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Chronic Diseases Journal

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1. Perlman AI, Sabina A, Williams AL, Njike VY, Katz DL. Massage therapy for osteoarthritis of the knee: a randomized controlled trial. Arch Intern Med 2006; 166(22): 2533-8.

2. Buckwalter JA, Marsh JL, Brown T, Amendola A, Martin JA. Articular cartilage injury. In: Robert L, Robert L, Joseph V, editors. Principles of Tissue Engineering. 3rd ed. Burlington, MA: Academic Press; 2007. p. 897-907.

3. Kuczmarski RJ, Ogden CL, Grammer-Strawn LM, Flegal KM, Guo SS, Wei R, et al. CDC growth charts: United States. Advance data from vital and health statistics. No. 314. Hyattsville, Md: National Center for Health Statistics, 2000. (DHHS publication no. (PHS) 2000-1250 0-0431)

4. World Health organization. Strategic directions for strengthening nursing and midwifery services [online]. Available from: URL:http://www.wpro.who.int/themesfocuses/theme3/focus2/nursingmidwifery.pdf2002

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Table of Contents

Original Articles

Case Reports

Chronic Diseases Journal

Risk factors for gestational diabetes mellitus in Sanandaj, Iran

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Original Article

Abstract

BACKGROUND: Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance that is detected for the first time during the most recent pregnancy. It can lead to serious complications for mother and infant. The current study aimed to determine the important risk factors for GDM in Sanandaj, Iran during 2010-2011.

METHODS: This was a case-control study in which 220 people were chosen for each group from referees to the healthcare centers and diabetes center in Sanandaj. Data were collected through interviews and review of medical records. Data analysis conducted using chi-square test and logistic regression.

RESULTS: In the present study, diabetic mothers were older and more obese than non-diabetic mothers. In the logistic regression, variables such as familial history of diabetes in first-degree relatives, history of gestational diabetes, age ≥ 30 years, history of stillbirth, history of macrosomia, and body mass index above 30 were considered as the most important independent risk factors for gestational diabetes respectively. However variables such as smoking, blood pressure, and history of infant death showed no statistical significant difference between the two groups.

CONCLUSION: The most important risk factors for developing GDM included history of diabetes among relatives (family history), mothers with a history of gestational diabetes, and history of macrosomia. Therefore, controlling these factors can reduce the incidence of diabetes during pregnancy.

KEYWORDS: Gestational Diabetes, Risk Factors, Logistic Regression

Date of submission: 7 Oct 2013, ***Date of acceptance:*** 9 Dec 2013

Citation: Zokaie M, Majlesi F, Rahimi-Foroushani A, Esmail-Nasab N. **Risk factors for gestational diabetes mellitus in Sanandaj, Iran.** Chron Dis J 2014; 2(1): 1-9.

Introduction

Diabetes is the most common metabolic disorder which has been the seventh leading cause of death in the United States in 2007.[1] It will be the seventh leading cause of death in the world in 2030[1,2] and the most common metabolic disorder affecting pregnancy.[1,3-5] According to different studies, prevalence of gestational diabetes mellitus (GDM) in Iran is consistent with the international level and varies from 2 to more than 10%.[6] Increase in gestational diabetes in recent years in all ethnic groups is possibly related to the lifestyle factors in general population (sedentary lifestyle and dietary changes).[6-8] Advanced maternal age during pregnancy is another reason for this increase.[4,9] Abnormal glucose metabolism during pregnancy could have adverse outcomes for both mother and baby,[10] and is among strong risk factors for adverse pregnancy outcomes and increases morbidity and mortality during

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childbirth.[11] In addition to recurrence risk of gestational diabetes in subsequent pregnancies, there is a chance for developing the disease in their later years of life.[11] Consequently 35 to 60% of the patients will develop diabetes over the next 10 to 20 years.[1] Offspring of diabetic mothers (ODM) are at higher risk of developing diabetes.[12]

In meta-analysis of over 110 articles on gestational diabetes, Shannon has reported the following risk factors which are associated with gestational diabetes: Maternal obesity (> 120% of ideal body weight), first-degree relative history of diabetes, previous history of microcosmic babies, history of stillbirth, unexplained infant death, age over 35 years, glucosuria (two or more than two times) during recent pregnancy, and eventually race and ethnicity.[13]

In a systematic review of 41 articles on diabetes risk factors by Souza, many variables including past obstetric history of mother's low birth weight, maternal short stature, history of smoking, high parity, race, low levels of physical activity, weight gain during pregnancy, and socio-economic factors had contradictory results and are still not unanimously agreed upon.[14] In most national studies, role of risk factors such as miscarriage, stillbirth, abnormal birth history, and history of hypertension and preeclampsia results have shown contradictory outcomes.[15-19] According to the National Center for Disease Control, guidelines warning signs after screening of pregnant mothers include the history of stillbirth, history of two or more spontaneous abortions, history of high-birth-weight baby 4 kg or more, first-degree family history of diabetes and obesity equal to or greater than 30 kg/m^2 mean body mass index (BMI) before pregnancy.[20] Owing to the importance of GDM and its adverse consequences for mother and baby, as well as contradictory information about risk factors for gestational diabetes throughout the world including Iran, and insufficient measurement of the variables related to gestational diabetes in the country level, and because no comprehensive study in this field has been conducted in the Kurdish population, this study aimed to determine the risk factors for GDM in Sanandaj during 2010 to 2011.

Materials and Methods

This was a case-control, non-matched population-based study done in 2010 to 2011 in pregnant women referred to the health and diabetes center in Sanandaj, Iran. The minimum sample size required for this study was considered based on exposure in controls (P0 = 0.15) and cases (P1 = 0.26). With regard to the odds ratio (OR) equal or more than 2 for each risk factor, with a confidence level of 95% and the power 80% (β = 80), 208 cases were enrolled in the study. In this study, case and control groups were defined early in the study. Cases were chosen among pregnant women who according to their GDM screening and based on the national guidelines their positive test results were available in their patient records. Controls were pregnant women who were considered healthy based on the gestational diabetes screening tests records. Among health records at health centers in Sanandaj during 2010 to 2011, and according to the figure 1, samples were selected. Then, after applying the following exclusion criteria, 220 patients were selected; history of overt diabetes mellitus, history of taking medications that affect glucose metabolism such as corticosteroids, endocrine disorders such as connective tissue disease, toxic goiter and active thyroid, and evidence of no laboratory tests such as glucose tolerance test (GTT) in patient file record.

After determining distribution in separate health centers, controls were selected based on the registered records of pregnant women in centers using simple random sampling. Finally, 220 controls were chosen from selected health centers after applying the following exclusion criteria in the control group; laboratory evidence suggestive of GDM, overt diabetes, exposure to endocrine disorders and impaired glucose metabolism, history of taking medication that impairs glucose metabolism, and incomplete records despite maternal interviews for extraction of variables.

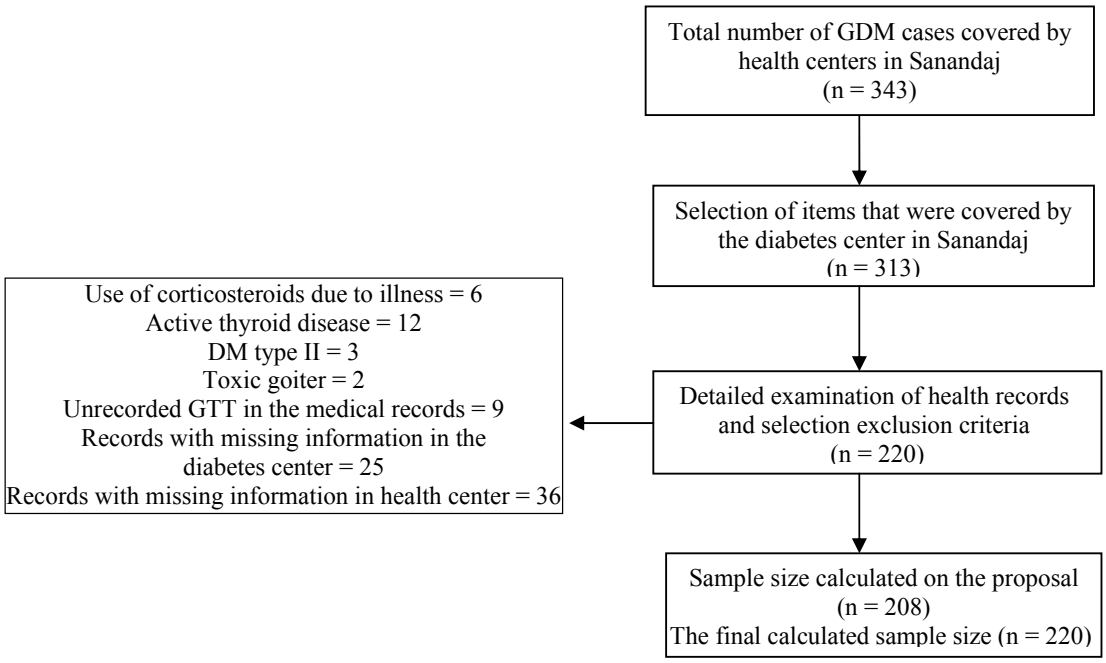

Figure 1. Sampling flowchart

GDM: gestational diabetes mellitus

DM: Diabetes mellitus

While reviewing health records of mothers in the health centers and their medical records in the diabetes center, telephone interviews with mothers were conducted by the researcher in order to extract information and control the recorded data. In this study, mothers were classified into three age groups i.e. less than 25 years, 25 to 30 years and over 30 years. Mothers' body mass index (BMI) before the pregnancy were divided into three groups; normal, pre-pregnancy (less than 25), overweight (30-25) and obese (greater than 30). Mother's education level was divided into three groups; less than primary education, guidance and high school, diploma or higher. Smoking habit divided into never used to smoke, active smoker and quit smoking. Previous history of macrosomia and birth records of infants greater than 4000 grams, history of gestational hypertension with blood pressure greater than 140/90 mmHg measured twice with an interval of more than 6 hours without proteinuria and after week 20 of gestation. In this study, history of polyhydroamnious was defined as increased fluid volume more than 2000 cc according to ultrasound report.

After data collection, data were entered into SPSS for Windows (version 16.0, SPSS Inc., Chicago, IL, USA) and were analyzed. Chi-square test and calculation of crude OR were used for univariate analysis. To remove the effect of confounding variables, variables with a significance level of less than 0.25 entered into the logistic regression analysis. Then, after calculation of OR, value less than 0.05 was considered as a significance level.

Results

The mean age of the study subjects and control group were 32.27 ± 5.41 and 27.29 ± 5.41 years, respectively. In this study, 91.4% of the cases were in the age group 25 years and over. Mothers with gestational diabetes were older and fatter than healthy mothers (Table 1).

Table 2 shows comparison of variables including educational status, smoking, number of pregnancies (of 3 or more) and height of case and

control groups

Table 1. Mean quantitative variables related to demographic characteristics of women participating in the study

Variables	Case (n = 220) (Mean ± SD)	Control (n = 220) (Mean ± SD)
Maternal age	32.27 ± 5.41	27.29 ± 5.06
Mother BMI	28.16 ± 3.92	25.68 ± 4.01
Systolic blood pressure	108.97 ± 11.43	108.25 ± 9.26
Diastolic blood pressure	68.90 ± 8.8	68.52 ± 8.45
Weight gain during pregnancy	10.22 ± 3.20	12.50 ± 3.47
Parity	1.48 ± 1.08	1.29 ± 0.93

BMI: Body mass index

Compared with healthy mothers, mothers who developed GDM were among those who had the following risk factors; family history of diabetes, previous history of gestational diabetes, history of macrosomia, history of stillbirth, history of infertility, abnormal birth history, two or more previous miscarriages, and history of gestational hypertension. The difference between the two groups regarding maternal employment variables, smoking, history of hypertension, and history of infant death with an unknown cause was not statistically significant (P > 0.05) (Table 2 and Table 3).

After entering the univariate analysis significant risk factors into regression model, age over 30 years, having a BMI 25 or more, family history of diabetes in relatives, history of gestational diabetes, macrosomia and history of stillbirth remained in the model (P < 0.05), finally, results showed that women over age 30, maternal overweight, mothers who had a history of diabetes in their first-degree relatives, those who have a history of gestational diabetes, mothers with a history of macrosomia, and finally, mothers with a history of stillbirth had a higher chance of getting gestational diabetes. (Table 4).

Discussion

The results of our study showed that family history of diabetes in first-degree relatives, was identified as the most important risk factor (OR = 7.18). Family history of diabetes in relatives increases the risk of gestational diabetes which was considered as an important risk factors in the studies done by Kanadys in Poland[21] and Rahimi

Table 2. The relationship between demographic variables and recent pregnancies in study subjects

Variables	Case (n = 220) [%]	Control (n = 220) [%]	OR (CI)	P
Age groups				
Age group under 25 year	19 (8.6)	79 (35.9)	1	-
Age group older than 30 years	134 (60.9)	58 (26.4)	9.60 (5.33-17.29)	< 0.001
Age group between 30-25 years	67 (30.5)	83 (37.7)	3.35 (1.85-6.08)	< 0.001
BMI groups				
BMI under 25	42 (19.1)	98 (44.5)	1	-
BMI over 30	84 (38.2)	35 (15.9)	5.60 (3.28-9.56)	< 0.001
BMI between 25-30	94 (42.7)	87 (39.6)	2.52 (1.58-4.01)	< 0.001
Education				
Secondary and higher education	69 (31.4)	80 (36.4)	1	-
Guidance and secondary education	34 (15.5)	54 (24.5)	2.16 (1.29-3.60)	0.003
Primary and lower education	117 (53.1)	86 (39.1)	1.57 (1.03-3.41)	0.035
Smoking	3 (1.4)	1 (0.5)	3.02 (0.312-29.33)	NS (P = 0.315)
Mother's occupation (housewife)	198 (90)	200 (90.9)	-	NS (P = 0.935)
Maternal height ≤ 150 cm	16 (7.3)	4 (1.8)	4.23 (1.39-12.88)	0.001
Weight gain ≥ 11 kg	113 (62.08)	86 (44.79)	2.01 (2.01-4.50)	0.001
Number of deliveries ≥ 3	48 (28.1)	15 (6.8)	3.81 (2.06-7.04)	0.001
Parity ≥ 3	129 (58.6)	123 (55.9)	1.11 (0.76-1.63)	NS(P = 0.563)
Having high blood pressure	6 (2.7)	2 (0.9)	3.05 (0.610-15.31)	NS (P = 0.154)

OR: Odds Ratio; CI: Confidence interval; BMI: Body mass index; NS: Non significant

Table 3. Relationship between maternal related variables in previous pregnancies of study subjects

Variables	Case (n = 220)	Control (n = 220)	OR (CI)	P
Family history of diabetes	74 (%33.6)	24 (%10.9)	4.14 (2.49-6.87)	< 0.001
Previous history of gestational diabetes	27 (%14.9)	5 (%2.8)	5.99 (2.25-15.95)	<0.001
Previous history of macrosomia	26 (%14.7)	4 (%2.4)	6.93 (2.36-20.32)	<0.001
History of stillbirth	29 (%16.4)	4 (%2.4)	7.88 (2.70-22.97)	< 0.001
History of infertility	32 (%14.5)	10 (%4.5)	3.57 (1.71-7.46)	< 0.001
History of congenital malformation	9 (%5.1)	1 (%0.6)	8.78 (1.10-70.12)	0.014
History of 2 ≥ previous miscarriages,	11 (%8.6)	2 (%1.6)	5.64 (1.22-25.99)	0.013
History of gestational hypertension	12 (%6.6)	3 (%1.7)	4.09 (1.13-14.76)	0.02
History of infant deaths with unknown cause	7 (%4.0)	3 (%1.8)	2.22 (0.56-8.74)	NS (P = 0.241)

OR: Odds Ratio; CI: Confidence interval; NS: Non significant

Table 4. Analysis of multivariable associated with diabetes in pregnancy using unconditional logistic regression

Variables	OR	95% (CI)	P
Age group 25-30 years	1.40	0.29-6.79	0.674
Age over 30 years	5.77	1.27-26.10	0.023
BMI between 25-30	2.91	1.16-7.30	0.023
BMI over 30	3.69	1.40-9.68	0.008
Family history of diabetes in relatives	7.18	2.94-17.55	0.001
Maternal history of gestational diabetes	6.25	1.52-25.74	0.011
History of macrosomia	5.27	1.12-24.67	0.035
History of stillbirth	5.63	1.33-23.86	0.019

OR: Odds Ratio; CI: Confidence interval; BMI: Body mass index

et al. in Kermanshah.[22] These results have already been obtained in the literature[5] and many other prospective[23-25] and cross-sectional studies are already in the literature.[26,27] But some of the studies done inside Iran did not find any significant association between the history of diabetes in first degree-relatives and GDM[15,18,28,29], which could be due to high prevalence of type II diabetes in these communities.

In the fifth international conference on diabetes, the history of GDM as a variable in the previous pregnancies was as a risk factor of gestational diabetes.[9] In our study after history of diabetes in the first degree relatives, history of GDM as a variable was mentioned as the second important risk factor in GDM (OR = 6.25). This variable remained in the model in other studies of regression determining diabetes during pregnancy (OR = 5.09- 21.93).[7,18,22,30-32]

In a study conducted by Cheung et al., the risk factors for GDM women born in the four Asian countries, i.e. China, the Philippines, Sri Lanka and Vietnam showed that history of GDM was the only significant risk factor in all four groups (OR = 14.5).[33] The study of Tabatabaei on pregnancy and diabetes did not show any statistical significant association between this variables and GDM.[15]

In our study, increasing age was associated with more chances of gestational diabetes so that the risk of gestational diabetes in women over 30 years was 5.77 times more than women under 25 years. The results are consistent with most of the national and international studies.[3,6-8,13,29,34-36] In a study done by Hadaegh et al. in Bandar-Abbas, relative risk of gestational diabetes in 35-39 year old group were 15 times more than age groups under 20 years.[29] In a study conducted by Tabatabaei, with every year increased in maternal age, the risk became 1.18 times more.[15] Although several studies have reported age as a risk factor for gestational diabetes, each reported a different age number.[21,32,37,38] Perhaps age difference of the demographic profile, young population and pregnancy in the lower age group in developing countries comparing to developed ones is one of the reasons for age differences in various

studies. In a study done in Lithuania and Philippines, There was no statistical significant association between age and GDM.[35,39] The possible explanation for this could be socio-cultural desire of these people to family formation in lower age groups compared with western countries, leading to fewer numbers of marriages above 30 years in these studies.

History of stillbirth in the diabetes protocol of Iranian Center for Non Communicable Disease Management has been listed as a risk factor for gestational diabetes.[20] This variable was among other significant factors that increased the chances of GDM to 5.63 times more, and was consistent with some international and national studies.[13,19] However, in some national studies,[16-18,22] there was no statistical significant association between stillbirth and gestational diabetes. In this study, history of two and more than two abortions after doing univariate tests was identified as risk factor for gestational diabetes. However, after entering into the logistic regression model, no significant association was found with gestational diabetes. This finding was in accordance with the results of national and international researchers.[17,19,30,35,40,41] The conflicting results could be due to inclusion of one miscarriage (instead of at least two miscarriages), as a risk factor in some studies.[22]

In the diabetes management Protocol of the Iranian non-communicable diseases center and literature,[5] macrosomia is one of the most important risk factor for GDM. In our study, history of macrosomic infants was recognized as an independent risk factor for gestational diabetes which increased the risk of diabetes by 5.27 times. Finding was consistent with the results of many other studies.[7,13,16-19,21,40,42,43] Furthermore, in Mirfeizi et al. study in Karaj, macrosomia has been suggested as the most important risk factor for GDM (OR = 10.47).[40] However, in other national and international studies, there was no association between macrosomia and GDM.[22,28,30,39]

Among other interfering risk factors is high BMI which is an independent risk factor, significantly associated with our study. Chances of developing gestational diabetes in overweight and obese group were 2.91 and 3.69 more times, respectively than those who had a BMI less than 25. This was consistent with the meta-analysis results of Torloni et al.[42]

Some cohort studies have suggested that smoking is among the risk factors that is related to the gestational diabetes,[23,44,45] although some other studies (national and international), showed inconsistent results.[32, 46-49] In our study, association between smoking and gestational diabetes was not significant. These differences are supposed to represent the following points in the studies: Studies' lack of power, difference in diagnostic methods, different definitions of exposure time (such as categorizing woman who smoke just one cigarettes as smokers), different controls for confounding factors as well as change in smoking habits as a result of pregnancy or giving wrong information about smoking habits because of under recognized adverse effects of smoking during pregnancy.[14,45,47-49] A cross sectional study in Scandinavian countries[50] showed that smoking more than 10 cigarettes per day during pregnancy affect glucose homeostasis and cause GDM. This study has been confirmed by others.[23]

Among the strengths of this study was that the researcher used standard definitions of protocols of Non-Communicable Disease Prevention Center and office of Iranian Mothers Health Organization, which was due to the variety in definitions of variables in other studies. In order to minimize the information bias, researcher collected the data himself. Considering the fact that abortion is introduced as risk factor for GDM in some studies,[16,21,22], and stillbirths is introduced as risk factor for GDM in other studies,[13,19] therefore it is possible that this problem can be due to lack of correct differentiation between stillbirths and abortion at the time of data registration. Therefore, it is suggested that in future studies particularly in retrospective ones, accuracy of abortion and stillbirths be checked in

the time of data collection. It can be noted that one of the limitations of this study was limiting samples to those who were supported by the health centers or province diabetes center which caused a relative decrease in our study's population-based findings. However, this can be disregarded owing to high coverage of diabetes screening at these two centers during pregnancy.

Conclusion

In this study, after identifying significant independent risk factors for GDM in Kurdish ethnicity, for the first time most important risk factors for developing GDM identified as the history of diabetes among first-degree relatives (family history), mothers with a history of gestational diabetes, and history of macrosomia.

Therefore, it is recommended that detected risk factors in this study be prioritized for education of mothers who are willing to have birth. In addition, these risk factors should be considered more in screening and follow-up of mothers at risk of GDM to prevent any adverse effects of the disease in mothers and their children.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

Hereby, many thanks go to the staff of the Deputy of Health as well as Diabetes Center, Kurdistan University of Medical Sciences for their cooperation and assistance in this study.

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Chronic Diseases Journal

Comparison of diagnostic indices of MRI and EMG in diagnosis of lumbar radiculopathy

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Original Article

Abstract

BACKGROUND: lumbosacral radiculopathy is one of the most common disorders that can be examined by neurologists. Electromyography (EMG) and magnetic resonance imaging (MRI) are used to inspect this disease; however, the application of MRI and EMG in patients with back pain is still under study. This study was designed and implemented to compare the diagnostic values of MRI and EMG in the diagnosis of lumbar radiculopathy.

METHODS: This was cross-sectional study which included 62 patients with suspected lumbosacral radiculopathy in a referral neurology clinic in Sanandaj, Iran, in 2009-2010. EMG was considered as the gold standard test. Inclusion criteria were being older than 20 years of age, and suffering from back pain or radicular pain in the lower limbs for more than four weeks. Data were entered into SPSS software and the diagnostic indices and agreement were calculated.

RESULTS: The percentage of agreement between MRI and EMG results were calculated as 80.6%. The sensitivity of MRI compared with EMG at different levels was calculated between 44.4% and 79.6% and its specificity was calculated between 46.1% and 94.3%. In total, sensitivity and specificity of MRI were 68.9% and 86.3%, respectively. The Lasègue's sign, used for detection of disc herniation, had the sensitivity, specificity, and positive and negative predictive value of 28.8%, 50%, 75%, and 11.9%, respectively.

CONCLUSION: MRI and EMG tests have no superiority over one another for the evaluation of lumbar radiculopathy and it is necessary to do both. The Lasègue's sign is also not an appropriate test for detection of lumbar spine disc herniation, and it is not helpful in diagnosing or ruling out the disease.

KEYWORDS: Radiculopathy, Magnetic Resonance Imaging, Electromyography

Date of submission: 28 Oct 2013, ***Date of acceptance:*** 1 Dec 2013

Citation: Khomand P, Ahsan B, Fazel S, Ghafari A. **Comparison of diagnostic indices of MRI and EMG in diagnosis of lumbar radiculopathy.** Chron Dis J 2014; 2(1): 10-4.

Introduction

Prevalence of back pain varies from 12% to 33% in different societies. Its prevalence in a person's life can vary from 11% to 84%.[1,2] Lumbosacral radiculopathy is a complication in the lumbar nerve roots that leads to symptoms in the lower limbs and it is one of the most common disorders that is evaluated by neurologists.[3,4] Electromyography (EMG) can be used to diagnose lumbar radiculopathy; however, this test can diagnose the problem as long as the nerve root is physiologically affected. Instead, magnetic resonance imaging (MRI) can also detect lesions that have not caused physiological disorders in the nerve.[5] MRI can provide anatomical evidences and is useful in choosing a treatment process, but it could also have false positive results.[6-8] The effectiveness of MRI in the evaluation of patients with back pain is still controversial.[8] This study was designed and implemented to compare the

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diagnostic value of MRI and EMG in the diagnosis of lumbar radiculopathy.

Materials and Methods

This was a cross-sectional and descriptive-analytical study. Patients who suffered from back pain and radicular lower limb pain with paresthesia and motor-reflex deficit and who referred to the Neurology Clinic of Tohid Hospital between 2009 and 2010 were enrolled in the study.

Inclusion criteria were being older than 20 years of age, and suffering from back pain or radicular pain in the lower limb for more than four weeks. Exclusion criteria included diabetes, vasculitis, Guillain-Barré syndrome, motor neuron disease (MND), tumors, and metastases. First, samples were clinically examined by a neurologist and the result of Lasègue's sign was registered, and if necessary MRI was requested. MRI report was prepared by a radiologist and was entered into the questionnaires. Then, EMG/NCV (nerve conduction velocity) electrodiagnostic test was performed by a neurologist without the knowledge of the MRI result.

To determine radiculopathy in different muscles of lower extremity, EMG/NCV was performed on the sensory-motor nerves and lower limb muscles; based on the sum of NCV and EMG findings in the involved nerve roots, they were identified and were registered in the questionnaires. EMG was considered as the gold standard test. MRI was considered positive when disc herniation, bulging, protrusion, extrusion, degenerative joint disease (DJD), and Spondylolisthesis was observed with different grades. 73 patients who had inclusion criteria were evaluated, and 62 patients signed informed consent forms and were entered into the study.

Frequencies and percentages were calculated after entering data into SPSS for Windows (version 11.5, SPSS Inc., Chicago, IL, USA). Chi-square and Fisher's exact tests were used to compare nerve root involvement between male and female participants. Then diagnostic indices together with 95% confidence intervals were calculated.

Results

37 participants were male (59.7%) and 25 (40.3%) were female. Their mean age was 40.5 ± 11 years. Using EMG as a diagnostic test, 8 patients (12.9%) had normal test results, and there was L3 involvement in 9 patients (14.5%), L4 involvement in 18 patients (29%), L5 involvement in 40 patients (64.5%), and S1 involvement in 49 patients (79%). No Significant difference was observed between the sexes regarding different levels of involvement (Table 1). In 10 cases (16.1%) involvement was observed at one level, in 31 cases (50%) at two levels, in 8 cases (12.9%) at three levels, and in 5 cases (8.1%) at four levels. In 6 patients (9.7%) MRI test result was reported normal. The percentage of MRI and EMG agreement was calculated as 80.6%. In total, sensitivity and specificity of MRI were 68.9% and 86.3%, respectively. The sensitivity and specificity of MRI compared with EMG at different levels (lumbar and sacral roots) were calculated from 44.4% to 79.6% and from 46.1% to 94.3%, respectively. Defect in 36 (31.3%) nerve roots were seen in EMG, but MRI had missed them; however, 18 impaired (13.6%) roots were seen in MRI but EMG had missed them. Compared with other levels, L5 and S1 had more cases of positive MRI but negative EMG (Table 2).

Table 1. Involvement of different levels based on electromyography (EMG) test in both sexes

Involvement level	Male	Female	Significance level
L3	6 (16.2%)	3 (12%)	0.72
L4	10 (27%)	8 (32%)	0.77
L5	23 (62.2%)	17 (68%)	0.78
S1	32 (86.5%)	17 (68%)	0.11

Based on Fisher's exact test, no significant difference was observed in the involvement level between the two sexes.

52 patients (83.9%) had disc herniation in the lumbar vertebrae. The Lasègue's sign, used for detection of disc herniation, had the sensitivity, specificity, positive and negative predictive value of 28.8%, 50%, 75%, and 11.9%, respectively, in comparison to MRI.

Table 2. Comparison of the diagnostic value (95% confidence interval) of magnetic resonance imaging (MRI) with electromyography (EMG) in different lumbar levels

Assessed level	MRI	EMG		Sensitivity	Specificity	Positive predictive value	Negative predictive value
		Positive	Negative				
L3	Positive	4	3	44.4	94.3	57.1	90.9
	Negative	5	50	(13.7-78.8)	(84.3-98.8)	(18.4-90.1)	(89-97)
L4	Positive	11	2	61.1	95.4	84.6	85.7
	Negative	7	42	(35.7-82.7)	(84.5-99.4)	(54.4-98.1)	(72.7-94.1)
L5	Positive	26	6	65	72.7	81.2	53.3
	Negative	14	16	(48.3-79.4)	(49.8-89.3)	(63.5-92.8)	(34.3-71.7)
S1	Positive	39	7	79.6	46.1	84.8	37.5
	Negative	10	6	(65.6-89.7)	(19.2-74.8)	(71.1-93.6)	(15.2-64.7)
Total roots	Positive	80	18	68.9	86.3	81.6	76
	Negative	36	114	(59.7-77.2)	(79.3-91.7)	(72.5-88.7)	(68.3-82.5)

MRI: Magnetic resonance imaging; EMG: Electromyography

Discussion

In the present study, the agreement between MRI and EMG was approximately 80.6%. MRI and EMG revealed 98 and 116 lesions, respectively. Approximately 13.6% of the MRI detected lesions were failed by EMG.

In the early stages of the lesion, MRI may show lesions that EMG fails to report. However, as an alternative, EMG can indirectly detect inflammatory lesions and nerve root stretches which cannot be examined by MRI. Therefore, with respect to the high agreement of MRI and EMG, in case of EMG failure, using MRI for an accurate diagnosis in the nerve root lesions instead of using more invasive approaches seems to be beneficial. On the other hand, MRI could be useful alone in mild cases to predict and prevent formation of larger physiopathologic lesions.

In a prevalence study involving patients with abnormal EMG radiculopathy, 84% of patients had radiculopathy symptoms.[3] In a study by Koushan et al., abnormalities in EMG and MRI were reported as 89% and 93%, respectively.[9] It seems that selecting patients based on clinical criteria is a reasonable choice and clinical findings are quite valuable.

Prevalence of radiculopathy in lumbar vertebrae increases from top to bottom. L1 radiculopathy is rare and L5 radiculopathy is the most common.[10] In another study, L5 was the most common involved root.[11] In the present study, people who had clinical symptoms for over 4 weeks were evaluated. Higher incidence of involvement in S1 in our study could possibly result from the presence of cases with more severe disease, and association with the deformities related to the L5/S1 including changes in DJD, Spondylolisthesis, discopathy, and pressure on the S1.

In the study by Koushan et al.,[9] the percentage of agreement was 88% and it was 61% in the study by Reza Soltani et al.[11] Probably, the agreement increases as the severity of the disease increases.[11] Therefore, it is expected that different agreement levels be observed in different studies based on patient type and severity of the disease. Although MRI and EMG results are roughly consistent, each of these tests provides different information.[10,12] Type of patients and their clinical symptoms affect MRI outcome.[9,13]

As MRI can detect disorders that have not caused pressure or defect in nerve roots, we expected to observe high sensitivity in MRI, but the result was different. However, in several previous studies, the sensitivity of MRI, compared with electrodiagnostic tests, was reported from 50% to 64% based on the type of patients.[14-16] In our study, we selected EMG as the gold standard, while EMG is not a complete gold standard and its sensitivity, compared with clinical symptoms, is reported from 55% to 86%.[12,14,16,17] In the study by Koushan et al., the sensitivity and specificity of MRI were 27.3% and

96.5%, respectively.[9] Other studies showed that MRI is the main tool for assessing the vertebra structure and the nerves involvement regions; therefore, performing MRI together with electrodiagnostic tests can be very useful in understanding how to treat complications.[9,18] Some other studies have also shown the superiority of MRI and electrodiagnostic test over one another.[11] Hence, in Lumbar radiculopathy cases both tests are needed.

In addition, one of the possible causes of the low sensitivity of MRI in this study could be the lumbar radiculopathy caused by another radiculitis existing in the province or in our patients. Inflammatory causes can be associated with normal MRI. MRI can detect special complications which need surgery, and in primary examinations MRI is better than CT scan since it can detect inflammations, intra vertebra pathologies, and vascular problems. It may also have a high rate of false-positive results.[10] It is suggested that the causes of lumbar radiculopathy be studied with high precision and the causes of inflammatory back pain be determined.

The most common presentation of lumbar radiculopathy is the pressure on nerve root caused by the disc herniation between the vertebrae which had a prevalence of 83.5% in our study.[10] In other studies, the prevalence of lumbar disc herniation and dislocation in people with radiculopathy have been reported from 65% to 88%.[3,19] This shows that MRI is important for assessing the disc of people with radiculopathy and can facilitate choosing the treatment method. Moreover, Lasègue's sign result cannot be trusted as diagnostic test or screening tool in confirming herniation of lumbar vertebral disc.

Conclusions

Though it seems that MRI has higher specificity and sensitivity for detection of disk herniation, for diagnosis of lumbar roots lesions EMG is the method of choice. However, MRI and EMG tests have no superiority over one another for the evaluation of lumbar radiculopathy and it is necessary to do both. The Lasègue's sign is also not an appropriate test for detection of lumbar spine disc herniation, and it is not helpful in diagnosing or ruling out the disease.

Conflict of Interests

Authors have no conflict of interests.

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Chronic Diseases Journal

Association of chronic medical conditions with preterm labor

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Original Article

Abstract

BACKGROUND: Prematurity is the most common cause of neonatal death and according to Millennium Development Goal (MDG), two-thirds of all under-five deaths should be reduced by 2015. Therefore, this study examined factors related to preterm birth in Sanandaj, Iran in 2012.

METHODS: This case-control study has been conducted on 600 pregnant women; cases were 200 women with preterm labor and controls were 400 women with term labor, in Be'sat Hospital, Sanandaj, Iran, in 2012. Results were analyzed by Chi-square, Mann-Whitney U and logistic regression tests.

RESULTS: In univariate analysis, overt diabetes ($P = 0.030$), chronic hypertension ($P < 0.001$), preeclampsia and eclampsia ($P < 0.001$), had significant correlations with preterm labor. However, multivariate analysis results showed that factors like preeclampsia and eclampsia ($P < 0.001$) and chronic hypertension ($P = 0.030$) had significant correlation with the incidence of premature birth. In univariate and multivariate analysis, anemia ($P = 0.340$) had not any association with the preterm labor.

CONCLUSION: The results of this study showed some chronic maternal conditions such as chronic hypertension and diabetes mellitus, which are important pre-existing medical disorder complicating pregnancy and control of blood pressure and blood sugar before pregnancy, and have an important effect in decreased of preterm labor and complications. But others such as mother's anemia were not responsible for the prematurity.

KEYWORDS: Prematurity, Diabetes, High Risk Mothers, Hypertension

Date of submission: 2 Oct 2013, ***Date of acceptance:*** 4 Dec 2013

Citation: Derakhshi B, Esmailnasab N. **Association of chronic medical conditions with preterm labor.** Chron Dis J 2014; 2(1): 15-20.

Introduction

Premature birth is defined as delivery before 37 completed weeks of gestation and after congenital anomalies; it is the most common cause of death and disease in newborns.[1] It is one of the big challenges in the care of pregnant women during prenatal care.[2] Each year, 13 million premature babies are born in the world, of which 3.1 million of them die in the neonatal period. Statistics shows the rate of premature birth in the United States increased by 21% compared to 1990;[3] although the incidence of preterm birth remains at 12% higher than in many developed countries.[4] Premature births are the cause of 27% of annual infant mortality worldwide, 70% of perinatal mortality in developing countries, and 50% of neurological disorders.[5]

Although in most cases the reason for preterm labor cannot be found, the known risk factors are exclusive of labor itself. These factors include demographical factors, obstetric history, cervical and uterine factors, multigravity, bleeding and chronic diseases. One of the most common and avoidable factors is maternal chronic medical conditions including pre-pregnancy diabetes mellitus, chronic hypertension (essential or pregnancy induced), untreated anemia and urinary tract infections (UTI), which are

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responsible for large number of preterm labor.[6-15]

In pregnancy, chronic hypertension is associated with increased incidences of placental abruption, acute renal failure, cardiac decompensation, cerebral accidents and preterm labor in mothers.[7] Diabetes also increases the risk of preterm delivery not only as an independent factor, but also through its complications, including increased risk of infection, increased abnormal amniotic fluid (polyhydroamnious); severe hypertension and worsening of diabetic nephropathy could impose delivery to mother and fetus.[7,8]

In Kurdistan province, the most common causes related to neonatal mortality were prematurity that accounts for 42.5% of all perinatal deaths.[16] Despite high incidence of preterm labor as a major health problem in this province, unfortunately, no study has ever been performed on the role of mothers underlying medical condition and preterm labor. So this study has been designed and implemented to investigate the role of chronic diseases such as diabetes mellitus, chronic hypertension, anemia and UTI before pregnancy on the incidence of preterm birth after excluding confounding factors (maternal age, preeclampsia and eclampsia, bleeding etc.).

Materials and Methods

This case-control study has been conducted on 600 pregnant mothers in Be'sat Hospital, Sanandaj, Iran, in 2012. Cases included mothers who were delivered before 37 weeks and after 20 weeks of gestational age and preterm labor was approved by their medical care records and ultrasounds. The control group was mothers delivered between 37 to 42 weeks of pregnancy.

Sample size of 196 cases were calculated, considering type I error 5%, power 85%, acceptable Odd Ratio (OR = 2) and control group prevalence of risk factors about 20%. To increase the accuracy of the test, for each case two controls were selected.

For data collection, a trained midwife checked mothers in the postpartum ward (where mothers are transferred to shortly after childbirth) as well as the medical records of the newborns (including ultrasound and medical reports). Then in case of encountering preterm infant, those cases were enrolled in the study. Thereafter, two other newborns, closest in time to the birth of the preterm, were selected as the controls. Furthermore, maternal deaths during childbirth were recorded each day for identifying bias in the study.

Hypertension is defined as blood pressure ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic (preferably confirmed by two readings, 4 to 6 hours separately). Diabetes mellitus is defined as fasting blood sugar (FBS) above 126 in two separate measurements or random FBS more than 200 with classic symptoms of hyperglycemia. Anemia is defined as hemoglobin less than 12 mg/dl and hematocrit < 36% in complete blood count (CBC) done in first prenatal visit.

Data were analyzed using SPSS for Windows (version 11.5, SPSS, Inc., Chicago, IL, USA). Then quantitative and qualitative data were compared between the two groups using t-test, Mann-Whitney U-test and chi-square test, respectively. At this stage, variables with P value less than 0.05 were entered into the logistic regression model. After preparing the model, variables with high P value were excluded from the model which resulted in a model that could explain maximum likelihood estimation of variances.

Results

Out of a total 600 cases, 10 infants died, 9 were preterm and 1 had cardiac anomalies. Mann-Whitney U test showed no statistically significant difference between the two groups.

Given the following string variables; preterm labor in history of previous premature babies (OR = 4.8; P < 0.001), number of dead children (OR = 2.58; P = 0.011), olygohydramnious (OR = 3.3; P < 0.001), premature rupture of membranes (OR = 3.5; P < 0.001); double and multiple pregnancies (OR = 10.8; P < 0.001), overt diabetes mellitus (OR = 3.5; P = 0.030), chronic hypertension (OR = 2.6; P < 0.001),

preeclampsia and eclampsia (OR = 3.5; P < 0.001), infertility (OR = 3.9; P < 0.001) and cervical insufficiency (OR = 7.3; P < 0.001) in univariate analysis showed statistically significant association with preterm labor. However, mother's age, occupation and education, showed no statistically significant association with the preterm labor (Table 1).

Based on multivariate analysis, amniotic fluid reduction (OR = 3.7; P < 0.001), double and multiple pregnancies (OR = 12.1; P < 0.001), chronic hypertension (OR = 2.04; P = 0.030),

Table 1. Comparison of maternal variables between case and control groups

Variable	Status	Groups [n (%)]		Total [n (%)]	OR (CI 95%)	P
		Preterm	Term			
Previous delivery	NVD	77 (34.1)	149 (65.9)	266 (100)	0.665 (0.411-1.077)	0.096
	C/S	33 (25.6)	96 (74.4)	129 (100)		
Previous child death	No	184 (32.2)	387 (67.8)	571 (100)	2.58 (1.22-5.49)	0.011
	Yes	16 (55.2)	13 (44.8)	29 (100)		
Amniotic fluid status	Normal	152 (29.3)	366 (70.7)	518 (100)	3.325 (2.059-5.380)	< 0.001
	Abnormal	47 (58.0)	34 (42.0)	81 (100)		
Premature rupture of membranes (PROM)	No	97 (23.9)	309 (76.1)	406 (100)	3.571 (2.483-5.134)	< 0.001
	Yes	102 (52.8)	91 (47.2)	193 (100)		
Twin	Single	146 (27.4)	387 (72.6)	533 (100)	10.807 (5.822-20.408)	< 0.001
	Twin and more	53 (80.3)	13 (19.7)	66 (100)		
Infant gender	Girl	75 (29.8)	177 (70.2)	252 (100)	1.329 (0.938-1.882)	0.109
	Boy	125 (36.0)	222 (64.0)	347 (100)		
History of prematurity	No	182 (31.7)	392 (68.3)	574 (100)	4.846 (2.069-11.352)	< 0.001
	Yes	18 (69.2)	8 (30.8)	26 (100)		
History of overt diabetes mellitus	No	193 (32.8)	395 (67.2)	588 (100)	3.582 (1.036-12.383)	0.032
	Yes	7 (63.7)	4 (36.4)	11 (100)		
Gestational diabetes mellitus (GDM)	No	166 (33.0)	337 (67.0)	503 (100)	1.096 (0.694-1.730)	0.695
	Yes	34 (35.1)	63 (64.9)	97 (100)		
Chronic hypertension	No	156 (30.2)	361 (69.8)	517 (100)	2.611 (1.631-4.176)	< 0.001
	Yes	44 (53.0)	39 (47)	83 (100)		
Preeclampsia and eclampsia	No	166 (30.5)	378 (69.5)	544 (100)	3.519 (1.997-6.201)	< 0.001
	Yes	34 (60.7)	22 (39.3)	56 (100)		
Infertility	No	175 (31.2)	386 (68.8)	561 (100)	3.939 (1.999-7.761)	< 0.001
	Yes	25 (64.1)	14 (35.9)	39 (100)		
Urinary tract infection (UTI)	No	169 (34.0)	328 (66.0)	497 (100)	0.847 (0.534-1.344)	0.481
	Yes	31 (30.4)	71 (69.6)	102 (100)		
Anemia	No	140 (32.3)	294 (67.7)	519 (100)	1.200 (0.824-1.747)	0.341
	Yes	60 (36.4)	105 (63.6)	80 (100)		
Place of residence	City	115 (31.2)	254 (68.8)	369 (100)	1.280 (0.904-1.811)	0.164
	Village	84 (36.7)	145 (63.3)	229 (100)		
Mother's job	Housekeeper	194 (33.3)	388 (66.7)	582 (100)	0.833 (0.289-2.399)	0.735
	Employed	5 (29.4)	12 (70.6)	17 (100)		
History of cervical insufficiency	No	174 (30.8)	391 (69.2)	589 (100)	7.303 (3.241-16.455)	< 0.001
	Yes	26 (76.5)	8 (23.5)	34 (100)		
Age groups	18-35 years old	175 (33.8)	343 (66.2)	518 (100)	1.960 (0.677-5.676)	0.215
	Less than 18 years old	7 (50.0)	7 (50.0)	14 (100)		

OR: Odd Ratio; CI: Confidence interval; NVD: Normal vaginal delivery; C/S: Cesarean section

previous history of preterm labor (OR = 3.8; P = 0.011) were all significantly associated with the incidence of preterm labor. However, in multivariate analysis, pre-pregnancy diabetes mellitus (P = 0.230), was not associated with prematurity (Table 2).

In both univariate and multivariate analyses, anemia (P = 0.340) and UTI (P = 0.480) were not associated with prematurity (Table 1).

Discussion

In univariate analysis, history of previous premature babies, number of dead children, premature rupture of membranes (PROM), olygohydramnious, double and multiple pregnancies, overt diabetes mellitus, chronic hypertension, preeclampsia and eclampsia, infertility and cervical insufficiency had statistically significant relation with the occurrence of preterm labor. But mother's age, occupation, anemia and urinary tract infections had no statistically significant relation with the occurrence of preterm labor. However, after logistic regression analysis, abnormal amniotic fluid, PROM, double and multiple pregnancy, hypertension, preeclampsia and eclampsia, maternal age of over 35 years, and previous preterm labor were significantly associated with the incidence of preterm labor. In univariate analysis, variables that were statistically significant and were associated with prematurity could be considered as risk factors for screening high risk women who should receive more attention during pregnancy. However, these factors could be correlated; hence some of them were not significant in multivariate analysis.

In univariate analysis, data showed a statistically significant association between diabetes mellitus and prematurity (but not gestational diabetes mellitus). But in multivariate analysis, there was no association between the pre-pregnancy diabetes mellitus which was in accordance with some other studies. It might be related to the small sample size in our study or it may be neutralized with others variable (such as age, hypertension, etc) in multivariate analysis. On the other hands, one of the important complications of diabetes is chronic hypertension, so diabetes can be affected by the hypertension. However, based on gynecology and obstetrics clinical references and most studies, as an independent risk factor, diabetes can directly or indirectly (e.g. by increasing risk of infection, and polyhydroamnious, hypertensive disorders and severe diabetic nephropathy) trigger a preterm delivery.[8,13,17] In Sibai et al., women with diabetes mellitus had significantly higher rates of both indicated preterm delivery and spontaneous preterm delivery did women in the control group.[13]

In this study, chronic hypertension had a significant association with preterm labor. In multivariate analysis, preeclampsia and

Table 2. Multivariate analysis of factors influencing prematurity

Variables	B	Standard error	Wald	P	Adjusted OR	95% CI for OR	
						Lower	Upper
Amniotic Fluid Reduction	1.316	0.272	23.370	< 0.001*	3.729	2.187	6.358
Twin	2.494	0.362	47.576	< 0.001*	12.107	5.961	24.592
Sex (male)	0.222	0.204	1.184	0.277	1.248	0.837	1.860
Previous preterm labor	1.353	0.533	6.435	0.011	3.867	1.360	10.996
Overt diabetes mellitus	1.032	0.870	1.407	0.236	2.807	0.510	15.445
Hypertension	0.714	0.333	4.592	0.032*	2.041	1.063	3.921
Preeclampsia and eclampsia	0.962	0.395	5.940	0.015*	2.618	1.207	5.676
Cervical insufficiency	0.529	0.471	1.265	0.261	1.698	0.675	4.271
Age group	-	-	8.067	0.018*	-	-	-
< 18 years	0.766	0.637	1.446	0.229	2.151	0.617	7.497
> 35 years	-0.961	0.379	6.428	0.011*	0.383	0.182	0.804

* Statistically significant; OR: Odd Ratio; CI: Confidence interval

eclampsia also had a significant association with preterm labor. According to many studies, hypertensive disorders in pregnancy include four categories, uncontrolled chronic hypertension, preeclampsia superimposed on chronic hypertension, gestational hypertension and preeclampsia and eclampsia. Therefore, it seems that chronic hypertension, itself, and in addition through superimposing preeclampsia and other complications can investigate the pregnancy's outcome.[2,18] In Sibai et al., mothers with chronic hypertension compared with control group, had higher rates of indicated preterm delivery.[13] In Xiong's study,[19] gestation was 0.6 week shorter in women with severe preeclampsia than in normotensive women. But the risk of preterm labor was not increased with any classification of pregnancy-induced hypertension. Although most studies confirmed a significant association between preeclampsia with preterm birth,[17,20,21] our objective was to remove the effect of preeclampsia and eclampsia and examine the role of chronic hypertension.

In our study, there was no association between mother's anemia before pregnancy and prematurity. Perhaps, the development of prenatal care and giving ferrous sulfate supplementation in early pregnancy reduced the rate of anemia in all the pregnant women. The result of Kang and Lin's study[22] was also similar to us. But in Bora et al.,[23] maternal anemia was increased preterm labor and each 10 µg/l decrease in maternal hemoglobin was associated with 0.18 week decrease in gestational length.

In this study, the most cause of hospitalization of mothers was urinary tract infections and a high percentage of mothers suffered from vaginal discharge and dysuria, but genitourinary infections were not associated with preterm labor. In the study of Ebrahimi,[24] UTI was more common in preterm labor but without any significant association with preterm labor. In some others, women with UTI especially acute pyelonephritis had threatened preterm labor.[25-27]

Conclusion

The results of this study showed that some chronic maternal conditions such as chronic hypertension and diabetes mellitus are important pre-existing medical disorder complicating pregnancy and control of blood pressure and blood sugar before pregnancy have an important impact on declining preterm labor and complications. But others such as mother's anemia were not responsible for the prematurity.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

This article was extracted from the thesis of Ms. Bahareh Derakhshi; the Student Research Committee of Kurdistan University of Medical Sciences is greatly appreciated for the approval of this thesis. We would like to thank Ms. Azar Derakhsh and Nahid Saidi Mordi for the data collection.

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Chronic Diseases Journal

The transtheoretical model: Changes in health beliefs among female adolescents in Iran during 3 years

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Original Article

Abstract

BACKGROUND: The present study aimed to track adolescents' attitudes towards changes in their health behavior considering perceived benefit and barrier in different stages of physical activity during a three-year transitional period from junior high school to high school.

METHODS: Data were collected amongst female adolescents in 2010 (n = 558) using random cluster sampling method, of whom 400 were provided by follow-up data in 2013. The stages of change and health beliefs regarding physical activity were measured using self-reported questionnaires. The research data were, then, analyzed in statistical analysis system (SAS), using inferential statistics.

RESULTS: The baseline participants had a mean age of 14.28 ± 1.54 and at follow-up were 17.52 ± 1.82. At the baseline and follow-up, proportions of participants in pre-adaption and adaption stages were 26.7%-73.3% and 72.3%-27.7%, respectively. At baseline, pre-contemplators showed significantly lower positive attitude and greater agreement for most of the barrier items than those on other stages. In the baseline, female in action and maintenance stages endorsed greatest agreement for the barrier item i.e. having too much homework. In comparison to females, in the maintenance stage pre-contemplators were more likely to agree that a "not knowing how to do a certain type of exercise"(OR = 10.30, CI = 4.42-23.99). At the follow-up, in the pre-contemplators and maintenance stages, the greatest amount of agreement for the barrier item was "not enough time".

CONCLUSION: This study revealed transition from junior high school to high school and showed lower physical activity in females. Consequently, perceived barriers increased and perceived benefits decreased in the transition from junior high school to high school.

KEYWORDS: Physical Activity, Female Adolescents, Tracking, Transtheoretical Model

Date of submission: 6 Oct 2013, ***Date of acceptance:*** 9 Dec 2013

Citation: Mohammadkhani M, Taymoori P, Roshani D. **The transtheoretical model: Changes in health beliefs among female adolescents in Iran during 3 years.** Chron Dis J 2014; 2(1): 21-31.

Introduction

The benefits of doing physical activity on health is well-established.[1,2] Regular physical activity has favorable effects on weight maintenance, psychological well-being in adolescents, and enhancement of mood, self-concept and self-esteem. Physical inactivity in female adolescent is a risk factor for obesity, higher triglyceride levels, anxiety and depression.[3,4] Adolescent is very significant in terms of physical activities because their attitudes to physical activities are being adopted during youth period.[1,5] Despite the importance of physical activity in youth, studies always show that participation in

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physical activity declines during adolescence.[6] This decrease in tendency have been observed in both cross-sectional and longitudinal studies.[7,8] Evidence has revealed that in Iranian students aged 12-14 years, the average time spent in daily sports activities was 45.7 minutes compared to 38.2 minutes among in those aged 15-17 years.[9] Several studies have shown that tracking of physical activity may differ between males and females.[10-13] Another study on Iranian adolescents showed that 35.9% of females in comparison to 61.4% of males reached the action and maintenance stages of physical activities. Furthermore, the average time spend on physical activities amongst females was 31.82 minutes on a daily basis.[9]

According to some studies, health beliefs on physical activities influence exercise behavior.[14] Perceived benefits and perceived barriers are the most major cognitive variables that are dependent on physical activity.[15,16] Empirical studies showed that exercise in adolescents was directly influenced by perceived benefits and inversely by perceived barriers.[17,18] Females compared to males have less perceived benefits and more perceived barriers in doing physical activity.[19] Due to cultural issues and a decline of physical activity during transition from junior high school to high school amongst female adolescents in Iran, we recruited only females in our study. There are various models to examine health behavior and to conduct educational interventions. One of the used models for the health behavior is transtheoretical model.[20] This model is useful to identify and promote these behaviors in adolescents.

Transtheoretical model (TTM) can help to comprehend behaviors such as physical activity, cancer screening, and smoking cessation. It engages pros and cons as benefits and barriers of the health belief model (HBM). According to TTM, a behavioral change necessitates changes in pros and cons and movements in all stages. Cons/barriers toward a health behavior overcome pros/ benefits. However, an equal balance between benefits and barriers can be observed. Consequently, when benefits are more than barriers action plan can be achieved.[20] This study utilized five stages of physical activity: (pre-contemplation, contemplation, preparation, action, and maintenance). The present study aimed to track adolescents' attitudes towards changes in their health behavior considering perceived benefit and barrier in different stages of physical activity during a three-year transitional period from junior high school to high school.

Materials and Methods

Participants

This was a longitudinal study in 2010. Adolescents were identified using random cluster sampling method. According to the results of a pilot study and using a 0.95 confidence level, it was concluded that a sample size of 558 would be enough. Eight junior high school females and high schools females were selected randomly in Sanandaj, Iran. Participants provided contact information; they were again contacted in 2013 for the follow-up study. Due to change of address, access to 158 students was not possible. Therefore, size of sample for the follow-up was 400.

Instruments

Health beliefs related physical activity

In this study the questionnaire of perceived benefit was as: perceived benefits are defined as positive or reinforcing aspects of physical activity and were examined using a modified version of the scale developed by Garcia et al.[21] The eight items measurement tool was adopted using a five-point Likert Scale (1 = strongly disagree to 5 = strongly agree). Perceived barrier: these refer to real or imagined obstacles that make participation in physical activity difficult or impossible and were measured using a modified version of the scale developed by Garcia et al.[22] The 10 items used a five-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). Stage of change in physical activity was measured by stages of exercise change questionnaire (SECQ) by Kearney et al.[23] This questionnaire used various studies. Reliability of test retest was 85% by Philippaerts et al. in 2003.[24]

The kappa index of reliability for stage of change over a 2-week period study was 0.90 (n = 50). Cronbach's alpha reliability coefficients for the benefit and barrier subscales were 0.83 and 0.78, respectively. Content validity was used in order to determine the scientific validity of the tool for data collection.

The instruments were translated into Persian then validated using the standard back transition technique. Five bilingual Iranian Health Behavior researchers, Health Education researchers, exercise psychologist, and experts on Instrument development were asked to evaluate the pilot instrument for appropriateness and relevance of items. The instruments were then revised and modified. The questionnaire was pilot tested on 50 participants who were selected randomly (from eight females' high school in Sanandaj). This was a separate source of participants from those who took part in the larger study and their data were not included in the analyses. Revisions and presentation were based on empirical findings and recommendations from a pilot study. In order to create each stage of physical activity adoption of participants, this study utilized five stages of physical activity as follows:

- Pre-contemplation: No intention to take action within the next 6 months.
- Contemplation: Intends to take action within the next 6 months.
- Preparation: Intends to take action within the next 30 days and taken some behavioral steps in this direction.
- Action: Changed overt behavior in less than 6 months.
- Maintenance: Changed overt behavior for more than 6 months.[25]

***Ethics*:** Both protocols were evaluated by the Regional Committee Ethics for Medical Researches and were approved by the Kurdistan University of Medical Sciences. The baseline and the follow-up study carried out in the schools after agreement of school authorities in Sanandaj.

Data Analysis

Statistical analysis system (SAS) software, version 9.2 was conducted for the statistical analyses. Univariate analysis was performed for all outcomes on benefits and barriers for each stage of the physical activity. Because response on individual benefit and barrier items were based on multinomial responses classified as (1) strongly disagree, (2) disagree, (3) neutral, (4) agree and (5) strongly agree; therefore we adopted a proportional adds model for cumulative logics to examine differences in all five stages. Original score item was dependent variable and categorical stage was the independent variable. We modeled the higher score (greater agreement) as the outcome. In each logistic regression analysis, the reference stage group was pre-contemplation, means that contrasts based on the analysis compared the other four groups with the pre-contemplation group in terms of the probability of agreeing. Odds ratios (OR) and 95% confidence intervals (CI) were used to describe contrasts.

Results

Mean age of participants were 14.4 (standard deviation; SD = 1.6) years (range = 12-17 years) in this study. Among the 558 participants, at the baseline and follow-up, proportions of participants in pre-adaption and adaption stages were 26.7-73.3% and 72.3-27.7%, respectively.

Differences in perceived benefit and barriers according to the stage

Distributions of response for perceived benefit and barriers as well as the results compared results across the stages are shown in tables 1 and 2. Tables 3 and 4 illustrate the baseline and follow-up with estimated OR and 95% CIs for two-level comparison (i.e. agreement vs. disagreement) between stages.

The greatest amount of agreement for the benefit items was reported by females in the action and maintenance stages. However, amongst the six benefits there was the least amount of agreement with "make more friends". There were significant differences between pre-contemplation, action and maintenance stages for this item. Actors displayed the most endorsement (98.5%) for the item "feel happier" compared with

Table 1. Perceived benefit items by stage of physical activity at baseline

Benefits	Agree (%)					Significant contracts	OR	CI	P
	Pre-contemplation (Pre)	Contemplation (C)	Preparation (P)	Action (A)	Maintenance (M)				
Look better	40.5	78.2	54.1	89.2	87.7	Pre vs. C	0.18	0.058-0.62	0.006
						Pre vs. P	0.57	0.24-1.37	0.214
						Pre vs. A	0.08	0.03-0.20	0.0001
						Pre vs. M	0.09	0.04-0.20	0.0001
Have more energy	67.5	78.2	72.9	96.0	96.0	Pre vs. C	0.57	0.17-1.93	0.374
						Pre vs. P	0.77	0.30-1.97	0.591
						Pre vs. A	0.08	0.02-0.28	0.0001
						Pre vs. M	0.08	0.03-0.23	0.0001
Feel happier	62.1	86.9	85.4	98.5	97.4	Pre vs. C	0.24	0.06-0.98	0.04
						Pre vs. P	0.28	0.09-0.79	0.01
						Pre vs. A	0.12	0.04-0.33	0.0001
						Pre vs. M	0.04	0.01-0.13	0.0001
Have fun	54.0	65.2	70.9	89.2	96.0	Pre vs. C	0.62	0.21-1.83	0.395
						Pre vs. P	0.48	0.19-1.18	0.113
						Pre vs. A	0.14	0.05-0.35	0.0001
						Pre vs. M	0.05	0.01-0.13	0.0001
Make more friends	21.6	30.4	39.6	73.6	73.5	Pre vs. C	0.63	0.19-2.06	0.445
						Pre vs. P	0.42	0.15-1.11	0.081
						Pre vs. A	0.09	0.04-0.24	0.0001
						Pre vs. M	0.10	0.04-0.23	0.0001
Get stronger	54.0	78.3	66.7	89.3	94.9	Pre vs. C	0.32	0.10-1.06	0.063
						Pre vs. P	0.58	0.24-1.42	0.238
						Pre vs. A	0.14	0.05-0.35	0.0001
						Pre vs. M	0.06	0.02-0.15	0.0001
Love myself more	51.3	52.1	52.1	83.3	80.1	Pre vs. C vs. P	0.96	0.34-2.74	0.95
						Pre vs. P	0.97	0.41-2.29	0.946
						Pre vs. A	0.21	0.09-0.48	0.0002
						Pre vs. M	0.26	0.12-0.54	0.0004
Feel healthier	64.8	82.6	98.0	92.1	97.4	Pre vs. C	0.38	0.10-1.38	0.145
						Pre vs. P	0.03	0.005-0.31	0.002
						Pre vs. A	0.11	0.04-0.33	0.0001
						Pre vs. M	0.04	0.01-0.14	0.0001

Abbreviations: Pre-contemplation; C: Contemplation; P: Preparation; A: Action; M: Maintenance; CI: Confidence Interval; df: Degree freedom; NS: not significant; OR: Odds Ratio

Estimated odds ratio and 95% Confidence Interval are presented for each two-level comparison; P < 0.04-0.001

those in other adoption. Significant differences were seen between pre-contemplators and the other stages for this item. The most agreement with a benefit item among pre-contemplators was “Have more energy". The ORs of this item is 92% higher in the action and maintenance groups relative to the pre-contemplation group (Table 1). The results from the comparisons across barrier items showed that participants in the pre-adoption stages had significantly greater agreement than those in action and maintenance stages for most of the barriers. In comparison to females in the maintenance stage pre- exercise" (OR = 10.30) "and exercise made me tried" (OR = 13.29). Actors was reported the least amount of agreement with "Too bad weather". Contemplators were more likely to agree that a "not knowing how to do a certain type of the differences for this statement across the stages were significant except between pre-contemplators, contemplation and preparation

Table 2. Perceived barrier items by stage of physical activity at baseline

Barriers	Agree (%)					Significant contracts	OR	CI	P
	Pre-contemplation (Pre)	Contemplation (C)	Preparation (P)	Action (A)	Maintenance (M)				
Not enough time	62.1	56.5	72.9	25.5	25.5	Pre vs. C	1.26	0.43-3.64	0.664
						Pre vs. P	0.61	0.24-1.53	0.292
						Pre vs. A	4.80	2.15-10.68	0.001
						Pre vs. M	4.79	2.29-10.03	0.001
Too many chores to do	70.2	78.2	54.1	22.6	25.0	Pre vs. C	0.65	0.19-2.21	0.497
						Pre vs. P	2.00	0.80-4.94	0.133
						Pre vs. A	8.11	3.49-18.88	0.001
						Pre vs. M	7.09	3.26-15.40	0.001
Not good place to exercise	45.9	69.6	56.3	12.7	15.3	Pre vs. C	0.37	0.12-1.11	0.077
						Pre vs. P	0.66	0.27-1.56	0.346
						Pre vs. A	5.81	2.43-13.88	0.001
						Pre vs. M	4.70	2.21-10.00	0.001
Too bad weather	56.7	78.2	56.3	9.8	14.8	Pre vs. C	0.36	0.11-1.19	0.095
						Pre vs. P	1.02	0.43-2.42	0.962
						Pre vs. A	12.07	4.80-30.34	0.001
						Pre vs. M	7.55	3.53-16.17	0.001
Have not right equipment	43.2	60.9	45.8	18.6	11.8	Pre vs. C	0.49	0.17-1.41	0.187
						Pre vs. P	0.90	0.38-2.13	0.811
						Pre vs. A	3.32	1.46-7.55	0.004
						Pre vs. M	5.73	2.62-12.53	0.001
Not knowing how to do a certain type of exercise	78.3	65.2	67.6	22.6	26.0	Pre vs. C	1.93	0.60-6.17	0.265
						Pre vs. P	2.37	0.89-6.28	0.081
						Pre vs. A	12.45	5.01-30.93	0.001
						Pre vs. M	10.30	4.42-23.99	0.001
Have too much homework	62.1	65.1	54.1	27.4	26.1	Pre vs. C	0.87	0.29-2.59	0.811
						Pre vs. P	1.39	0.58-3.33	0.460
						Pre vs. A	4.34	1.96-9.60	0.003
						Pre vs. M	4.67	2.23-9.76	0.001
Not anyone to exercise with me	48.6	65.2	45.9	16.7	10.7	Pre vs. C	0.50	0.17-1.47	0.212
						Pre vs. P	1.12	0.47-2.64	0.796
						Pre vs. A	4.73	2.06-10.84	0.002
						Pre vs. M	7.89	3.59-17.35	0.001
Not like to exercise	51.3	73.9	62.5	19.6	17.9	Pre vs. C	0.37	0.12-1.15	0.087
						Pre vs. P	0.63	0.26-1.51	0.303
						Pre vs. A	4.32	1.92-9.71	0.004
						Pre vs. M	4.85	2.31-10.18	0.001
Exercises made me tired	78.3	60.9	60.4	28.4	21.4	Pre vs. C	2.33	0.74-7.33	0.148
						Pre vs. P	2.37	0.89-6.28	0.081
						Pre vs. A	9.12	3.73-22.29	0.001
						Pre vs. M	13.29	5.65-31.21	0.001

Abbreviations: Pre-contemplation; C: Contemplation; P: Preparation; A: Action; M: Maintenance; CI: Confidence Interval; df: Degree freedom; NS: not significant; OR: Odds Ratio; Estimated odds ratio and 95% Confidence Interval are presented for each two-level comparison; P < 0.04-0.001

Table 3. Perceived benefit items by stage of physical activity at follow-up

Benefits	Agree (%)					Significant contracts	OR	CI	P
	Pre-contemplation (Pre)	Contemplation (C)	Preparation (P)	Action (A)	Maintenance (M)				
Look better	57.7	69.7	61.1	76.6	94.0	Pre vs. C	0.59	0.24-1.41	0.239
						Pre vs. P	0.86	0.37-2.02	0.742
						Pre vs. A	0.41	1.14-1.16	0.095
						Pre vs. M	0.08	0.02-0.31	0.002
Have more energy	57.7	85.2	84.0	85.1	83.6	Pre vs. C	0.23	0.09-0.59	0.002
						Pre vs. P	0.25	0.10-0.63	0.003
						Pre vs. A	0.23	0.07-0.73	0.010
						Pre vs. M	0.26	0.09-0.73	0.01
Feel happier	65.4	87.7	89.6	87.2	95.6	Pre vs. C	0.26	0.10-0.70	0.007
						Pre vs. P	0.22	0.08-0.57	0.002
						Pre vs. A	0.27	0.08-0.89	0.030
						Pre vs. M	0.08	0.02-0.36	0.008
Have fun	42.3	83.6	76.4	80.8	89.6	Pre vs. C	0.14	0.05-0.35	0.001
						Pre vs. P	0.22	0.09-0.54	0.008
						Pre vs. A	0.17	0.06-0.50	0.001
						Pre vs. M	0.08	0.02-0.25	0.001
Make more friends	34.6	41.8	43.1	61.7	40.3	Pre vs. C	0.73	0.30-1.78	0.499
						Pre vs. P	0.70	0.29-1.67	0.423
						Pre vs. A	0.32	0.12-0.89	0.020
						Pre vs. M	0.78	0.30-2.01	0.614
Get stronger	61.6	85.2	70.8	68.1	85.1	Pre vs. C	0.27	0.10-0.70	0.007
						Pre vs. P	0.65	0.27-1.56	0.346
						Pre vs. A	0.75	0.27-2.03	0.572
						Pre vs. M	0.28	0.09-0.79	0.010
Love myself more	46.2	64.8	61.6	70.2	70.2	Pre vs. C	0.46	0.19-1.09	0.080
						Pre vs. P	0.53	0.22-1.22	0.138
						Pre vs. A	0.36	0.13-0.98	0.040
						Pre vs. M	0.37	0.14-0.92	0.030
Feel healthier	84.6	87.7	91.0	97.8	98.5	Pre vs. C	0.77	0.23-2.54	0.669
						Pre vs. P	0.54	0.16-1.82	0.326
						Pre vs. A	0.12	0.01-1.13	0.669
						Pre vs. M	0.08	0.00-0.78	0.030

Abbreviations: Pre-contemplation; C: Contemplation; P: Preparation; A: Action; M: Maintenance; CI: Confidence Interval; df: Degree freedom; NS: Not significant; OR: Odds Ratio; Estimated odds ratio and 95% Confidence Interval are presented for each two-level comparison; P < 0.04-0.001

stages. Thorough questions, we found statistically significant differences between pre-contemplation, action and maintenance stages but no significant differences were seen between pre-contemplation, contemplation and preparation (Table 2).

In maintenance, females displayed the most percentage (98.5%) for "feel healthier". Significant differences were seen between pre-contemplation and maintenance stage for this item. Pre-contemplator was reported the least amount of agreement with "make more friends". No Significant differences were found between the stages and pre-contemplation except between pre-contemplators and actors for this item. Significant differences were seen between the pre-contemplators and female in other stage on their perceptions on the following three items benefits: "feel happier", "having fun", and "having more energy"(Table 3).

Table 4. Perceived barrier items by stage of physical activity at follow-up

Barriers	Agree (%)					Significant contracts	OR	CI	P
	Pre-contemplation (Pre)	Contemplation (C)	Preparation (P)	Action (A)	Maintenance (M)				
Not enough time	88.5	85.2	66.0	48.9	55.3	Pre vs. C	1.32	0.36-4.88	0.1670
						Pre vs. P	3.95	1.13-13.81	0.0300
						Pre vs. A	7.99	2.11-30.29	0.0020
						Pre vs. M	6.21	1.70-22.70	0.0050
Too many chores to do	88.4	86.9	61.8	57.5	41.8	Pre vs. C	1.15	0.31-4.29	0.8270
						Pre vs. P	4.73	1.35-16.50	0.0100
						Pre vs. A	5.67	1.49-21.55	0.0100
						Pre vs. M	10.67	2.91-39.04	0.0003
Not good place to exercise	84.7	73.0	53.5	46.8	28.4	Pre vs. C	2.03	0.65-6.36	0.2190
						Pre vs. P	4.78	1.57-14.58	0.0050
						Pre vs. A	6.24	1.86-20.94	0.0030
						Pre vs. M	13.89	4.22-45.67	0.0001
Too bad weather	76.5	68.9	52.8	38.2	34.4	Pre vs. C	1.50	0.56-4.05	0.4150
						Pre vs. P	2.98	1.13-7.86	0.0200
						Pre vs. A	5.37	1.81-15.90	0.0020
						Pre vs. M	6.37	2.24-18.08	0.0005
Have not right equipment	46.2	50.8	48.6	29.8	20.9	Pre vs. C	0.82	0.35-1.93	0.6660
						Pre vs. P	0.90	0.39-2.09	0.8170
						Pre vs. A	2.02	0.74-5.45	0.1640
						Pre vs. M	3.24	1.23-8.56	0.0100
Not knowing how to do a certain type of exercise	46.2	65.6	58.3	44.7	38.8	Pre vs. C	0.45	0.19-1.06	0.0670
						Pre vs. P	0.61	0.26-1.41	0.2510
						Pre vs. A	1.06	0.40-2.77	0.9030
						Pre vs. M	1.35	0.54-3.37	0.5180
Have too much homework	69.3	86.9	50.7	63.8	53.7	Pre vs. C	0.34	0.12-0.91	0.0300
						Pre vs. P	2.18	0.89-5.35	0.1860
						Pre vs. A	1.27	0.45-3.54	0.6410
						Pre vs. M	1.93	0.74-5.06	0.1770
Not anyone to exercise with me	53.8	45.9	40.3	31.9	15.0	Pre vs. C	1.37	0.58-3.21	0.4620
						Pre vs. P	1.73	0.74-4.00	0.2010
						Pre vs. A	2.48	0.92-6.66	0.0690
						Pre vs. M	6.64	2.39-18.48	0.0003
Not like to exercise	65.4	59.0	52.1	34.0	18.0	Pre vs. C	1.31	0.54-3.17	0.5470
						Pre vs. P	1.73	0.72-4.15	0.2140
						Pre vs. A	3.66	1.33-10.03	0.0100
						Pre vs. M	8.65	3.11-24.03	0.0001
Exercises tires me	73.1	64.1	54.9	51.1	46.3	Pre vs. C	1.47	0.57-3.79	0.4170
						Pre vs. P	2.23	0.88-5.64	0.0890
						Pre vs. A	2.60	0.92-7.34	0.0710
						Pre vs. M	3.15	1.17-8.48	0.0200

Abbreviations: Pre-contemplation; C: Contemplation; P: Preparation; A: Action; M: Maintenance; CI: Confidence Interval; df: Degree freedom; NS: not significant; OR: Odds Ratio; Estimated odds ratio and 95% Confidence Interval are presented for each two-level comparison. P < 0.04-0.001

Participants reported greatest amount of agreement for the barrier item "not enough time". The differences for this statement across the stages were significant except between pre-contemplators and contemplators. Those in the contemplation stage showed the most agreement with the perceived barrier items" too many chores to do" and "have too much homework" (86.9%). The differences for first item across the stages were significant except between pre-contemplators and contemplators but in the second item, significant differences were seen between the pre-contemplators and contemplators. No statistical significant difference was seen between the pre-contemplators and female in the other stages on their perceptions on the following item barrier "not knowing how to do a certain type of exercise" (Table 4).

Discussion

This study provides the first evidence about differences in perceived benefit and barrier items in female adolescents regarding physical activity behaviors across stages of changes during transition from junior high school to high school. These findings are an importance start for further studies about a theory based on interventions designed to increase physical activity amongst Iranian female adolescents. Such interventions would appear to be necessary because more than half of the female adolescents in this study in pre-adaption stages of exercise change their behavior at follow-ups. At the baseline and follow-up, in pre-adaption and adaption stages, percentage of participation was 26.7-73.3% and 72.3-27.7%, respectively. These findings are similar to several studies.[17,18,26,27] Perceived benefits and barriers were found to be significant for predictors of stage of behaviors change in females in our findings. This is similar to the findings of other studies showing that perceived benefits and barriers predicted the stage of behavior change for exercise.[9,19,28] To develop interventions promoting physical activity, it is critical to understand factors regarding stages of adaption. Our study illustrated that attitudes to physical activity differentiated in stages of physical activity adoption.

While previous studies examined differences in individual perceived benefit, and it reported the perceived benefit as a mediator.[19] In Taymoori et al. study also found, perceived benefit influenced direct effects on regular physical activity.[28] This study is the first research that examined differences in perceived benefits items in female adolescents according to preparation stages for physical activity. Perceived barrier is another concept that can be linked to physical activity.[29] The results of our study indicated that barrier had a direct path with physical activity. In the first phase of the study, the most important perceived barriers "did not know how to do a certain type of exercise" and "exercise made me tired". It is likely that causes are lack of suitable places and access to safe recreational facilities. According to previously mentioned reasons, it is possible that one cause can be having limited sorts of sports especially at schools. Economic problems could also be another cause. Some of the reasons are as follows: swimming opportunity is limited, lack of knowledge about exercise, social and family norms regarding inaccessibility of outdoor exercises for females, lack of walking path, cultural limitation regarding some activities and lack of a role model. In Iranian culture, Parents are concerned about unsuitable facilities and they also think that homework or family responsibilities are more important than physical activity.

Indeed, we found both direct and indirect effects of perceived benefit and barrier on physical activity. Consequently, effects of perceived benefits on perceived barriers lead to an increase of physical activity. For example, the incentives for being physically active could be body fitness. This is very significant for females in Iranian culture. Although female students do not have enough time for physical activity and must take a lot of time for academic success, they spend little time for exercise due to mentioned incentive. However, the relationship between perceived benefits and perceived barriers suggest the

perception of high perceived benefits to overcome barriers may increase physical activity indirectly.

In order to improve physical activity, adolescents should be consulted to choose their preferred activities and not only competitive sports. Although females are influenced by external motivations, the agreements of their parents, friends and teachers could be beneficial as well. Sending educational messages to students such as "active life span" could create interests amongst females and it also could encourage them to exercise regular physical activity. For instance, raising awareness programs such as a lecture about the advantages of physical activity can be beneficial, as well. In addition, the duration of exercise should be increased gradually and exercise for a long period of time should not be done suddenly.

Three years later, follow-up showed that physical activity was less than the baseline. During the three-year period, perceived benefits decreased, and perceived barriers increased. At follow-up, participants reported the greatest amount of agreement for the barrier "not enough time". In Iran, entrance to high school coincides with preparing for university entrance examination. In recent years, a substantial increase to continue further education can be observed amongst female adolescents.[30] Thus; they spend a great deal of time for studying. This leads to having insufficient time for physical activities. Yet, results of several studies indicated that physical activity during the three years decreased to a greater extent in female adolescents compared to males.[17,18,31,32] Thus, daily time management during their study is of paramount significance.

Schools play a major role in promoting involvement of children in recreational activities that they can enjoy for a lifetime. By involving adolescents on a daily basis in physical activity, teaching the personal value of regular activity, and encouraging continuing involvement in moderate or vigorous activities both at school and at home, schools contribute to the goal of an "active" generation. School-based programs should be supplemented by family-based activities. Family-based programs encourage parents to be active with their adolescents in building relationships. According to the three-year period of this study, longitudinal studies identifies in a short period of time changes in beliefs associated with physical activity is recommended. Furthermore, tailored interventions to improve positive attitudes related to exercise and to support physical activity behavior in females is essential.

Limitations

There were several limitations to the present study. The data were measured by a self-report questionnaire. Despite acceptable internal consistency reliability of the instrument used in the current study, there is still a need to explore other possible benefit and barrier items that tap individual and normative expectations as suggested by Rakowski et al.[33] Physical activity Behavior has not been evaluated. The most important limitation of this study, which is common in longitudinal studies and may cause lots of bias, is the loss to follow-up and declined response rate in repeated measurement.

Recommendation for future studies

According to a decline of physical activity in female adolescents during transition from junior high school to high school and a decrease in perceived benefits and increase in perceived barriers, it is necessary to plan and carry out studies in future in order to do tailored interventions. It is also important to do such research to positively influence cognitive and psychosocial factors regarding exercise and increase physical activity in female adolescents during high school.

Conclusion

According to the results of this study, several barriers were responsible for the decline in physical activity among females, such as transition from junior high school to high school, importance of academic success and cultural barriers for female adolescents.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

The present study was the result of the first author's thesis which was funded by Kurdistan University of Medical Sciences.

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Chronic Diseases Journal

Strategies for enhancing nurses' clinical judgment in care for patients with chronic diseases: A grounded theory study in Iran

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Original Article

Abstract

BACKGROUND: A varying background in situations of chronic diseases affects the selection of strategies in clinical judgments. This study explained the strategies used to enhance the clinical judgment in chronic diseases situations.

METHODS: This article was the part of a grounded theory study. Obtained data from open and semi-structured interviews were analyzed simultaneously with data collection and according to the Corbin and Strauss approach. The first experienced nurse was selected with purposive sampling and 25 other participants were selected on the basis of the theoretical sampling from different wards of the clinical and educational care centers of Sanandaj, Iran from 2011 to 2013.

RESULTS: As shown in results, the core variable "situation-based efforts for enhancing clinical judgment" represented the main process used by participants in the promotion of clinical judgment in situations of chronic disease. The main categories included a "comprehensive collaboration", "inclusive education", "matching of clinical judgment skills", "maintaining patient's and nurses' autonomy" in a clinical judgment.

CONCLUSION: Participants were trying to use strategies appropriate to different situations for clinical judgment in terms of chronic diseases conditions. Applying these processes with regard to the present context, can enhance the clinical judgment in chronic diseases situations.

KEYWORDS: Clinical Judgment, Chronic Diseases, Nurses, Grounded Theory

Date of submission: 2 Oct 2013, ***Date of acceptance:*** 4 Dec 2013

Citation: Seidi J, Alhani F, Salsali M. **Strategies for enhancing nurses' clinical judgment in care for patients with chronic diseases: A grounded theory study in Iran.** Chron Dis J 2014; 2(1): 32-40.

Introduction

Chronic diseases are different from acute diseases in terms of duration, severity and changes, care, treatment, clinical judgment, and decision-making. Chronic disease refers to a condition in which the disease process has persisted for a long time.[1] Patients with chronic diseases requires empowerment for self-care. Consequently patient seeks to enhance the knowledge and skills to manage their disease.[2-4] In this situation, integrating clinical and theoretical knowledge is necessary and critical for caregivers, and the type of care and clinical judgment is different from other clinical situations.[5] In Tanner's Clinical Judgment Model, emphasis is on the background role of nurses, context, and nurse's communication with patients which is the central point in the process of clinical judgment.[6] Based on social judgment theory, a person's judgment depends on reality of his social environment and this environment can be seen from different angles.[7] So the impact of disease chronicity as an environmental truth can affect the individual's clinical judgment. This could explain the need for

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strategies to enhance clinical judgment based on position and situation.

Clinical judgment as a concept, in terms of background in various fields of medicine, has many differences and similarities[8] with nurses' clinical judgment.[8,9] The challenge here is the participation of all care providers to enhance clinical judgment. Standing showed how two different approaches (cognitive continuum theory in medicine and nursing) could be unified in clinical judgment to achieve an ideal decision.[10] Standing, upgraded modified version of the cognitive continuum theory from 6 to 9 factors; nine factors from the bottom to the top included: intuitive judgment, reflective judgment, Patient and peer judgment, critical review of experimental and research evidence, action research and clinical audit, qualitative research, survey research and finally experimental research.[10] Nursing clinical judgment as a process includes patient's plan of care, previous knowledge and experience, determination of numerous symptoms, question and search for supplementary information, combining and interpreting the available data and prioritization.[8] About the components of clinical judgment, nurses use knowledge and skills of observation, interpretation, prioritization, intuition, and analogy to achieve clinical judgment.[11]

Criticizing previous studies found that clinical judgment is different in various medical professions. However, in enhancing clinical judgment, the important element is collaborative judgment of all medical professions. In this study, it is necessary to reveal the health care team's strategies of enhancing clinical judgment in situations of chronic diseases. On the other hand, different models and theories such as Standing Cognitive Continuum Theory of clinical judgment in Nursing,[10] Hammond Cognitive Continuum Theory,[12] Tanner Clinical Judgment Model,[6] Lens Model, Social Judgment Theory[7,13,14] all referred to the characteristics of clinical judgment; however, they have not succeeded in revealing processes and background in enhancing clinical judgment. It is therefore necessary to address this important issue. Furthermore, most of these studies were conducted in emergency situations [6,15-18] and few studies have been conducted in conditions of chronic disease and follow-up period after discharge.[19] Based on Benner's approach, variability of patients and environment are influenced by contextual factors and the type of response. Therefore, an experienced and professional nurse in clinical judgment must pay attention to variable and immediate situations of patient and the environment.[20] This is a gap in studies on the necessity and importance of strategies enhancing clinical judgment based on existing conditions. This study can reveal how nurses can apply strategies in enhancing clinical judgment in response to the conditions underlying chronic diseases.

Materials and Methods

Design

This qualitative study is part of a grounded theory one. One factor why we chose this method[21,22] was its suitability for complex and hidden processes[23] such as clinical judgment. Accordingly, since for clinical judgment nurses interact with people, this approach can reveal their concerns about clinical judgment.[19,24]

Participants

Clinical nurses with at least 3 years of experience, willing to participate and the ability to provide rich experiences were selected as key participants. First key participant was selected based on purposive sampling. Other participants were selected by theoretical sampling, in accordance with the given data, based on memos, information needs and high maximum variance. Twenty-six participants were recruited into the study including 14 clinical nurses, two nursing managers (matron and clinical supervisor), two trainers, two physicians, two senior nursing students, two patients and their family members, and two nutritionists and physiotherapists. They were selected in clinical departments of three universoity hospitals of Sanandaj, Iran. Then, 29 interviews were performed. Based on

participant's preference, location of interview were either clinical wards of three teaching hospitals in Sanandaj or School of Nursing and Midwifery, Kurdistan University of Medical Sciences, Iran.

Data Collection

For data collection, unstructured interview began with open-ended questions, with the term "clinical judgment" what type of working memory comes to your mind? After data analysis and emergence of the primary theory, the focus of subsequent interviews was based on analytical questions (based on guide produced from previous interviews). In this stage of data collection, guide interview questions were deep, semi-structured interviews; hence, based on reminder researchers were able to obtain relationship between the concepts and categories and reveal the participants' main concerns. For example, some questions from an interview guide were as follows: "Based on your experience, what factors and behaviors are effective in enhancing clinical judgment in chronic disease situations?" or, "how did you try to enhance clinical judgment chronic disease situations?". On the basis of participants' responses, exploratory questions asked until data saturation. Data collection was carried out simultaneous with the constant comparative analysis. The objective was to determine differences and similarities in data. After comparison of data, it was clear where and from whom to ask the next question (theoretical sampling). With question phrasal words (why, how, where, when, under what conditions, and what consequences), theoretical concepts were cleared. This process continued until achieving the following items: no emerging new data, transparency of connections between concepts and sub-categories, and the absence of new categories, evolution of axial categories, and the gradual emergence of the theory.

Data Analysis

Based on Corbin and Strauss approach (2008)[22] open coding was used in analyzing data for concept, for example "face to face training, group training, etc." were made under the category "education to patient and family". At this stage, the axial coding was done to link concepts and categories. For example, "staff training", "clinical education", and "education to patients and families" sub-categories formed the axial category "health care team comprehensive education with the patient and family". This category, along with "health care team comprehensive partnership with the patient and family in clinical judgment", "matching clinical judgment skills to chronic disease situations" analyzing data for context using memos based on paradigm model, paradigmatic components including casual condition, context condition, phenomena, intervention condition and strategies were determined (Figure 1). In this article "situation-based efforts in enhancing clinical judgment" was determined as a strategy (process). In the next stage, main process was linked to structural conditions of phenomena (causal conditions, context and intervention conditions and outcomes). The categories were linked around the central variable (Schematic view 1). From the beginning until the end of the study MAXQDA software version 2010 was used for data analysis.

Rigor

For credibility we used member check, data collecting, concurrent continuous comparative analysis of data, participants trust, listening carefully and drowning in data. For dependency, various interviews data was combined. In addition to date, recorded interviews and manuscripts preserved for two years after the study for possible access of participants and observers. For confirmability, transcripts were evaluated by panel of experts and multi observers. Transferability of the study was promoted by maximum variation sample.

Ethical Considerations

After approval of the proposal by the Ethics Committee of Tarbiat Modares University, permission to enter the field of research was obtained. The objective of the study and methods of interview were described for participants. The

participants were assured of the confidentiality of their name and information. Participation or refusal to participate in the study was optional. Written informed consent was obtained from participants for interviews and recordings.

Results

Characteristics of participants are presented in table 1. Strategies employed by participants included "comprehensive collaboration", "inclusive education", "matching of clinical judgment skills", "maintaining patient's and nurses' autonomy" in clinical judgment. Indeed these categories were reflecting situation-based strategies in response to the main concern of participants (barriers to clinical judgment in situations of chronic disease). The core category titled "situation-based efforts on enhancing clinical judgment" would cover all the categories. This strategy was facilitated with the support of nurses and patients and limited by emerging barriers to clinical judgment in chronic disease situations. So the outcome of this process was "relative enhancement of clinical judgment in chronic diseases situations" (Figure 1).

Comprehensive Collaboration

In chronic diseases situations, patients and families, healthcare professionals had interaction in clinical judgment. In most cases, patients were consulted. Then follow-up care after discharge was performed by nurses.

"…We follow up their home care, upon their request after calling us, we provide consultation and help then in judgment and decision-making". (Nurse 16)

Patients and their families influenced clinical judgment of physicians and nurses by providing their care and treatment experiences. ".... In our judgment, listening to previous favorite songs could help to improve patient's memory. The nurse accepted, and in fact it was very helpful ...." (Brother of patient 1)

In chronic diseases situations there was ample time and opportunity for interaction between individuals. The complexity of chronic diseases required further interaction between individuals for clinical judgment. Thus, unlike other clinical situations, nurses and physicians were trying to participate in team clinical judgment.

"… While caring for patients with chronic mental diseases, we have more interaction with physicians and they check and accept our opinions well…" (Nurse 1)

Other care providers such as nutritionists, occupational therapists, physiotherapists, laboratory experts, and other members, interacting with physicians, nurses, patients and families, were trying to participate in the team clinical judgment.

"…During respiratory therapy for patient, nurse as a respiratory therapist proposed postural positions considering patient's condition and I accepted her view". (Physiotherapist)

Inclusive education

Participants' willingness for required education in conditions of care of patients with chronic diseases was different with other clinical situations, which was due to enough time to

Table 1. Individual characteristics of the participants

Participant	Gender		Age (year)	Educational level			Time of service as nurse (mean of years ± month)
	Male	Female		BSc	MSc	PhD	
Practicing nurses	7	7	26-47	12	2	-	14 ± 6
Nurse managers	1	1	34-44	1	1	-	18
Nurse educators	1	1	32-38	-	1	1	8 ± 4
Physicians	0	2	34-49	-	-	2	16
Junior students	1	1	23-24	-	-	-	-
Nutritionist	1		37	1	-	-	14
Physiotherapist		1	34	1	-	-	8
Hospitalized patients and their family members	1	1	36-52		-	-	-

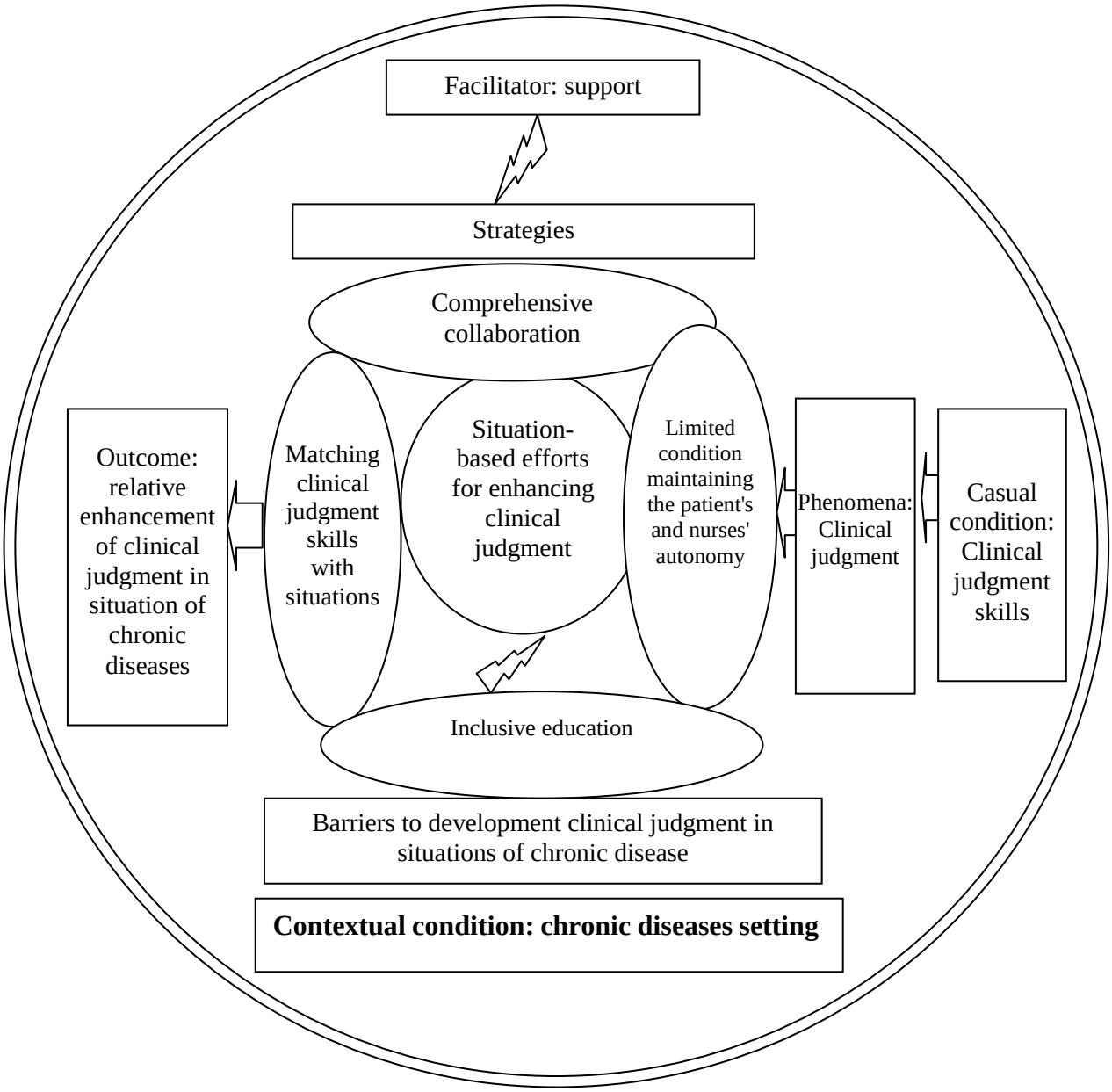

Figure 1. Psycho-social process for nurses' clinical judgment in the care for patients with chronic diseases

clinical judgment, the nature of chronic diseases, long-term care of chronic patients and patients' different needs. In the field of clinical education there was sufficient time to collect information and evidence to enhance clinical judgment. Participants used approaches such as holding conferences, case report, and providing educational pamphlets.

".... In turn, in the internal ward, a patient was chosen and was presented to others as a case report." (Student 1)

In the field of personnel education, physicians and nurses had more interaction with patients and their family. There was ample opportunity for the exchange of information between clinical individuals. "With the case report, conference and preparing educational pamphlet we were seeking to educate and to monitor students in clinical judgment." (Instructor 1)

Chronic diseases situation gave the

opportunity of face-to-face training or follow-up after discharge to participants. These trainings provided better clinical judgment in participants:

"During hospitalization of diabetic patients in the ward, I gave them face-to-face training and telephone counseling." (Nutritionist)

Matching clinical judgment skills with chronic disease situations

Experiences of participants in matching clinical judgment skills such as knowledge and experience, evidence documentation, reasoning, critical thinking, intuition and considering professional ethics in different clinical situations were not the same. In conditions for care of chronic patients, there was enough time to use scientific contents such as the results of scientific papers, and educational materials, which ended up in creating guide lines:

"...Some colleagues argued based on their experiences, we matched their experience with clinical evidence and condition. Then we conclude the right judgment." (Nurse 15)

Protocols and guidelines were considered as standard evidence that in chronic disease situation their effectiveness and accuracy in judgment was confirmed by reasoning skill and matching with other evidence and experience:

"...We have the ample opportunity to match the guidelines for the care of chronic respiratory disease with evidence such as the results of research papers and experience". (Nurse 10)

In chronic disease situations and in terms of professional ethics, participants respected each other's opinions and beliefs and in case of errors, they corrected each other's opinions by reasoning and based on their experience:

".... After transferring patient to internal ward, the nurse had the opportunity to communicate and interact with the patient after taking patient's history and to adapt patient's condition with physician order". (Physician 1)

Maintaining autonomy of patients and nurses in clinical judgment

In the caring of patients with chronic disease, authority of nurses, patients and families in clinical judgment was more because they had more time. Besides, the nature of the chronic disease had forced physicians and nurses with independent interventions led patients to empowering and maintain independence in self-care, particularly in the field of clinical judgment:

"...We conducted independent nursing interventions such as teaching bud lips breathing or respiratory physiotherapy. These interventions caused patient independence in clinical judgment." (Nurse 13)

Under the care of patients with chronic diseases, nursing duties were more extensive and enabled them to use helping nursing models to preserve patient independence:

"…Based on Orem's Self-care Model, we encourage the patient to do self-care ...". (Nurse 16)

Chronic diseases situations require specialized nurses in care for patients with chronic diseases. Specialist nurse was able to judge specialized clinical judgment in the field chronic diseases.

"... We have reflected specialization of nursing in the care of chronic diseases to the Ministry's Committee" (Nursing director 1).

Discussion

In the present study, all the clinical individuals (Table 1) in chronic diseases situations were seeking clinical judgment enhancement. Everyone in the group tried to encourage patients and families to participate in the clinical judgment and decision-making. In this condition, the opportunity to interact was more and therefore the opinion and experience of nurses and patients and other healthcare team members were considered by physicians. Patients and families were more closely connected to healthcare team members; consequently in the chronic diseases situations, physicians were more confident in comparison to nurses and clinical experts. Elliot in a study on caring chronic patients found that, in the process of clinical judgment "mutual interacting" could be the core of participation of patient and family. Dialogue and consultation to the patients were including strategies used to achieve mental and social process.[19] The results of

this study were similar to recent study from this point of view that they were seeking to interact with patients and patient participation in the clinical judgment. But the difference was that in the recent study, participants were seeking inclusive interaction and participation of all clinical individuals in the clinical judgment.

In the present study, there was required and appropriate time for the inclusive education of patients and family and health care team. Therefore, type of training methods differed from other clinical situations. For example, nurses by educating patients and their families, in face-to-face or by telephone counseling after discharge were trying to enhance their clinical judgment. According to Smith, providing telephone counseling and using algorithms of causes and solutions to overcome crying infants were trying to counsel parents of those infants. By necessary training to parents, they tried to change their judgment about their crying children. And the modification of judgment led to the parents' adaptation with their children and appropriate intervention was conducted by parents.[25]

In this study, matching clinical judgment skills to situations of chronic diseases was appropriate strategy for enhancing clinical judgment. In this study guidelines and the experience and knowledge of people would be adapted with evidence such as the results of scientific work and research papers. Then, based on the evidence their correctness was argued. Cranley found that inappropriate combining of clinical knowledge and experience with time and place was the basic barrier for estimating probabilities by the nurse in the clinical judgment.[26] For example, intuition based on experience or knowledge alone cannot be the basis of correct clinical judgment, but integrating with other sources such guidelines would be helpful.[27] On the other hand, clinical judgment is "used reasoning" required for clinical individuals concurrent with the continuing interaction with their patients.[28] In Hammond's cognitive continuum, intuitive judgment facilitates reaching speeds to judgment which is appropriate for emergency. However, clinical judgment stemming from reasoning specifies the method to achieve judgment that suits for situations such as chronic diseases.[7] In fact the most appropriate skill for clinical judgment is between reasoning and intuition.[29]

In the present study, the majority of participants were seeking to maintain the independence of patients and nurses. Having sufficient time the independent nursing interventions such as counseling and education, using nursing models such as the Orem self-care model was conducted. This caused that patients and families have more independence for their clinical judgment and self-care. In many studies, nursing models such as Orem's self-care model was able to maintain patients' independence, judgment and decision-making in self-care.[2,4] Duties of nurses in this study were more extensive than in other clinical situations and that would provide background for the independent clinical judgment. Organizational support can develop nurses' tasks.[30] Relying on skills such as experience, reasoning, evidence, ability to communicate and interactions can maintain professional independence for clinical judgment.[31,32] In the chronic diseases situations, achieving these criteria is easier than other clinical situations.[19,33] Finally, the participants in this study were trying in situation-based effort to enhance clinical judgment based on chronic diseases conditions. This was an abstract concept covering all major categories of the study which had other sub-categories. In fact criteria for enhancing clinical judgment as sub-strategies such participation, education, independence and clinical judgment skills in many of the studies were consistent with the results of the present study.[34-36] The difference between this study and other studies was that this study revealed process of enhancing clinical judgment in the chronic diseases situations.[37-39]

Limitation of this study was that the structure of clinical judgment and its relation to process was not presented. Although it has been illustrated in figure 1, the focus of this study was on introducing used strategies in enhancing

nurses' clinical judgment. The reason was that the article is part of an original grounded theory study. Another limitation of the study was low transferability of the study, which is the nature of a qualitative study.[40]

Conclusion

Based on the situations, participants used different strategies for achieving the right clinical judgment. In fact core variable was a strategy that participants in relation to the condition and care of patients with chronic diseases were seeking integration of enhancing clinical judgment criteria such as participation, education, clinical judgment skills, and maintaining independence of patients and nurses in clinical judgment.

It is necessary that clinical nurses, nursing management, physicians, patients, family and other individuals interacting together on the clinical situation of chronic diseases use different strategies to form other situations to perform right clinical judgment. This requires further clinical research and training in situations of chronic diseases. Therefore it is recommended that studies make appropriate tools with respect to condition of patients suffering from chronic diseases in the future, until criteria in enhancing clinical judgment in the patient care are evident.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

The authors acknowledged all the participants who agreed to participate in the study. This study is written based on PhD dissertation; therefore, the financial support from the School of Medical Sciences, Tarbiat Modares University, is also highly appreciated (No: 52/112071).

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Chronic Diseases Journal

Investigation of renal osteodystrophy among hemodialysis patients referring to Towhid Hospital, Sanandaj, Iran

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Original Article

Abstract

BACKGROUND: Renal osteodystrophy is a major complication among dialysis patients that can lead to muscle weakness, and bone pain and fractures by minor trauma. In the present study, the frequency of these symptoms and status of blood markers among dialysis patients are discussed.

METHODS: In a crass-sectional study, blood sample was obtained from 82 hemodialysis patients for calcium (Ca), phosphorus (P), alkaline phosphatase (ALP), and parathyroid hormone (PTH) level measurement. Radiography of the right hand was performed for 57 patients. Data analysis was performed via SPSS by using chi-square test, Fisher's exact test, and Pearson correlation coefficient.

RESULTS: The prevalence of osteodystrophy among dialysis patients was 72% (59 patients), including 29 patients with high bone turnover and 30 patients with adynamic bone disease. Moreover, 24 patients (29.3%) were hypocalcaemic and 25 patients (30.5%) were hypercalcemic. In addition, 25 (30.5%) patients had hyperphosphatemia. In the present study, 82 patients, 40 male (48.8%) and 42 female (51.2%), were recruited. Patients' mean age ± standard deviation was 55.77 ± 14.99. There was a relation between increase in age and adynamic bone disease (P = 0.004). Calcium level had a significant association with radiologic manifestation of renal osteodystrophy (P = 0.007). PTH levels had moderate correlation with ALP level (r = 0.55).

CONCLUSION: In the present study, there was a relation between age and adynamic bone disease; meaning that by increasing of age, the prevalence of adynamic bone disease also increased. There was a strong positive correlation between PTH and ALP.

KEYWORDS: Renal Osteodystrophy, Hemodialysis, High Bone Turnover, Adynamic Bone Disease

Date of submission: 5 Oct 2013, ***Date of acceptance:*** 19 Dec 2013

Citation: Sedighi-Gourabi V, Afkhamzadeh A, Nikkhu B, Rahimi-Rastgoo B, Habibi S, Moradinia Gh. **Investigation of renal osteodystrophy among hemodialysis patients referring to Towhid Hospital, Sanandaj, Iran.** Chron Dis J 2014; 2(1): 41-5.

Introduction

Renal osteodystrophy is a chronic kidney disease-mineral and bone disorder (CKD-MBD) which occurs due to renal failure. This disorder is a direct result of electrolyte abnormalities and endocrine disorders that accompany elevated serum phosphate levels, low or normal serum calcium, and parathyroid function stimulation.[1] The disruption is divided into two groups based on metabolic bone status; high exchange bone disease [high parathyroid hormone (PTH)] and low exchange bone disease (low PTH), or

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adynamic bone disease.[2] A sample of high exchange bone disease is osteitis fibrosa which is developed due to high levels of PTH and manifests as pain and fragile bones. Other examples of disease with low bone turnover are adynamic bone disease (ABD) and osteomalacia. The cause of adynamic bone disease is not fully known; however, it is known that, diabetes, medications, and dialysis solutions with high concentrations play a role in its creation. In adynamic disease, the number of osteoblasts and osteoclasts are also reduced. The risk of bone fractures in adynamic patients is high.[3]

Osteodystrophy is most common in dialysis patients. These patients suffer from bone pains, increased incidence of bone fracture and deformity, myopathy, muscular pain, and tendon rupture.[4] This disease is associated with disability and reduced quality of life.[5,6] In developing countries, the prevalence of this disease varies from 33.3% in Egypt to 81% in Brazil.[7]

Most researchers use PTH, total alkalin phosphatase (ALP), calcium, and phosphorus as replacement for bone biopsy which is a gold standard diagnosis.[8] PTH measurement is a suitable screening instrument for differential diagnosis of high bone exchange (osteitis fibrosa) and adynamic bone disease.[5] Measuring PTH and ALP increases the accuracy of disease diagnosis.[9] Renal osteodystrophy manifestations in plain radiography include subchondral resorption of bone, soft tissue calcification osteopeny, amyloid repletion, and fracture.[10]

The present study is designed and conducted for investigating renal osteodystrophy in hemodialysis patients.

Materials and Methods

In a crass-sectional study, blood sample was obtained from 82 hemodialysis patients for Ca, P, ALP, and PTH levels measurement. The patient's blood samples were sent to the laboratory of Tovhid Hospital. In this study, PTH levels above 300 pg/ml show high exchange bone disease and PTH levels below pg/ml represent adynamic bone disease. The normal amount of calcium was considered to be 8.4-9.5 mg/dl, of phosphorus 3.5-5.5 mg/dl, and of PTH was 100-300 pg/ml.

Radiography of the right hand, including wrist, hand, was performed for 57 patients and results were interpreted by one radiologist. Radiological manifestation is positive in case of presence of at least 1 of these findings: disseminated demineralization of bones; osteolytic lesions; osteosclerosis; bone resorption; soft tissue calcification; osteopenia; amyloid deposition; and fracture predisposition.

A checklist including demographic data, duration of disease, frequency of dialysis per week, and radiography reports was completed. Data analysis was performed via SPSS for Windows (version 16; SPSS Inc., Chicago, IL, USA) by using chi-square test, Fisher's exact test, and Pearson correlation coefficient.

Results

The prevalence of osteodystrophy among dialysis patients was 72% (59 patients), including 29 patients with high exchange bone disease, and 30 patients with adynamic bone disease. In addition, 23 patients (28%) had normal PTH.

In the present study, 82 patients, 40 male (48.8%) and 42 female (51.2%), were recruited. Patients' mean age ± standard deviation was 55.77 ± 14.99 (range: 16-91 years). The largest and smallest age groups were 61-70 years (26.8%) and below 40 years (14.6%), respectively. During the study, 25 patients died. The frequency of dialysis for most of the patients (50 patients; 61%) was three times per week, 9.8% of patients had dialysis once a week. Moreover, 29 patients (35.4%) had PTH levels above 300 pg/ml that indicate high bone exchange disease.

Normal PTH range was observed in 23 patients (28%). In addition, 30 patients (36.6%) had a PTH level of below 100 pg/ml that indicates adynamic bone disease. There was a relation between increase in age and adynamic bone disease (P = 0.004) (Table 1).

In terms of Ca levels, 24 patients (29.3%) were hypocalcaemic, 33 patients (40.2%) were normal, and 25 patients (30.5%) were hypercalcemic. In

terms of P levels, 25 patients (30.5%) had hyperphosphatemia, 57 patients (69.5%) were normal, and none of the patients had low phosphorus.

Radiography of the wrist was performed for 57 patients. The mean levels of calcium, alkaline phosphatase, and parathyroid hormone were not significantly different between the two groups of positive and negative radiological manifestations. However, the mean level of phosphorus was significantly different between the two groups ($P < 0.05$) (Table 2). However, Ca and P had no association with positive radiologic manifestation based on Fisher's exact test ($P > 0.05$) (Table 3). PTH levels had moderate correlation with ALP level ($r = 0.55$).

Discussion

The prevalence of renal osteodystrophy based on PTH level was 72%, which consisted of 35.4% high bone exchange disease and 36.6% adynamic bone disease. In a study, the prevalence of renal osteodystrophy, high bone exchange disease,

Table 1. Association between bone diseases and variables among hemodialysis patients

Variables \ Bone disease	High exchange No (%)	Normal No (%)	Adynamic No (%)	P
Sex				
Man	15 (37.5)	14 (35.0)	11 (27.5)	0.201
Woman	14 (33.3)	9 (21.4)	19 (45.2)	
Age				
< 40 y	9 (75.0)	2 (16.7)	1 (8.3)	0.004
41-60	15 (41.7)	9 (25.0)	12 (33.3)	
> 60 y	5 (14.7)	12 (35.3)	17 (50.0)	
Dialysis frequency				
Once per week	1 (12.5)	1 (12.5)	6 (75.0)	0.483
Twice per week	6 (25.0)	9 937.5)	9 (37.5)	
Three times per week	22 (44.0)	13 (26.0)	15 (30.0)	
Radiologic manifestation				
Positive	6 (31.6)	6 (31.6)	7 (36.8)	0.902
Negative	14 (31.8)	12 (31.6)	12 (31.6)	

Table 2. Association between Ca and P, and radiological manifestation among hemodialysis patients

Variables \ Radiologic manifestations	Normal No (%)	Abnormal No (%)	P
Calcium			
Positive	8 (42.1)	11 (57.9)	0.70
Negative	14 (36.8)	24 (63.2)	
Phosphorus			
Positive	8 (42.1)	11 (57.9)	0.22
Negative	10 (26.3)	28 (73.7)	

Table 3. Mean of blood indicators among hemodialysis patients based on radiologic manifestations

Indicators	Radiologic manifestations	No	Mean	t	P
PTH	Positive	19	320.95	0.672	0.18
	Negative	38	389.24		
ALP	Positive	19	345.74	0.101	0.72
	Negative	38	339.42		
Ca	Positive	19	8.88	0.090	0.90
	Negative	38	8.90		
P	Positive	19	5.55	1.635	0.02
	Negative	38	5.13		

PTH: Parathyroid hormone; ALP: Alkalin phosphatase

and adynamic bone disease were 55.3%, 28.1%, and 27.1%, respectively; these results are in accordance with the present study.[11] In another study, total prevalence, and the prevalence of high bone exchange disease and adynamic bone disease were 87%, 45%, and 42%, respectively; this is higher than our study findings considering the proportion of the two diseases.[12]

In the present study, we did not find any relation between sex and renal osteodystrophy. However, in the study by Gupta, female gender had association with renal osteodystrophy.[13] This difference in findings might be because of the small sample size of our study. Regarding age, adynamic bone disease increased along with increase in patients' age (P = 0.004). This finding was in agreement with the study by Hernandez et al.[14]

Considering calcium level, 29.4% of patients were hypocalcemic and 30.4% were hypercalcemic, which is in accordance with the study by Lye and Lee in which the prevalence of renal osteodystrophy was 24.4%.[15] In the present study, 30.5% of patients were hyperphosphatemic, but there were no hypophosphatemic patients, which is reasonable considering the nature of chronic renal failure. However, in the study of Lye and Lee, the prevalence of renal osteodystrophy was higher (75.4%). This can explain the relative efficiency of chelation therapy in our patients and effect of phosphorus chelator treatment in our patients. In an Indonesian study, 61% of the patients were hypocalcemic and 10% were hypercalcemic.[16] In another study, hypocalcaemia was associated with dialysis frequency and efficiency of dialysis.[17] In the present study, phosphorus level had no association with PTH level; this is in agreement with the results of the study conducted in Gorgan.[18]

Among the 57 candidates on whom hand radiography was performed, 23.2% had radiologic manifestations. This rate was 26% in the study by Gupta[13], 94% in the study by Lacativa et al.[19], and 3.35% in the study by Odenigbo et al.[20] This difference might be because of ethnic variations and imaging techniques.

A limitation of our study that reduced the prevalence of renal osteodystrophy was lack of access to digital radiography with higher quality and clearer radiographs. Radiologic findings in our study are consistent with the study by Odenigbo et al.[20], but are not in accordance with the study by Lacativa et al.[19] There was no significant relation between dialysis frequency and renal osteodystrophy which is not in agreement with the study by Lugon et al., this may be related to sample size.[17] In our study, the mean blood level of ALP, PTH, and Ca were 320 Iu/I, 372 pg/ml, and 8.95 mg/dl, respectively; this is in accordance with the studies by Nouri Majelan and Sanadgol, and Buargub et al.[1,11]

There was a strong positive correlation between ALP and PTH that is similar to the results of studies by Nouri Majelan and Sanadgol, and Couttenye et al.[1,21] This is a valuable finding in that it makes it possible to use ALP instead of PTH in medical centers which do not have access to PTH measurement for renal osteodystrophy patients.

In our study, PTH level for high bone exchange disease was higher than 300 pg/ml. Based on this range, the prevalence of renal osteodystrophy was 35.4%. In the study by Atsumi et al., the prevalence of renal osteodystrophy was also 35%.[22]

We had one limitation in this study; we were not able to perform drug assessment accurately because of irregular drug taking by patients.

In the present study, there was a high prevalence of renal osteodystrophy (approximately two-thirds of patients). With increase in age, the prevalence of adynamic type of osteodystrophy (PTH levels below 100 pg/ml) increased and high exchange bone disease decreased. This finding shows that more attention should be paid to adynamic osteodystrophy in the elderly and high exchange bone disease and its treatment in younger patients.

Acknowledgments

The present study is derived from a medical

student thesis and was financially supported by the Vice-chancellor in Research Affair of Kurdistan University of Medical Sciences.

Conflict of Interests

Authors have no conflict of interests.

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Chronic Diseases Journal

Comparison of the effects of gonadotropin-releasing hormone and raloxifeneon the size of uterine leiomyoma

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Original Article

Abstract

BACKGROUND: Uterine leiomyoma is a prevalent benign tumor. Several studies have shown the positive effects of raloxifene in the treatment of leiomyomas. Since raloxifene has fewer side effects than the gonadotropin-releasing hormone (GnRH) agonist, if proven effective, it can be applied easily. This study aimed to compare the medical effects of raloxifene and GnRH on uterine leiomyoma size.

METHODS: This clinical trial included 53 women with uterine leiomyoma. Participants were randomly divided into 2 groups of raloxifene and GnRH. The GnRH group received 1 dose per month (intramuscular injection) and the raloxifene group received 60 mg raloxifene orally/day for 3 months. The size of the leiomyoma, prior and during the intervention, was determined by a sonographist. During the study, repeated measurement was used for comparing the trend of alterations in the tumor size.

RESULTS: Analysis of changes in leiomyoma tumor size (log of tumor size) by repeated measurement showed that decrease in tumor size in the raloxifene group was significantly higher than GnRH group (P = 0.042). The trends of changes in endometrial thickness were different in the 2 groups and the reduction of thickness was more significant in the GnRH group (P = 0.026).

CONCLUSION: This study showed that raloxifene is an appropriate medicine to reduce the size of uterine leiomyoma and is more effective than GnRH.

KEYWORDS: Uterus, Leiomyoma, Gonadotropin-Releasing Hormone, Raloxifene

Date of submission: 24 Oct 2013, ***Date of acceptance:*** 13 Nov 2013

Citation: Zandvakili F, Seyedoshohadaie F, Rezaiee M, Soofizade N, Farhadifar F, Ghaderi E. **Comparison of the effects of gonadotropin-releasing hormone and raloxifeneon the size of uterine leiomyoma.** Chron Dis J 2014; 2(1): 46-51.

Introduction

Uterine leiomyoma, also called uterine fibroids, is a prevalent benign tumor that affects about 25% of women around their menopausal age. This is a tumor formed in uterine smooth muscles and approximately one-third of patients have to undergo hysterectomy.[1] Uterine leiomyoma can cause complications such as miscarriage, premature labor, detachment of the placenta, and bleeding.[2,3]

Several non-surgical treatments for the disease have been proposed.[4,5] Gonadotropin-releasing hormone (GnRH) drugs, raloxifene, and letrozole are among medications proposed for the

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treatment of uterine leiomyomas and they are still under study.[4-10] The hyperestrogenemia state induced by GnRH agonist is recognized as an effective treatment.[1,11] This drug is also associated with some side effects including climacteric like symptoms, hot flashes, vaginal dryness, osteoporosis, and decreased libido.[12,13]

Raloxifene is a non-steroidal drug that is derived from benzophenone. This drugs is a selective estrogen receptor modulator (SERM) and acts as an estrogen agonist in the central nervous system, and skeletal and cardiovascular metabolism; however, it has a weak antagonistic effect on breast and uterine activity.[14-16] This drug also prevents osteoporosis.[17] Several studies have proved the positive effects of raloxifene in the treatment of leiomyomas.[8-10] A study by Palomba et al., administration of raloxifene had led to the reduction of leiomyoma size in menopausal women, though it had not been effective in premenopausal women.[18] There is no other study showing the same effect, and the effect of this drug is still a controversial issue and more research is needed in this area.[19,20]

Since raloxifene has fewer side effects than the GnRH agonist, if proven effective, it can be applied easily. This study aimed to compare the medical effects of raloxifene and GnRH on uterine leiomyoma size.

Materials and Methods

This study was a randomized controlled clinical trial (RCT registration code: IRCT2014032816490N2) on 53 women with uterine leiomyoma referring to the gynecologic clinic of Be'sat Hospital in Sanandaj, Iran. In the first step, 61 women were evaluated. 8 women did not meet our inclusion criteria and were excluded from the study (Figure 1). After approval of the ethics committee of Kurdistan University of Medical Sciences, signed consent forms were obtained from all the patients. Then, participants were randomly divided into 2 groups of raloxifene and GnRH using simple random sampling method.

This study included women at child bearing age with a history of leiomyomas having a minimum size of 40 mm and a maximum of 60 mm in one dimension. Exclusion criteria included history of any metabolic, neoplastic, infectious diseases, blood disorders, venous thrombosis, liver disease, active rheumatoid arthritis, hormone therapy and surgery in the last 6 months, hypoechoic mass or calcified leiomyomas, endometrial abnormalities in sonography, lesions of the cervix and having body mass index (BMI) greater than 30 or less than 18 kg/m^2.

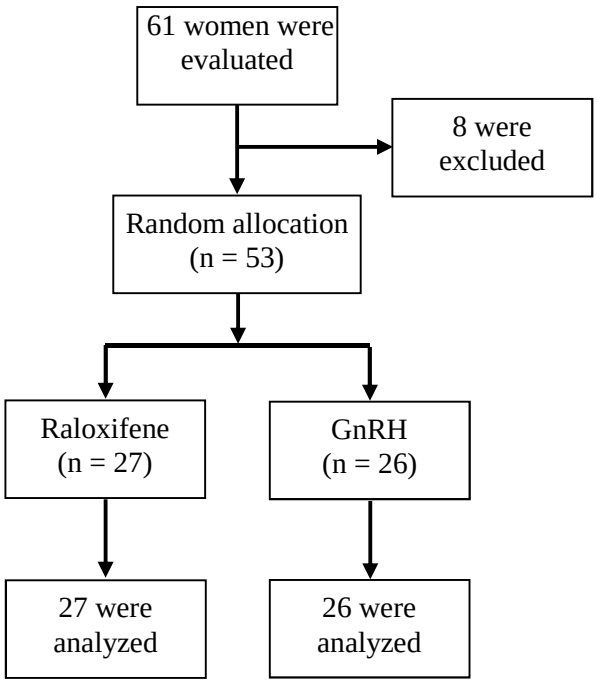

Figure 1. Participants profile in raloxifene and gonadotropin-releasing hormone (GnRH) groups during the study

After random assignment of the patients, the GnRH group received 3.75 mg of GnRH/month via intramuscular injection, and the raloxifene group received a daily dose of 60 mg oral raloxifene. Treatment duration was 3 months for both groups. Initial investigation and administration of drugs were performed by the same gynecologist.

Using transvaginal sonography, our sonographist determined the size of leiomyoma tumorbefore and three months after intervention. The size of leiomyoma was measured in 3

dimensions (D1 × D2 × D3 × 0.52). Thebiggest leiomyoma was studied when there were more than 1 tumor. Furthermore, endometrial thickness was measured for each case. Tumor size was measured by the same sonographist with no knowledge of the type of intervention. We used Simadzu SDU 2200 ultrasound machine (SIMADU, Japan) for performing sonography.

Data were entered in SPSS for Windows (version 11.5; SPSS Inc., Chicago, IL, USA). We used chi-square and Fisher's exact tests to compare qualitative variables and Student's independent t-test and Mann-Whitney test to compare quantitative variables between the 2 groups. During the study, repeated measurement was used to detect the changes in the tumor size. The sphericity assumption was assessed via Mauchly's sphericity test.

Results

This study included 53 participants, 27 in the raloxifene group and 26 in the GnRH group. Only 1 participant had history of smoking. Mean age of the participants was 42.1 ± 7.9 years, and their age ranged from 21 to 51 years; the mean of parity was 2.1 ± 1.8. 43 (81.1%) were married and the rest were single (virgin, divorced, or widowed). In addition, 5 patients (9.4%) had hypertension. Menorrhagia was observed in 50 patients (94.3%), pelvic pain in 31 patients (58.5%), and flushing in 7 patients (13.2%). No statistically significant differences were observed between the 2 groups regarding the above-mentinsed variables (Table 1).

Mean of leiomyoma size (mm3) decreased from 213.4 ± 356.5 to 77.2 ± 136.8 mm3 in the raloxifene group and from 113.4 ± 73.4 to 96.9 ± 74.6 mm^3 in the GnRH group (Table 2). Figure 2 indicates analysis of changes in leiomyoma tumor size (log of tumour size) by repeated measurement. Tumour size was significantly higher in the raloxifene group compared toGnRH group (P = 0.042). The trends of changes in endometrial thickness were different in the 2 groups and the reduction of thickness was more significant in the GnRH group (P = 0.026).

Table 1. Comparison of individual characteristics between raloxifene and Gonadotropin-releasing hormone (GnRH) groups

Variables	Raloxifene (n = 27)	GnRH (n = 26)	P
Age	42.4 ± 4.8	39.6 ± 8.2	0.143†
Parity	1.88 ± 1.39	2.36 ± 2.1	0.68†
BMI	28.8 ± 5.3	27.7 ± 3.9	0.559†
Smoking	0 (0%)	1 (3.8%)	0.491††
Hypertension	2 (7.4%)	3 (11.5%)	0.669††
Married	22 (81.5%)	21 (80.8%)	0.947††
Menorrhagia	25 (92.6%)	25 (96.2%)	1††
Tension sense	16 (61.5%)	21 (80.8%)	0.126
Pelvic Pain	15 (57.7%)	15 (57.7%)	1
Hot flash	5 (19.2%)	2 (7.7%)	0.419††

† Mann-Whitney test
†† Fisher's exact test
Others were tested by chi-square test
GnRH: Gonadotropin-releasing hormone
BMI: Body mass index

Discussion

In this study, both groups were similar regarding basic variables; however, at the beginning of the study the average size of leiomyomas in the raloxifene group was bigger than what was found

Table 2. Mean and standard deviation of leiomyoma sizes (mm^3) and endometrial thickness (millimeters) during the study

Indicator		Raloxifene (n = 27)	GnRH (n = 26)	P†
Leiomyoma sizes	Month baseline	213.4 ± 356.5	113.4 ± 73.4	0.042
	Month 1	119.9 ± 204	89.9 ± 71.9	
	Month 2	84.7 ± 131.8	83.6 ± 71.9	
	Month 3	77.2 ± 136.8	96.9 ± 74.6	
Endometrial thickness	Month baseline	5.8 ± 1.8	6.2 ± 2.5	
	Month 1	5.3 ± 1.6	5.4 ± 2.2	0.026
	Month 2	6.4 ± 8.9	4.7 ± 1.4	
	Month 3	4.7 ± 1.1	4.5 ± 1.4	

† Repeated measurement; GnRH: Gonadotropin-releasing hormone

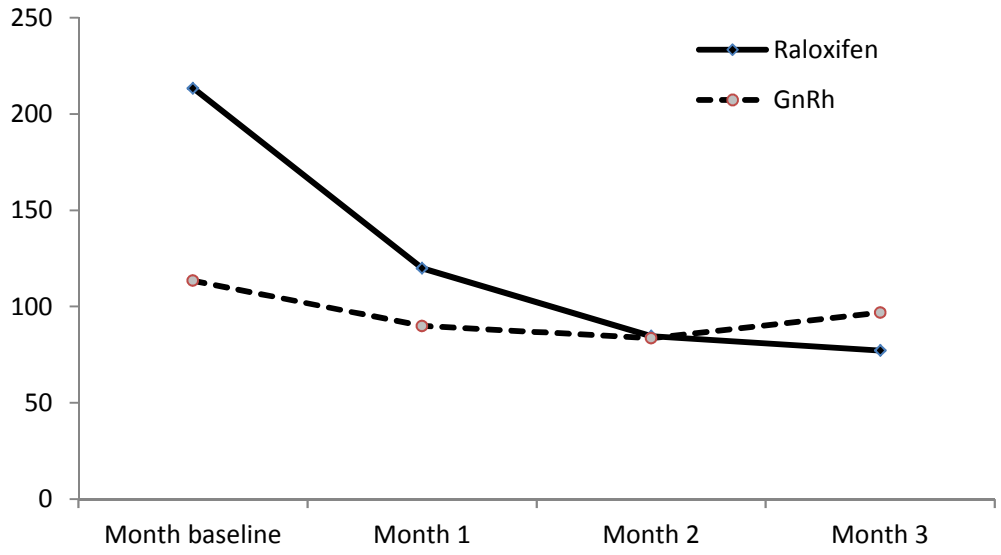

Figure 2. Trend of leiomyoma sizes (cm^3) in raloxifene and Gonadotropin-releasing hormone (GnRH) groups during the study

in the GnRH group. The logarithm of tumor size was used for improving the precision of the statistical tests. Based on the results, prescribing raloxifene for 3 months was more effective than GnRH in reducing the size of uterine leiomyomas. The endometrial thickness had a greater reduction in the GnRH group compared to the raloxifene group.

Leiomyomas are estrogen-dependent tumors. GnRH is one of the most common drugs used for leiomyomas and its effects usually begin within 3 months.[21] Although, GnRH is recognized as an effective treatment for reducing the size of leiomyoma, vriable results have been reported in different studies.[5,10,22] GnRH is more effective in women under 35 years; therefore, the variations in the results of different studies might be attributed to age.5 The wide age range in our study increased the external validity. This drug, which induces hypoestrogenism can cause vascular vasoconstriction in leiomyoma, but it may also have some other side effects such as insulin resistance, hyperlipidemia, and osteoporosis. Thus, the long-term administration of the drug can lead to several complications.[12,13,23] Raloxifene is a kind of selective estrogen receptor modulator (SERM), which can prevent osteoporosis in menopausal women.17 This drug can also prevent collagen synthesis in leiomyomas.[20] Raloxifene decreases the proliferation of endometrial tissue and this mechanism can affect leiomyomas.[24] In our study, raloxifene was effective in reducing the size of leiomyomas. In some studies, administration of an appropriate dose of raloxifene in premenopausal women failed to significantly reduce the size of leiomyomas.[18,25]

However, in a study, the simultaneous administration of raloxifene and GnRH for a long time (18 cycles) in premenopausal women prevented osteoporosis and any increase in the levels of glucose and lipids with no special side effects. For a better therapeutic effect 6 cycles of treatment are necessary. However in our study, Raloxifene did not reduce the vasomotor symptoms associated with the GnRH.[26] In a study by Palomba et al., raloxifene had no effect on the size of leiomyomas and menstrual bleeding in premenopausal women.[18]

However, in the raloxifene group we found no new case of tumor and no increase in the size of tumors. Administration of raloxifene was not as

effective as GnRH in reducing the size of endometrial thickness. Hence, raloxifene is a suitable medication for asymptomatic postmenopausal women as the drug does not have a great effect on the endometrial thickness and the vasomotor system.[27]

Jirecek et al. showed that raloxifene prevented the growth and progress of the leiomyoma; however, there was no significant difference in the clinical symptoms between the 2 groups and the drug was well tolerated.[28] Raloxifene can also reduce the risk of breast cancer and has a beneficial effect on skin elasticity.[29,30]

One limitation of our study was that we did not assess the signs and symptoms of the patients and only the size of leiomyomas was studied. Thus, we recommend further studies for evaluation of the effect of raloxifene on the patient's signs and symptoms.

Conclusion

This study showed that raloxifene is an appropriate medicine to reduce the size of uterine leiomyoma and it is more effective than GnRH.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

This study was financially supported by the Vice Chancellor for Research Affairs, Kurdistan University of Medical Sciences.

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Chronic Diseases Journal

Pancytopenia as a rare complication of acute Brucellosis: A case report

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Case Report

Abstract

Human Brucellosis still challenges many physicians, especially in developing countries where it is still a very common, but sometimes ignored disease. Its reemergence in developed countries and its status as a class B bioterrorist agent has recently attracted much interest. Having over 500,000 new cases annually, Brucellosis is known as one of the most common zoonotic infections in the world and "the great imitator" because of many clinical and hematological manifestations. Brucellosis is still endemic in many developing countries and remains under-diagnosed and sometimes missed reported. Although this province (Kurdistan, Iran) is a Brucella endemic area with a very high prevalence and incidence rate, except for very few and negligible case reports, we did not find any reports or epidemiological study regarding this zoonotic infection. This is the first reported case of Brucellosis with pancytopenia from this western province of Iran which has been neglected. Our case was a 16-year-old girl referred with protracted fever during the last month and undetermined diagnosis. She also suffered from generalized pain, pale skin, sweating, anorexia, and weight loss. After clinical surveying, taking history, and physical examination, Brucella infection was suspected. Diagnosis confirmed by standard tube agglutination test (STA), 1/640. The patient was successfully treated with doxycycline, rifampicin, and ceftriaxone.

KEYWORDS: Brucellosis, Pancytopenia, Zoonotic Infection, Kurdistan, Iran

Date of submission: 1 Oct 2013, ***Date of acceptance:*** 15 Dec 2013

Citation: Afrasiabian Sh, Gharib A, Hassanzadeh K, Ahmadi A. **Pancytopenia as a rare complication of acute Brucellosis: A case report.** Chron Dis J 2014; 2(1): 52-55.

Introduction

Brucellosis or Malta fever is the most common zoonotic infection in the globe caused by a gram-negative, non-motile, facultative intracellular bacterium that belongs to the genus of Brucella.[1] It affects animals like sheep, goats, cattle, and pigs as the primary host and humans as the secondary.[2] It is still a common health problem in some Middle Eastern and Mediterranean countries including Iran.[3] Over the last ten years, the infection has re-emerged especially in Eastern Europe, the Balkans, and Eurasia. Brucellosis, although almost eradicated in many parts of the world, still remains widespread and endemic in developing countries.[4] It is very contagious for humans and the disease, unless diagnosed and treated both promptly and effectively, can become chronic, affecting multiple body systems.[5] The World Health Organization (WHO) has designated Brucellosis as a historically "neglected" zoonosis.[1]

In desirable situations and strong health systems less than 1 out of 8 Brucellosis case is diagnosed in opportune and reported.[1] While basic science and epidemiology of human Brucellosis is known, it is often under-detected

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and overlooked, therefore highlighting its status in endemic area and reporting rare cases may attract global attention.[6]

Kurdistan province of Iran is an endemic region of Malta fever with a very high prevalence and incidence rate.[3] Unfortunately no comprehensive and reliable epidemiological report from this area is available. So, in addition to case report, an estimation of this neglected important zoonotic infection in this province is presented.

Case Report

A 16-year-old girl referred to our university hospital from a rural clinic presented with prolonged fever and undetermined diagnosis. She suffered from generalized pain, pale skin, sweating, anorexia and weight loss over the previous one month. Physical examination showed fever (39° C), splenomegaly without hepatomegaly and lymphadenopathy.

In laboratory test results, hemoglobin (Hb), hematocrit (Hct), leukocytes and platelets count were decreased significantly. Laboratory analysis on the admission day showed leukopenia (white blood cell count = 3000/mm^3), thrombocytopenia (Plt = 35,000), and anemia (Hb = 7.72 g/dl, Hct = 26.02%). Evaluation of the peripheral blood smear (PBS) revealed neutrophils = 61%, lymphocytes = 27%, and eosinophils = 2%. The blood smear was also positive for anisocytosis, poikilocytosis, and hypochromia. Both urine and blood cultures were negative for pathogenic bacterial infections. The erythrocyte sedimentation rate and C-reactive protein (CRP) were 12 mm/1 h and 3+, respectively. The biochemical tests revealed an increase in the alanine aminotransferase (ALT) 149 U/l (normal range is 5-40), and aspartate aminotransferase (AST) 174 U/l (normal range is 5-40). The other laboratory results were within normal ranges.

Because of pancytopenia and weight loss, hematological malignancies were suspected. Normal erythroid and myeloid maturation in bone marrow aspiration ruled out an underlying malignancy. On the other hand, because of abnormal AST and ALT liver involvement was obvious. Although both urine and blood cultures were negative and white blood cells (WBC) count was decreased, protracted bacterial fever or viral infections were under discussion. At last, Malta fever and Typhoid fever were under suspicion. Antibodies against typhoid fever were only positive for O and H antigens at titer 1/80. However, standard tube agglutination (STA) for Brucella species was positive at a titer of 1/640.

Therefore, according to the clinical and laboratory findings treatment for Brucellosis was started and patient was administered doxycycline 100 mg orally twice daily, rifampicin 450 mg orally once daily, and ceftriaxone 4 g/day intravenously (all for eight weeks).[7] By the fifth day of the treatment, her fever subsided and hematological findings improved (Hb = 9.1 g/dl, Ht = 28.4%, Plt = 78000/mm^3, WBC = 2300/mm^3, neutrophils = 40%, lymphocytes = 59%, eosinophils 1%). PBS was still positive for anisocytosis, poikilocytosis and hypochromia.

The patient discharged from the hospital with the recommendation of ceftriaxone and rifampicin. After 8 weeks of treatment, all hematological parameters were within normal ranges and on later follow up samples showed no evidence of Brucella seropositivity.

Discussion

Malta fever is a systemic infection caused by Brucella species. These bacteria transmit from animals to humans and colonize in different body tissues, dominantly in lymphoreticular system.[8] Main reason for reporting this case is to advise physicians to consider Brucella infection in febrile patient who present with pancytopenia in the endemic areas, knowing that health education especially to villagers about routs of transmission, prevention methods, food supply, and delivery supervision could decrease the prevalence of the disease. The disease has a high morbidity and a broad spectrum of clinical manifestations ranging from asymptomatic disease to severe and/or fatal

illness.[2] As it is one of the leading infections causing fever of unknown origin, it can mimic those of other febrile illnesses.[9] The incubation period is usually one to four weeks.[8]

Hematological abnormalities include anemia, leukopenia, thrombocytopenia, pancytopenia, bleeding diathesis, and coagulation disorders, such as disseminated intravascular coagulation (DIC). Up to 87.5% of patients with pancytopenia induced by Brucella infection have positive blood cultures and almost all of them had positive Brucella antibody.[8]

Brucellosis is notorious for relapsing even after adequate treatment.[10] Relapse usually occurs within the first six months following completion of treatment. Causes of relapse include inadequate choice of antibiotics, shortened treatment duration, lack of adherence, or localized foci of infection. Relapse due to antibiotic resistance is rare;[10] hence, significant of its prompt and proper management.

Due to evading immune system and tendency to relapse, its eradication is very difficult.[2] Physicians in endemic areas always say "everything can be Malta fever until proven different".[1] Non-specific complications may initially lead clinicians to a differential diagnosis other than Brucella.[9] Hematologic complications during the course of Brucellosis, with numerous patterns of cytopenia or lymphocytosis has been reported.[11] However, one should always take into account the postscript to the above-mentioned rule, which says that "in endemic areas everything can be Brucellosis, but Brucellosis is not the only possible diagnosis." This has been demonstrated in some studies where hematologic complications that might have been attributed to concurrent. Brucellosis was actually due to underlying undiagnosed hematologic malignancies.[8,12]

In our case, in spite of living in a rural endemic area of Brucellosis and having a positive history of consumption of un-pasteurized dairy products, unfortunately there was no early diagnostic suspicion of Brucellosis and the patient suffered from a prolonged fever. Her family also tended as a shepherd. Although anemia in Brucellosis is expected due to bone marrow involvement, numerous other pathogenic mechanisms can be implicated.[10]

Brucellosis is a notifiable disease, yet its cases remain often unrecognized and underestimation; reflecting inadequacy of diagnostic laboratory services in most of the endemic area, especially un-developed countries.[13] The geographical pattern of this zoonotic infection is constantly changing.[14] The causes of its re-emergence and recent increase in the incidence of Brucellosis including socioeconomic changes, wars and political turbulence in some countries, inadequate control programs in un-developed countries, ease of human international travel recently, uncontrolled animal transportation across open borders, and at last Brucellosis is a complex disease that has different cycles of expansion and regression.[13,15]

Brucella bacteremia may be complicated by: infective endocarditis, fatal endotoxic shock that may be associated with DIC, multiorgan failure, microangiopathic hemolytic anemia (MAHA) with bleeding tendency and pancytopenia and death.[2] Despite the severity of these complications, the early use of appropriate antimicrobial therapy usually leads not only to clinical improvement but also to normalization of the hematological parameters and the coagulation profile.[9]

On a few occasions, Brucellosis has been encountered in patients with acute leukemia and solid tumors.[1,2] As reported cases of Brucellosis developed in patients with malignant disorders living in countries that are endemic for this infection, the dominant presenting features of Brucellosis were febrile neutropenia and pancytopenia.[2]

Kurdistan province of Iran with a population of 1.5 million people is an endemic region of Malta fever with a very high prevalence and incidence rate.[3] According to the statistics of Iranian Ministry of Health, in 2012 the incidence rate was 50/100000 (unpublished data). But upon over 15 years' experience of Brucella

treatment in this endemic area, it is obvious that its real burden is much higher, maybe over 10 times, i.e. 500/100000 new cases annually. Miss diagnosis, overlook, and finally and failure in reporting are the main reasons for mismanagement of the disease.

In conclusion, physicians should have a high index of suspicion regarding Malta fever when evaluating patients presenting with prolonged pyrexia, pancytopenia, and a history risk of consumption of non-pasteurized dairy products.

Conflict of Interests

Authors have no conflict of interests.

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Chronic Diseases Journal

Fibrosing mediastinitis: An unusual cause of superior vena cava symptoms

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Case Report

Abstract

Fibrosing mediastinitis is a rare benign disorder caused by the proliferation of acellular collagen and fibrous tissue within the mediastinum. Although many cases are idiopathic, many (and perhaps most) cases are thought to be caused by an abnormal immunologic response to *Mycobacterium tuberculosis* and *Histoplasma capsulatum* infections. Collagen formation leads to compression of vital structures, resulting in cough, chest pain, and dyspnea. The following case is a former healthy middle-age man who presented with an 8-year history of cough, chest pain, facial swelling, and trouble breathing, and was subsequently found to have fibrosing mediastinitis. Fibrosing mediastinitis should be considered in the differential diagnosis of cough, chest pain, and dyspnea, primarily when findings such as increased venous pressure are present on physical exam, and hilar abnormalities are seen on chest radiograph.

KEYWORDS: Fibrosing Mediastinitis, *Mycobacterium tuberculosis*, Superior Vena Cava Syndrome

Date of submission: 04 Sep 2013, ***Date of acceptance:*** 11 Nov 2013

Citation: Mozafari A, Choopankareh E, Chopani M, Baharvand A, Gharib A. **Fibrosing mediastinitis: An unusual cause of superior vena cava symptoms.** Chron Dis J 2014; 2(1): 56-9.

Introduction

Fibrosing mediastinitis also known as granulomatous or sclerosing mediastinitis is an uncommon benign disorder characterized by the proliferation of dense fibrous tissue within the mediastinum.[1] Osler in 1903 published the first major review on mediastinal fibrosis.[2] Since then, a few case series have been published with stray case reports.[3,4] Mediastinal structures are surrounded, constricted and sometimes invaded by the fibrous tissue, which may extend to affect other intrathoracic organs. The pattern of involvement of mediastinum is variable, and so are the clinical features.[5]

Venous structures (superior vena cava and pulmonary veins), due to thin walls and low intraluminal pressure, tend to be compressed earlier than the arteries and tracheobronchial tree and esophagus. For this reason, venous hypertension in the drainage area of superior vena cava is considered the hallmark of the disease. It is a rare cause of superior vena cava obstruction (1-2%).[6] Various hypotheses have been proposed for the fibrous lesions. Radiological, computed tomography (CT), and magnetic resonance imaging features help in diagnosis; however, histological confirmation is difficult. Medical therapy is discouraging; surgery has limitations while stenting of vessels and dilatation of bronchi and esophagus may provide some relief of disease.[3]

Case Report

A 47-year-old male, Iraqian by nationality attended the clinic due to 8-month history of dyspnea on minimal exertion, orthopnea, cough with scanty mucoid-white sputum and

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sometimes bloody expectoration, dull aching, and nausea. He described an 8-year history of progressive puffiness of face, swelling over both upper limbs and dilated neck vein, more after getting up in the morning and decreased over day. There was no history of fever, feet edema, urinary complaints, change in voice, and palpitation. Past history was not contributory. There was no history of drug intake or exposure to radiation. However, patient had a history of active smoking (15 pack/years). Personal and family histories were not contributory.

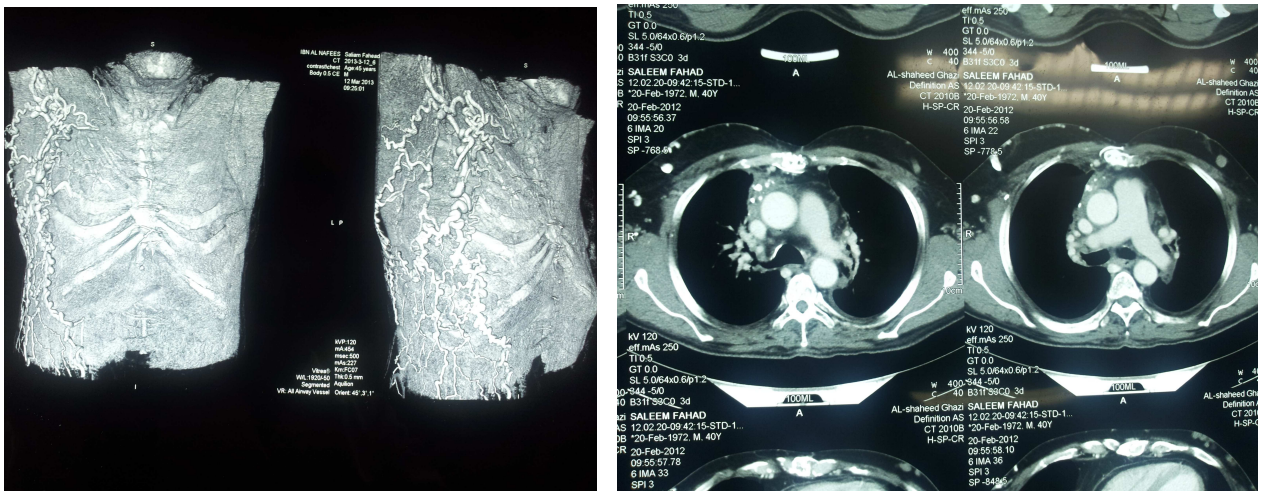
Clinical examination revealed blood pressure of 120/70 mmHg, pulse of 90/min, respiratory rate of 20/min, and temperature of 36.9° C. He had experience of puffiness of conjunctiva, face, and both upper limbs. The jugular veins were full and non-pulsatile, prominent veins were seen over arms, chest and anterior aspect of neck with flow away from mediastinum (Figure 1). Respiratory system examination revealed bilateral rhonchi and crepitations. Rest of the general physical and systemic examination was unremarkable.

Complete blood count revealed hemoglobin of 11.8 g%, a white blood cell of 4.9×10^9/l with 83% polymorphs, 13% lymphocytes, and normal platelets. Serum biochemical parameters were normal. On investigation, his electrocardiogram and two-dimensional echocardiogram were normal. Sputum for acid-fast bacilli and purified protein derivative test was negative.

The chest X-ray showed mild superior mediastinal widening (Figure 2). Chest CT demonstrated soft tissue density and intermingled calcifications adjacent to the superior vena cava, right pulmonary artery, and ascending aorta. The three-dimensional (3D) venographic reconstruction showed an extensive network of collateral circulation due to obstruction of the right and left brachiocephalic vein that extended toward the chest wall, upper limbs, and abdomen (Figure 3). No thrombi were observed in the vena cava. Based on these findings, a diagnosis of superior vena cava syndrome was made. There was no evidence of mediastinal mass or lymphadenopathy. Mediastinoscopy, mediastinotomy, or histopathological confirmation could not be done due to refusal for consent to undergo invasive interventions/procedure.

Figure 1. Chest wall and abdomen of patient demonstrated extensive engorgement of vessels

Figure 2. Chest radiography of this patient shows mediastinal widening



A **B**

Figure 3. Three-dimensional venographic and reconstruction computed tomography scan of the same patient; (A) Widespread arrangement of collateral circulation due to obstruction of the right and left brachiocephalic vein that extended toward the chest wall; (B) Soft tissue density and calcifications adjacent to the superior vena cava and great vessels

Discussion

Mediastinal fibrosis is a rare disease characterized by the proliferation of collagen tissue and establishment of fibrous tissue in the mediastinum.[1] In most cases, the cause of this process is unknown, although in endemic zones it has been related with *Histoplasma capsulatum* infection, specifically with an abnormal inflammatory response to the antigens of this fungus and, with other granulomatous diseases such as tuberculosis.[7] There is an idiopathic form with a possible autoimmune component that may be associated with fibrosing processes in other locations, such as retroperitoneal fibrosis, pseudo-tumor of the orbit and Riedel's thyroiditis. It affects young patients, with a slight predominance in males, and its symptoms are insidious and progressive, with a variable natural history.[8] The inflammatory process usually sets in the upper half of the mediastinum, in the paratracheal region. It is commonly located to the right, anteriorly to the trachea and close to the pulmonary hilum; however, it may also develop as a diffuse fibrosis in the mediastinum, extending from the brachiocephalic veins to the pulmonary bases. The symptoms are generally caused by obstruction of the superior vena cava, esophagus, trachea, bronchi, or pulmonary veins, also causing pulmonary arterial hypertension by direct compression of pulmonary arteries, or secondary to pulmonary venous compression.[9]

Investigations showed suggestive of idiopathic mediastinal fibrosis are mediastinal widening on chest X-ray and lung CT. Barium swallow and bronchoscopy may show areas of compression or distortion of the esophagus and bronchus. Venogram showing collaterals and mediastinal veins are diagnostic. Mediastinoscopy, mediastinotomy may be difficult, and histopathology may be confirmative and requires large sample of tissue if obtained surgically though rarely CT guided automated needle biopsy may be possible.[10]

Our patient presented with features of superior vena cava obstruction for which no clinical or radiological cause could be demonstrated; hence, a possibility of idiopathic mediastinal fibrosis was entertained as a diagnosis on exclusion of common causes, which was supported by the 3D angiographic study of the upper extremity and chest wall.

There is no curative treatment for this disease. Anti-fungal agents have been used in cases that may be related with histoplasmosis, although they

have not been effective.[11] The use of corticoids does not provide any benefit except in cases of autoimmune etiology, in which there may be a response. Therefore, therapeutic measures will be aimed at relieving obstructive symptoms in the airways, major vessels, and esophagus. When there is involvement of the vena cava, the placement of endovascular stents to the vessel is an option that produces a symptomatic improvement. Other techniques have been described, such as bypass surgery with saphenous vein grafts or bioprostheses.[12] We recommended palliation therapy such as endovascular stent in brachiocephalic vein to the patient. However, he did not submit this alternative management.

Conflict of Interests

Authors have no conflict of interests.

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