from server to client.

The second stage is establishing communication between client (android mobile) and server (laptop). Different input files related to body parameters are stored in the mobile. The laptop is turned into a server using mhotspot tool. Mhotspot is a software which converts laptop into a virtual wifi router and creates a secure wifi hotspot. By using the IP address of the laptop, mobile phone is connected to server. Then the home page will be loaded in the mobile. When the user name and password are entered in the mobile, they are verified with the database. If it is an authenticated user, all the keys will be generated in the server and displayed in the laptop. When a file is selected in the mobile, it will be uploaded into the server and reply is sent back to the mobile.

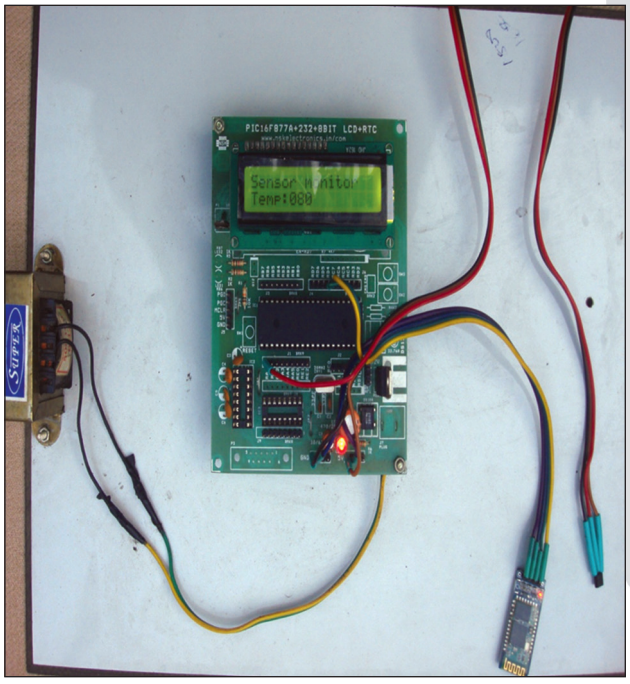

Figure 4. Temperature sensing circuit

The final stage of implementation is real-time implementation with the help of temperature sensor. The sensing circuit consists of LM35 temperature sensor, LCD, microcontroller16F877A, *USART (Universal Synchronous/Asynchronous Receiver/Transmitter)* and linvor Bluetooth device and it is shown in Figure 4. The pin diagram of the microcontroller is shown in Figure 5.

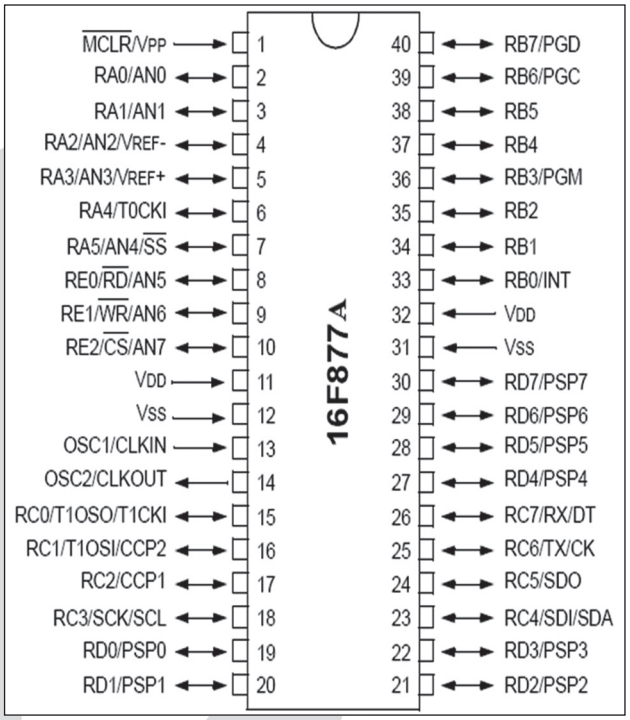

Figure 5. Pin diagram of microcontroller 16F877A

The block diagram of real time implementation is depicted in Figure 6. The temperature sensor senses the temperature of the patient. It is an analog form and it is given to microcontroller which has an inbuilt ADC (Analog to Digital Converter) to convert into a digital form. The value is displayed in LCD display. A serial Bluetooth device linvor is connected to RC6 and RC7 pins of microcontroller through USART (Universal Synchronous Asynchronous Receiver/Transmitter) which is used to establish a communication between sensor and a mobile.

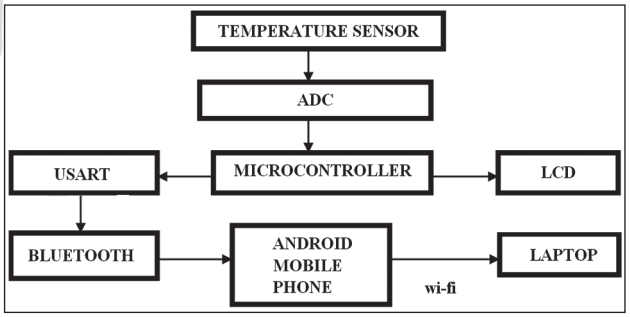

Figure 6. Block diagram of the real time implementation with temperature sensor

A package blue-ser is installed in a mobile phone. It has a java coding for android operating system to enable continuous automatic uploading. It is also connected with the Bluetooth adapter. A timer is set for 9s. When a Bluetooth socket is wirelessly connected with the mobile phone, the temperature values of a patient are continuously forwarded to android mobile phone at an interval of 9s.The blue-ser package forwards it to laptop through wifi communication. Here a laptop is created as a secure wifi hotspot using mhotspot software. Then the reply is given from laptop to mobile phone based on the temperature reading. Hence the continuous real time monitoring is supported.

The outdoor environment monitoring can also be supported here. GSM (Global System for Mobile Communications) technology is enabled in the mobile phone. The location of the patient is found out using latitude and longitude mobile tracking data. This means that the location can be automatically traced any time and also forwarded to the server side. Hence the doctors can track the location of the patient.

4. Performance and evaluation

In the proposed in-home patient monitoring system security is enhanced by double encryption. The key generation process is implemented by modified CP-ABE steps. Different key sizes like 512 bits, 1024 bits, 1536 bits and 2048 bits can be given to generate keys and the execution is repeated for ten iterations. During the authentication process, patient ID is encrypted with KGC's public key and given to KGC. This time is represented by encryption time1. KGC decrypts it by its private key and compares it with DB for authentication. This decryption time is represented by decryption time2. The data owner can create his own private and public key pair using UK1 and UK2. This time is represented by owner key generation time. Data owner encrypts its data with its private key DOPr and gives to DSC. This encryption time is represented by encryption time2. Authenticated user can get encrypted data from DSC and decrypts it by DOPu. This time is represented by decryption time2. The values are plotted in a graph and it is shown in Figure 7. It shows that there is no large deviation even when the key sizes are increased. When the key size is increased, the security is also improved. Thus the security is improved in the proposed in-home patient monitoring system when a key size of 2048 bits is used.

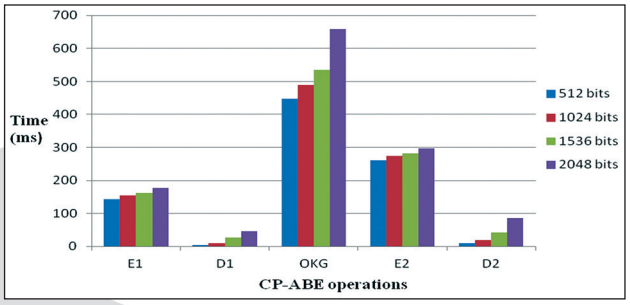

Figure 7. Average time requirement for CP-ABE operations

The modified CP-ABE scheme is compared with the existing CP-ABE scheme. In the existing CP-ABE, there is a single data encryption (E2). Also KGC generates UK1 by its private key, user ID and personalized secret information of user. Similarly DSC generates UK2 by its private key, user ID and personalized secret information of user. So it takes more time for generating UK1 and UK2 and automatically OKT, DE and DD are also increased when compared with the proposed scheme. The corresponding graph for table 2 is shown in Figure 8.

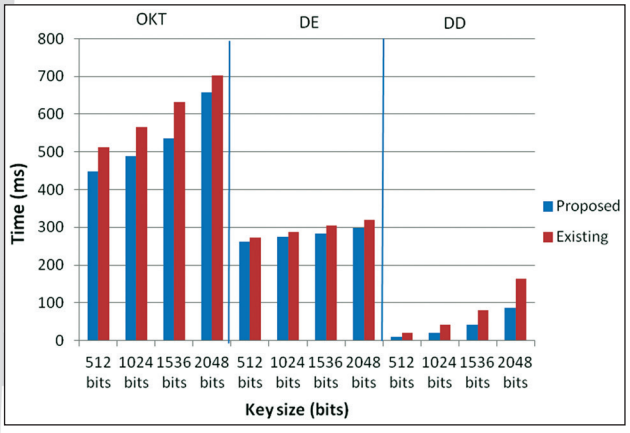

Figure 8. Comparison of proposed and existing systems

In the real time implementation, the temperature readings of a patient are automatically forwarded to server through the mobile phone. Then the response is immediately forwarded back to patient's mobile phone. Now the RTT (Round Trip Time) delay for this communication calculated and the process is repeated up to 100 iterations for pro-

posed and existing CP-BE scheme. The average values for every 20 iterations are also calculated and the corresponding graph is shown in Figure 9.

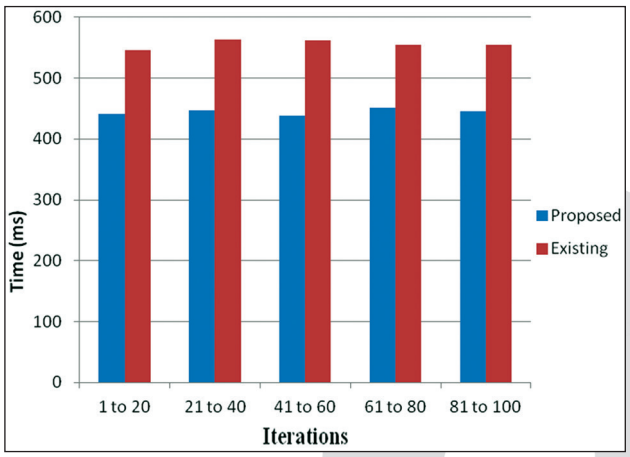

Figure 9. Average RTT values

The graph shows that the average RTT values for different iterations are constant. Hence it is concluded that the system is stable with respect to time. But the RTT values of existing system are higher than the proposed system.

During the data transmission, the temperature reading from the patient is transmitted to the server in terms of bytes. The number of bytes transmitted from the client side and number of bytes received at the server side are calculated. These are monitored for 50 seconds. Then the DDR (Data Delivery Ratio) for different data transmission are calculated by the formula

DDR= (No. of bytes received / No. bytes transmitted) X 100

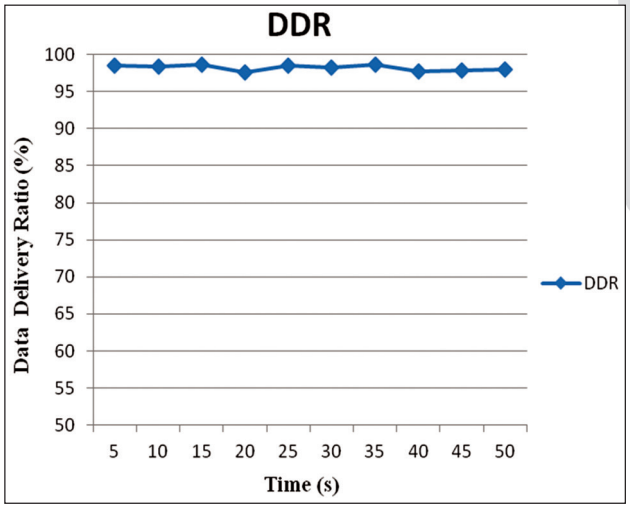

Figure 10. Data Delivery Ratio

The resulting graph is shown in Figure 10. The graph shows that high DDR (above 97.5%) is achieved constantly in the proposed system.

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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

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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)

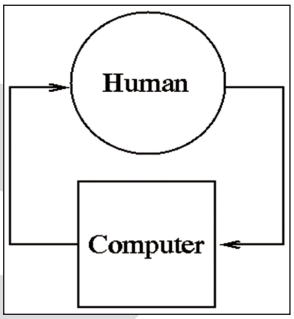

Figure 1. Text here

Conclusion

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Acknowledgements (If any)

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

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