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Frequency of metabolic syndrome in Behcet's disease and its relation with Behcet's disease activity

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Metabolic Syndrome, Behcet's Disease, Intensity

A B S T R A C T

Coronary artery disease is the most common cause of death and on time diagnosis and control is essential in improving health and increased longevity. It has been recognized that autoimmune mechanisms play a major role in the pathogenesis of atherosclerosis. In many cases, metabolic syndrome increases the risk of coronary artery disease, stroke and diabetes. The prevalence of this syndrome is high and in most cases it does not matter. The aim of this study was to investigate the prevalence of metabolic syndrome in Behcet's disease and its association with Behcet's disease intensity. In a cross-sectional and descriptive-analytic study that performed in internal medicine department of Tabriz University of Medical Sciences on patients with Behcet's disease, the prevalence of metabolic syndrome in Behcet's disease and its association with Behcet's disease intensity evaluated. 41 of patients (74.5%) were male and 14 of them (35.5%) were female. Mean age of patients was 38.80 ± 10.18 year. Metabolic syndrome was found in 14 patients (25.5%) of the studied patient's. The prevalence of metabolic syndrome in male patients with Behcet's disease was 24.4% in female patients with Behcet's disease was 28.6% that prevalence of metabolic syndrome was higher in female patients than male patients. In our study, prevalence rate of metabolic syndrome in patients with age less than 40 year was 17.24% and prevalence rate of metabolic syndrome in patients with age less than 40 year was 34.6% that prevalence rate of metabolic syndrome was increase with increase of patients age. Significant difference in eye score of patients at patients with and without metabolic syndrome ($P=0.326$). Significant difference in non-eye score of patients at patients with and without metabolic syndrome ($P=0.328$). Our results and various studies results suggest that in inflammatory diseases such as Behcet's, rheumatoid arthritis, psoriasis and IBD prevalence of metabolic syndrome is higher than other members of society, Note that this requires more and better screening period, the patients in terms of cardiovascular disease and diabetes for more highlights. Significant correlation was not found between Behcet's disease intensity and metabolic syndrome.

Introduction

Cardiovascular diseases are currently the most prevalent causes of death in the world.

Considering the mission of the medical community to improve the health and

lifetime of society members, it is evidently important to value these diseases and prioritize them in the research plans of the Health and Treatment Ministry (1).

Recently, a new horizon has been introduced into pathology of atherosclerosis. The horizon promoted attention to the role of self-immune mechanisms in the pathogenesis of this disease (1-2). According to the studies on inflammatory and rheumatic diseases such as RA (rheumatoid arthritis) and SLE (systemic lupus erythematosus), accelerated atherosclerosis is very common and is considered a cause of death. This is not mainly caused by consumption of medicines such as glucocorticoids. For instance, in an article published in 2010 by the European Rheumatology Association, it was stated that aside from usual risk factors of atherosclerosis, RA increases the risk of cardiovascular diseases such as type II diabetes (2-3).

Due to the significance of the issue, the Cardiovascular Diseases Association has also introduced an increase in high sensitivity CRP as a risk factor for cardiovascular diseases.

One of the possible risk factors of cardiovascular diseases is the metabolic syndrome (1). Behcet's disease is an inflammatory rheumatic disease that is more common in the Middle East and Iran than European and American countries. Hence, there has been little discussion on this disease in the major medical reference book. On the other hand, this disease is an important threat to eyesight in Iran and especially regions located on the Silk Road (e.g. Eastern Azerbaijan Province) (4-6).

The very few studies that have been performed on cardiac involvement have mostly focused on myocardial and

pericardium involvement. For example, in a study conducted in 2012 it was stated that most of the coronary artery obstructions are associated with Vasculitis and thrombosis. Little research has also been performed on the involvement of other factors of atherosclerosis in these diseases (1).

Hence, due to the significance of the Behcet's disease in Iran and in the Eastern Azerbaijan Province, the importance of coronary artery diseases to inflammatory rheumatic diseases, and the lack of Major Iranian and foreign studies, it was decided to study the prevalence of the metabolic syndrome in these patients. It is hoped that the results of this research contribute to the improvement of the condition of such patients. The objective of this research was to examine the frequency of occurrence of the metabolic syndrome with the Behcet's disease. It was also aimed to study the relationship between the metabolic syndrome and severity of the Behcet's disease.

Materials and Methods

In this cross-sectional descriptive-analytic study, which was carried out in the internal diseases department of the Medical Sciences University of Tabriz from 2013-2014, analyses were performed on patients suffering from the Behcet's disease. In this research, the frequency of occurrence of the metabolic syndrome and Behcet's disease as well as the relationship of the metabolic syndrome and Behcet's disease were studied.

A total of 55 patients with Behcet's disease were included in the study. The patients had visited the clinics of the Medical Sciences University of Tabriz for periodic check outs. They also met the inclusion criteria for the study.

Exclusion criteria included presence of the following diseases: liver disease, hypothyroidism, Cushing's syndrome, renal diseases accompanied by high protein excretion, renal failure developed prior to the Behcet's disease, history of previous diabetic diseases, and hereditary metabolic diseases.

All patients were examined by a rheumatologist and the project executive resident. A questionnaire containing questions about the following information was completed by the participants: demographic information; age of onset of symptoms; major disease symptoms such as canker sores; genital sores; ocular involvement; skin involvement; artery diseases and frequencies; gastrointestinal, joint, and neural involvements; and treatment method.

Afterwards, the activity of the Behcet's disease was measured against IBDDAM criteria. The prevalence of the metabolic syndrome in patients with Behcet's disease was studied and the simultaneous occurrence of the syndrome and activity of the disease was examined too.

In order to analyze the metabolic syndrome the following diagnostic criteria were used:

Adult Treatment Panel (ATP)-III Criteria

- 1- Abdominal circumference of higher than 102 cm in men and higher than 88 cm in women
- 2- Triglycerides level of higher than 150 mg/dl or consumption of drugs for a high level of triglycerides
- 3- HDL level of lower than 40 and 50 mg/dl in men and women, or consumption of drugs for treatment of low HDL

- 4- Fasting blood sugar level of higher than 100 mg/dl or consumption of drugs for high blood sugar levels
- 5- Blood pressure of higher than 130/80 or consumption of HTN drug

Patients meeting three of the above five criteria were considered to be suffering from the metabolic syndrome.

After 12 hours of fasting blood samples were taken from all patients to measure the levels of FBS, TG and HDL. Blood pressure and abdominal circumference values were obtained by the project executive resident. Patients meeting 3 criteria or more were considered to be metabolic syndrome patients.

Results of the research were compared to the results of the studies of prevalence of the metabolic syndrome in the general population of former studies.

International Criteria for Behcet's Disease (three points or higher shows presence of Behcet's disease):

- Genital sore: 2 points
- Ocular involvement: 2 points
- Canker sore: 1 point
- Erythema Nodosum or Pseudofolliculitis: 1 point
- Pathergy test:
- Venous or arterial thrombosis or aneurysm: 1 point

IBDDAM

In this method, activity of the disease is traced back to 12 months. Calculations in this method are performed as follows:

Scores of every attack are calculated from the previous examination to the current examination. Next, scores are summed up and the total score is divided by the number of months between the two examinations.

This process gives the mean monthly activity of the disease.

- Canker sore: 1 point for every 5 sores
- Genital sore: 1 point for every sore
- Pseudofolliculitis: 1 point for every 10 lesions
- Erythema Nodosum: 1 point for every 5 lesions
- Inflammatory Arthralgia: 1 point regardless of the number of involved joints
- Arthritis: 2 points for mono arthritis and 3 points for arthritis involving more than one joints
- Neural system involvement: 1 point for isolated headache (provided that it is caused by the Behcet's disease), 3 points for other slight central neural system involvements, and 6 points for moderate to severe involvement of the central neural system
- Gastrointestinal symptoms: 3 points for slight symptoms and 6 points for moderate to severe symptoms
- Epididymitis: 2 points
- Vascular thrombosis: 1 point for superficial thrombophlebitis and 2 points for deep venous thrombosis
- Positive Pathergy test result: 1 point

The score of ocular involvement was calculated separately. To this end, the eye was divided into three sections: anterior, posterior and retina. Next, one to four points was ascribed to every part based on the intensity and extent of the lesion.

Moral Considerations

In all of the project phases, no physical damage or financial loss was caused to the patients. The patients experienced no intervention too. Since the required tests were planned based on necessary periodic

follow up tests, no additional cost was imposed on patients. Patients' information also remained secret.

Result and Discussion

In this study, 55 patients with the Behcet's disease were studied and the following results were obtained:

Of the patients under study, 74.5% were male and 25.5% were female. The mean age of participants was also 38.80 ± 10.18 years. Canker sore, genital sore, Pseudofolliculitis, erythema Nodosum, active ocular involvement, Arthritis-Arthralgia, and Sacroiliitis were observed in 92%, 33%, 16%, 25%, 41%, 15.5%, and 1.8% of the patients, respectively. Information obtained from examination of patients is presented in Table I. The information was used as the basis for measuring the severity of the Behcet's patients.

A total of 14 patients (25.5%) under study were diagnosed with the metabolic syndrome. That is to say, 10 male patients and 4 female patients demonstrated the metabolic syndrome. No significant difference was observed between the results obtained from the two genders ($P=0.736$). Results of analysis of study parameters in patients with the metabolic syndrome are presented in Table I.

The ocular involvement score obtained by 42 patients was zero and the score obtained by 13 was higher than zero. Of the 42 patients with ocular involvement score of zero, 11 suffered from the metabolic syndrome and of the 13 patients with ocular involvement score of higher than zero, 3 patients suffered from the syndrome. No significant relationship was observed between the ocular involvement score and development of the metabolic syndrome ($P=0.568$).

The mean ocular involvement score of 21 patients was zero and that of 34 patients was higher than zero. Of the 21 patients with the ocular involvement score of zero, 3 suffered from the metabolic syndrome and of the 34 patients with the ocular involvement score of higher than zero, 11 suffered from the aforementioned syndrome.

No significant relationship was observed between the ocular involvement score and development of the metabolic syndrome ($P=0.135$). The mean ocular involvement score of patients with the metabolic syndrome was 5.12 ± 2.35 and that of patients without the syndrome was 1.35 ± 0.95 .

No significant difference was observed between the mean ocular involvement scores of patients with and without the metabolic syndrome ($P=0.328$). Table II shows the frequency of drugs used by patients based on gender and presence/absence of the metabolic syndrome. The data presented in this table reflect the absence of a significant relationship between drugs used by patients with the Behcet's disease and development of the metabolic syndrome.

ATP III criteria and patients' symptoms are shown in tables III based on gender and absence/presence of the metabolic syndrome. Figure I show the age distribution of patients with the Behcet's disease. The age range, abdominal circumference, ocular involvement score, and non-ocular involvement score values are also presented in Figures II to V.

The relationship of abdominal circumference with the levels of cholesterol ($P=0.032$, $r=0.297$), triglycerides ($P=0.010$, $r=0.349$), systolic blood pressure ($P=0.021$, $r=0.311$), and weight ($P<0.001$, $r=0.716$) was a direct significant linear relationship.

No significant linear relationship was observed between abdominal circumference of patients and non-ocular involvement ($P=0.261$, $r=0.154$). However, an inverse significant linear relationship was observed between the ocular involvement scores and weights of patients ($P=0.017$, $r=-0.375$).

In addition, a direct significant linear relationship was also found between the non-ocular involvement score and duration of presence of the Behcet's disease in patients ($P=0.004$, $r=0.528$). However, no significant linear relationship was observed between the non-ocular involvement score and ocular involvement score of patients ($P=0.400$, $r=-0.116$).

The Behcet's disease causes complications such as severe ocular involvement. Therefore, this disease is an important issue in countries that are located along the Silk Road. In Iran the prevalence of this disease is high (70 per thousand people). Similar to other rheumatic chronic diseases, the disease can also lead to major morbidity and mortality among patients. The mean mortality rate of this disease is 3.2-5% in the world over 7 years. Rupture of coronary/pulmonary arterial aneurysms, neurologic complications, and vascular thrombosis are the major causes of mortality of these patients (7-8).

Cardiovascular diseases are among the most common causes of death in the world. The metabolic syndrome leads to an increase in the probability of development of type II diabetes and coronary artery disease. Prevalence of this syndrome is increasing due to the modern lifestyle, increased obesity, decreased physical activity, and intake of fatty and salty food. Today, the role of inflammatory cytokines in the development of resistance to insulin, the metabolic syndrome, and atherosclerosis is known (9).

Table.I Clinical finding of patients based on gender and metabolic Syndrome

	Gender		Metabolic Syndrome		Total
	Male	Female	Yes	No	
Oral aphthae	21	9	22	8	30
Genital aphthae	8	1	5	4	9
Pseudofolliculitis	6	3	8	0	8
Erythema Nodosum	3	2	5	0	5
Ocular involvement	14	6	16	4	20
Arthritis	2	1	2	1	3
Sacroiliitis	1	0	1	0	1
Epididymitis	0	0	0	0	0
Gastrointestinal involvement	0	0	0	0	0
Neurological involvement	1	0	0	1	1

Table.II The frequency of drugs used by patients based on gender and metabolic syndrome

	Gender		Metabolic Syndrome		P
	Male	Female	Yes	No	
Prednisolone	33	12	11	34	0.703
Colchicine	14	5	6	13	0.522
Azathioprine	16	7	6	17	0.927
MTX	6	1	1	6	0.664
Cyclophosphamide	1	1	0	2	-
Warfarin	1	0	0	1	-
Sulfasalazine	1	0	0	1	-
Acid Folic	1	0	0	1	-

Table.III The ATP III criteria of patients based on gender and metabolic syndrome

	Gender		Metabolic Syndrome		Total
	Male	Female	Yes	No	
Waist circumference(> 88 cm in females and > 102 cm in males)	9	5	10	4	14
TG > 150 mg/dl	28	9	14	23	37
HDL(<40 mg/dl in males and <50 mg/dl in Females)	8	3	4	7	11
BS > 100 mg/dl	12	5	11	6	17
Blood pressure(SBP > 130 mmHg and DBP > 80 mmHg)	12	4	9	7	17

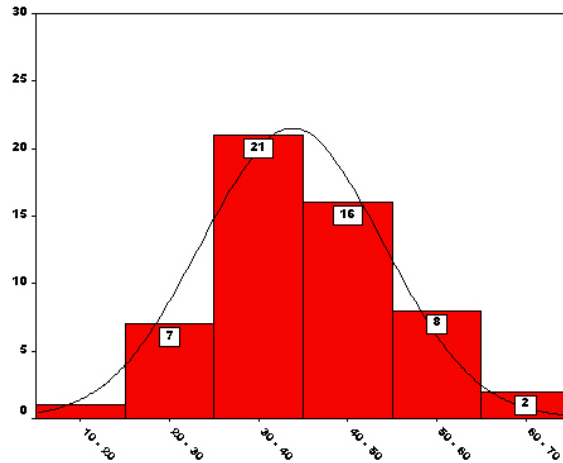


Figure.I Age distribution of patients with Behcet's disease

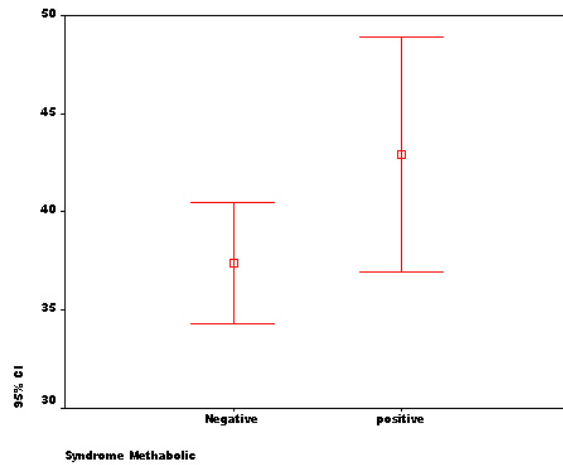


Figure.II Age distribution of patients with Behcet's disease with and without metabolic Syndrome

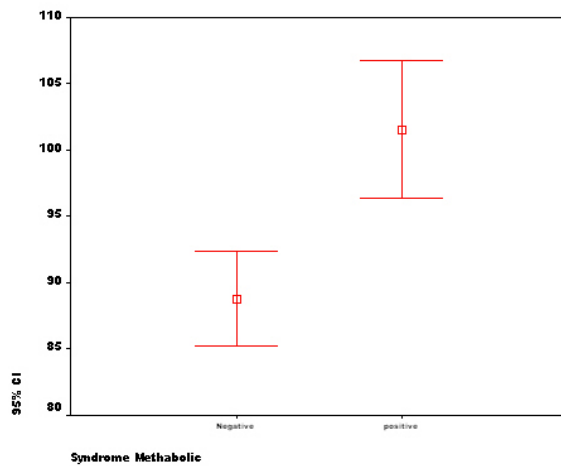


Figure.III Distribution of Waist circumference in Behcet's disease with and without metabolic Syndrome

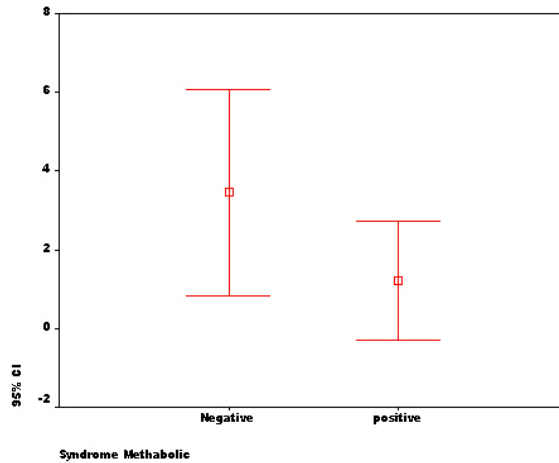


Figure.IV distribution of Ocular involvement score in Behcet's disease with and without metabolic Syndrome

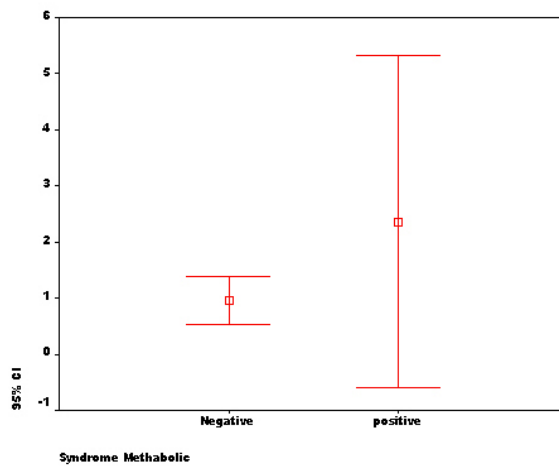


Figure.V Distribution of Non-Ocular involvement score in Behcet's disease with and without metabolic Syndrome

On the other hand, today more attention is paid to the role of obesity in the development of inflammation and the metabolic syndrome, which is especially caused by production of adipokine. Since patients with inflammatory rheumatic diseases have less physical activity compared to other people and since they use drugs such as glucocorticoids that cause

obesity, this problem is of greater significance (10).

In addition, a high level of hs-CRP can also be considered a risk factor to coronary vascular diseases. An evident increase in the outbreak of cardiovascular diseases with other rheumatic disease such as lupus, RA and psoriatic arthritis has been reported.

However, TNF- α , IL-6 and IL-1 play an important role in the pathogenesis of the Behcet's disease (11).

On the other hand, due to the severe potential involvements resulted from this disease, patients may need high dosages of glucocorticoids and cytotoxic drugs, which in turn theoretically increase the risk of development of the metabolic syndrome in such patients.

No comprehensive study has been so far conducted on the prevalence of the metabolic syndrome. An article was published in 2013 in Turkey by Talcin et al. The study was performed on 86 patients with the Behcet's disease in order to examine the prevalence of the metabolic syndrome in such patients. The prevalence of the metabolic syndrome in patients with the Behcet's disease and members of the control group was 35.4% and 20% respectively (with mean age of 39 ± 11 years) (12).

The prevalence of the metabolic syndrome in the patients under study in this research was 25.4%, which was lower than the figures reported by other studies conducted on rheumatic diseases such as RA (with prevalence of 39.2%) (13) and psoriasis (with prevalence of 35.4%) (12). However, in similar Iranian studies, the prevalence of this syndrome was reported to be between 30.1 and 32.1. In these studies, the prevalence of the metabolic syndrome in women was higher than men. Moreover, the prevalence was found to grow with an increase in age (14-15).

According to these studies, the prevalence of the metabolic syndrome in patients with the Behcet's disease was not higher than that of the ordinary people. Of course, this figure complies with the result of several studies

performed on ordinary people in the world (16-18). In the present study, no difference was observed between the genders and duration of disease and degree of development of the metabolic syndrome in patients with the Behcet's disease. These results do not comply with the results of studies that reported a higher prevalence of the metabolic syndrome in women and increase development of this syndrome with an increase in age (12, 19-20).

In this study, the prevalence of the metabolic syndrome in patients below 40 years and above 40 years was 17.24% and 34.6%, respectively. Although this disease was more common in patients above 40 years, no significant statistical difference was observed. The prevalence of the metabolic syndrome increases with an increase in age. This finding is in line with the findings of studies performed on the development of the metabolic syndrome in ordinary people (16-17).

No significant statistical difference was observed between most disease symptoms in assessing the patients by gender. Erythema Nodosum was more prevalent among women and was not present in patients without the metabolic syndrome. Neural involvement was only observed in a male patient. Interestingly, consumption of drugs, especially glucocorticoids did not increase the probability of development of the metabolic syndrome in the patients. It was perhaps caused by the proper control of inflammation and a reduction in cytokines. Abdominal circumference was the only metabolic syndrome parameter that was significant in patients with and without the metabolic syndrome.

According to information that presented concerning the relationship of inflammation and inflammatory cytokines with the

metabolic syndrome, it was assumed that in patients with ocular involvement or active diseases in other organs (except for the eyes), the metabolic syndrome was more prevalent. However, the results of this research did not reveal such a relationship.

On the other hand, no significant difference was observed between the ocular activity and extra-ocular activity in patients with or without the metabolic syndrome. This is perhaps immunomodulatory treatments were to some extent useful for minimizing the level of inflammatory cytokines such as TNF- α and IL-6. However, this was probably the case when the level of cytokines was measured. Valid electronic searches did not result in any study on the relationship of the metabolic syndrome and the activity of the Behcet's disease.

Due to the significance of the metabolic syndrome it is recommended to check the presence of the metabolic syndrome in patients with the Behcet's disease and inflammatory backgrounds by controlling lipids, blood sugar, weight and abdominal circumference on a regular basis and comparing the results with those of ordinary people. It is also recommended to provide accurate trainings to the patients and improve their life style to reduce vascular diseases including coronary vascular diseases.

Results of this study and other studies suggest that in patients with inflammatory diseases such as the Behcet's disease, RA, psoriasis and IBD, the prevalence of the metabolic syndrome is more than ordinary people. This calls for more attention and periodic screening of these patients to check them for cardiovascular diseases and diabetes.

Conclusion

A total of 41 male (74.5%) and 14 female (25.5%) patients were included in this study. The mean age of patients was 38.80 ± 10.18 years. A total of 14 patients (25.5%) under study were diagnosed with the metabolic syndrome. The prevalence of the metabolic syndrome in male and female patients with the Behcet's disease was 24.4% and 28.6%, respectively. Therefore, the prevalence of the metabolic syndrome in women was slightly higher than men. In this study, the prevalence of the metabolic syndrome in patients below and above 40 years old was 17.24% and 34.6%, respectively.

Therefore, the prevalence of the metabolic syndrome grows with an increase in age. Results of the present study and other studies suggest that in patients with inflammatory diseases such as the Behcet's disease, RA, psoriasis, and IBD, the prevalence of the metabolic syndrome is higher than ordinary people. This reflects the necessity of paying more attention and performing periodic screenings to check these patients with cardiovascular diseases and diabetes.

Suggestions

Considering the findings of this research it is recommended to reduce morbidity and mortality among these patients by using medical treatments and paying more attention to the physical activity, calorie intake and reduction in the weight of these patients.

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