Clinical presentations of Behcet's Disease in Upper Egypt

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Abstract

Background: Behçet's disease (BD) is an idiopathic, chronic, relapsing, multi-systemic vasculitis characterized by recurrent oral and genital aphthous ulcers, ocular disease and skin lesions.
Objectives: The purpose of this study was to investigate the clinical features of Behcet's Disease in Upper Egypt.
Patients and Methods: This study is a prospective observational study that conducted during the period extended from December 2017 to September 2018 in the Rheumatology Department of Sohag University Hospital. A total of 50 patient diagnosed as Behcet was included in the study.
Results: The results of this study cleared that, the higher symptoms were oral ulcer 50 (100 %), followed by genital ulcer 44 (88 %), the skin lesions appeared in 40 (80 %) and ocular lesions appeared in 34 (68 %).Meanwhile, the vascular lesions appeared in 13 (26 %) and neurological manifestations occur in 5 (10%).
Conclusion: The study concluded that, the BD is a serious disease affecting human and take many forms that includes oral, genital ulcer , skin and ocular lesions which are the predominant forms in Upper Egypt while, the vascular and neurological forms are of lower incidence.

Keywords: Behçet's disease; Clinical features; Upper Egypt.
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Introduction

Bechet's disease (BD) is considered a relatively rare disease that causes recurrent oral and genital ulcers in addition to a variety of systemic manifestations.

It characterized by manifestations such as, arterial aneurysms, mucocutaneous lesions, venous thrombosis, arthritis, central nervous system (CNS) lesions, intestinal ulcers, and pulmonary lesions **(Gul, 2005)**, Meanwhile Behçet's disease (BD) is a chronic inflammatory disease in which cardiovascular involvement has been found to range between 7% and 46% **(Gürgün et al., 2002)**.The clinical manifestations in BD are variable and characterized by unpredictable periods of recurrences and remissions, although the frequency and severity tend to abate with time **(Nair and Moots, 2017)**.

The mucocutaneous lesions are considered the main presentation of BD. The incidence of oral ulcers is 98%, the diagnosis by criteria of BD published by the ISGBD **(ISGBD, 1990)** needs the presence of oral ulcers. The tongue, buccal, pharyngeal and labial mucosal membranes are the most common site for oral aphthae. Being rounded, sharp, erythematous and elevated border with a diameter of 1 to 3 cm are the most characteristic shape **(Hamuryudan et al., 2012)**.

Genital aphthae have an incidence rate of 60% and is most likely occur with BD. The most common sites are scrotum in men and vulva and vagina in women, genital ulcers is similar to oral ulcers but differ in size and deepness being larger and deeper **(Kaneko et al., 2014)**. Other skin lesions are erythema nodosum, pseudofolliculitis, papulo-pustular lesions, and acneiform eruptions **(Yazici et al., 2018)**.

Eye involvement has an incidence rate of 70% and it is debilitating. If eye affection occur, blindness may occur in 25% of patients even if they was received treatment, although the use of immunosuppressant therapy improving the prognosis **(Ksiaa et al., 2019)**. Chronic relapsing bilateral non-granulomatous uveitis is the main ocular presentation which affects the anterior segment, the posterior segment or both (panuveitis) **(Tugal-Tutkun et al., 2017)**. Eye manifestations may occur in the form of cataract, glaucoma, as well as posterior segment involvement with vitritis, retinitis, and retinal detachment **(Accorinti et al., 2017; Ksiaa et al., 2019)**.

The cardiovascular manifestations are characterized by arterial and venous affection, and the incidence of venous involvement is 30% which is more than arterial lesions which is 5%. **(Saadoun et al., 2012)**.

The occurrence is not accurate as autopsy studies showed about 33% of patients had arterial lesions in 33%, and is asymptomatic **(Calamia et al., 2011)**. Cardiac involvement includes pericarditis, myocarditis, and endocarditis **(Geri et al., 2012)**. Aneurysms and/or thrombosis of the coronary arteries are observed complicated by hemorrhage, myocardial infarction and sudden death **(Seyahi, 2019)**.

The articular involvement occurs in 45-60 % of patients and includes arthralgia, monoarthritis or polyarthritis **(Ait Badi et al., 2008)**. Non-erosive, non-deforming oligoarthralgia commonly involving the knees, ankles, elbows, and wrists is the most frequent manifestation **(Mendes et al., 2009)**. Destructive changes rarely occur in patients with articular involvement **(Kaklamani et al., 1998)**.

While the Neurological manifestations are detected in 20 to 40% of cases **(Al-Araji and Kidd, 2009)**. Parenchymal and non-parenchymal lesions (i.e. cerebral venous thrombosis or arterial aneurism) lesions are forms of CNS affection in BD **(Saip et al., 2014)**. Parenchymal lesions (Neuro-BD) Occur in the form of headache, meningitis or meningoencephalitis, hemiplegia, or cranial nerve palsies which have acute onset **(Caruso and Moretti, 2018)**. Patients may develop Psychiatric manifestations including personality changes **(Uygunoglu and Siva, 2018)**.

Bechet's disease and intestinal inflammatory diseases cannot be differentiated easily. This perhaps gives a reason for the frequency difference, that fluctuates from 1 to 30% **(Hatemi et al., 2018b)**. Gastrointestinal involvement in patients with BD manifested by nausea, abdominal pain, and diarrhea, which may contain blood and perforation sometimes may occur **(Skef et al., 2015)**. The ileocecal region is the most commonly affected part of the gastrointestinal tract **(Kim and Cheon, 2016)**.

Patients and methods

Study design: This study is a prospective observational study.

Setting: This study was conducted from December 2017 to September 2018 in Rheumatology Department, Sohag University Hospital. A total of 50 patient diagnosed as Behcet was included in the study.

Inclusion criteria

- Patients diagnosed as Behcet according to 2006 classification criteria (ICBD ,.2006)
- Age (17-40) years
- Patients with disease duration more than 6 months

Exclusion criteria:

- Patients with concomitant systemic diseases such as, chronic obstructive lung disease, coronary artery disease, cancer, thyroid function disorder, hematological disorders, acute or chronic liver and renal diseases.
- Other autoimmune disease including rheumatoid arthiritis, systemic lupus erythromatosis, scleroderma, mixed connective tissue disease and polymyositis.
- Patients using contraceptive pills.

Patients with Metabolic diseases including Systemic hypertension, Hyperlipidemia, Obesity and Diabetes mellitus.

History of smoking

Methods

All patients and control cases were be subjected to the following:

- Full medical history from the patients, with the clinical examination including:
- General examination and vital signs
- Complete rheumatological examination
- Ophthalmological examination
- Dermatological examination
- Neurological examination
- Routine investigations (complete blood picture, erythrocyte sedimentation rate, liver functions and kidney functions)

Ethical considerations

Ethical approval was taken from Medical Research Ethics committee of Faculty of Medicine, Sohag University. An written informed consent was taken from all participants in the study after explaining the aim, benefits and risks of the study.

Statistical analysis

The statistical analysis was made using Statistical package for social sciences (IBM-SPSS), version 24 (May 2016); IBM- Chicago, USA will be used for statistical data analysis. Chi square test will be used to compare percentages of qualitative variables, and Fisher exact test will be used in stead of ordinary chi square test in cases of non parametric data.

Results

Clinical features of studied population

Table (1) and (**Fig.1**) cleared that, the clinical features of studied population that suffering from Behcet's disease was different among population.

The higher symptoms was oral ulcer 50 (100 %), followed by genital ulcer 44 (88 %) and ocular lesions appeared in 34 (68 %).

Meanwhile, the skin lesions appeared in 40 (80 %), and the vascular lesions appeared in 13 (26 %) and neurological manifestations occur in 5 (10%).

Table 1. Clinical features of studied population

Variable	Number (%)
Oral ulcer	50 (100%)
Genital ulcer	44 (88%)
Ocular lesion	34 (68%)
Skin lesion	40 (80%)
Neurological lesion	5 (10%)
Vascular lesion	13 (26 %)

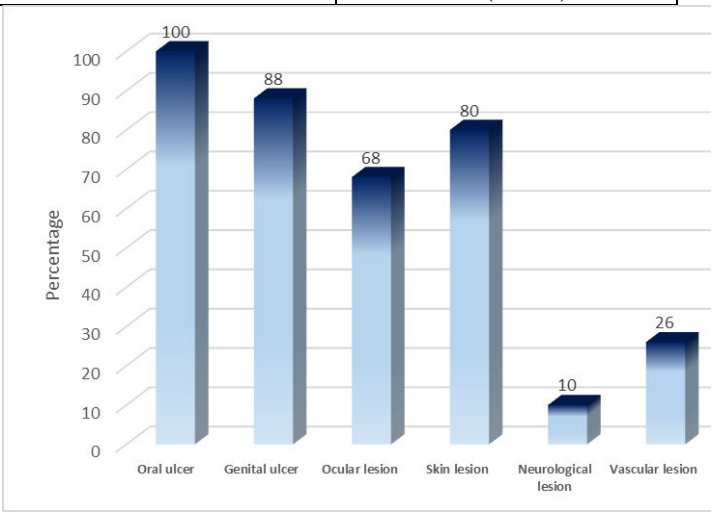

Fig.1. Clinical features of studied population

Patterns of BD

a- Oral pattern:

Table (2) cleared that, the number of patients suffering from oral pattern of Behcet's disease that take the form of ulcerations of oral cavity were 50

(100 %) of the examined patients. The tongue, buccal, pharyngeal and labial mucosal membranes are the most common site for oral aphthae. Being rounded, sharp, erythematous and elevated border

Table 2. Number of patients suffering from oral pattern of Behcet's disease.

Variable	Number (%)
Oral ulcer	50 (100%)

b- Genital pattern

Table (3) cleared that, the number of patients suffering from genital lesions of Behcet's disease were 44 (88 %). genital ulcers is similar to oral ulcers but differ in size and deepness being larger and deeper

The most common sites are scrotum in men and vulva and vagina in women**.**

Table 3. Number of patients suffering from genital pattern of Behcet's disease.

Variable	Number (%)
Genital ulcer	
No	6 (12%)
Yes	44 (88%)

c-Ocular pattern

Table (4) cleared that, the number of patients suffering from ocular lesions of Behcet's disease were 34 (68 %).

The ocular lesions differ according to the site of infection as it reached to 3 (6 %) Hypopyon &post uveitis, 2 (4 %) in Panuveitis, in IIOP 1 (2 %), Redness &blurring vision 2 (4 %), Retinal detachment 1 (2 %), Retinal fibrosis 1 (2 %), Retinal vascular occlusion 1 (2 %), Retinal vasculitis 1 (2 %),retinitis 1 (2%) and vitritis 4 (8%).

Table 4. Number and sites of lesions in patients suffering from genital pattern of Behcet's disease.

Variable	Number (%)
Ocular lesion	
No	16 (32 %)
Post uveitis	17 (34%)
Hypopyon &post uveitis	3 (6%)
	2 (4%)
Panuveitis	1 (2%)
IIOP	2 (4%)
Redness &blurring vision	1 (2%)
	1 (2%)
Retinal detachment	1 (2%)
Retinal fibrosis	1 (2%)
Retinal vascular occlusion	1 (2%)
Retinal vasculitis	4 (8%)
Retinitis	
Vitritis	

d-Skin pattern

Table (5) cleared that, the number of patients suffering from skin lesions of Behcet's disease were 40 (80 %). Skin lesions were in the form of erythema nodosum, pseudofolliculitis, papulo-pustular lesions, and acneiform eruptions.

Table 5. Number of patients suffering from skin pattern of Behcet's disease.

Variable	Number (%)
Skin lesion	
No	10 (20%)
Yes	40 80%)

e-Neurological pattern

Table (6) cleared that, the number of patients suffering from neurological pattern of Behcet's disease were 5 (10 %).

The neurological lesions taked the form of hemiplegia 3 (6 %), paraplegia 1 (2 %) and Transverse myelitis & encephalitis 1 (2 %).

Table 6. Number of patients suffering from neurological pattern of Behcet's disease.

Variable	Number (%)
Neurological lesion	
No	45 (90%)
Hemiplegia	3 (6%)
Paraplegia	1 (2%)
Transverse myelitis & encephalitis	1 (2%)

f-Vascular pattern

Table (7) cleared that, the number of patients suffering from vascular lesions of Behcet's disease were 13 (26 %).

The vascular lesions observed in DVT leg unilateral 3 (6 %), DVT on both L.L 1 (2 %), DVT recurrent 2 (4 %), DVT & atrial thrombosis 1 (2 %), DVT & pulmonary embolism 1 (2 %), S.V.C thrombosis 1 (2 %), Cerebral infarction 1 (2 %), Post vasculitis lesions 1 (2 %) and Recurrent stroke 2 (4 %).

Table 7. Number of patients suffering from vascular pattern of Behcet's disease.

Variable	Number (%)
Vascular lesion	
No	37 (74%)

DVT leg unilateral	3 (6%)
DVT on both L.L	1 (2%)
DVT recurrent	2 (4%)
DVT & atrial thrombosis	1 (2%)
DVT & pulmonary embolism	1 (2%)
S.V.C thrombosis	1 (2%)
Cerebral infarction	1 (2%)
Post vasculitis lesions	2 (4%)
Recurrent stroke	

discussion

Behçet's Disease can be considered as a chronic systemic inflammatory disease with an unknown etiology; characterized by manifestations such as mucocutaneous lesions, arterial aneurysms, venous thrombosis, arthritis, intestinal ulcers, central nervous system (CNS) lesions, and pulmonary lesions **(Gul, 2005)**.

This study targeted to investigate the clinical presentations of Behçet's Disease in upper Egypt.

Meanwhile, our results on the clinical features of studied population cleared that, the higher symptoms were oral ulcer 50 (100 %), followed by genital ulcer 44 (88 %) and ocular lesions appeared in 34 (68 %).

Meanwhile, the skin lesions appeared in 40 (80 %), and the vascular lesions appeared in 13 (26 %) and neurological manifestations occur in 5 (10%).

This results agreed with those of **(Koca et al., 2017)** where they reported that, Behçet's disease (BD) is a chronic inflammatory disease relapsing in character with mucocutaneous lesions, and it can affect neurological, ocular, and gastrointestinal systems. BD has been described as a triple symptom complex, i.e., oral aphthosis, genital ulcer, and uveitis. BD has a greater incidence and prevalence in the regions along the ancient Silk Road **(Verity et al., 1999 and Pineton de Chambrun et al., 2012).** As regards the disease prevalence in Egypt, **In a study of Gheita, (Gheita TA et al. 2019),** they evaluated the prevalence of adult Behçet's disease (BD) in adult Egyptian and studied the clinical pattern and influence of age at-onset and sex on disease phenotype, they provided that the current prevalence of BD in Egypt; 3.6/100,000 with no remarkable north-to-south gradient.

In a study of Abu Al-Fadl **(Abu Al-Fadl EM et al. 2019),** they studied the pattern of Behcet's disease among patients attending the Rheumatology and Rehabilitation department, Sohag University, It was found that the most common first manifestation in our study group was oral ulcers, followed by ocular manifestations, then CNS manifestations, articular or vascular manifestations and lastly genital ulcer or skin manifestations**.**

Meanwhile, our results on the patterns of BD cleared that, the number of patients suffering from oral pattern of Behcet's disease that take the form of ulceration of oral cavity were 50 (100 %) of the examined patients.

While, the genital pattern cleared that, the number of patients suffering from genital form of Behcet's disease were 44 (88 %) of the examined patients. While, the ocular pattern cleared that, the number of patients suffering from ocular form of Behcet's disease were 34 (68 %) of the examined patients.

Also, the ocular lesions differ according to the site of infection as it reached to 3 (6 %) Hypopyon &post uveitis, 2 (4 %) in Panuveitis, in IIOP 1 (2 %), redness &blurring vision 2 (4 %), Retinal detachment 1 (2 %), Retinal fibrosis 1 (2 %), Retinal vascular occlusion 1 (2 %), Retinal vasculitis 1 (2 %),retinitis 1 (2%) and vitritis 4 (8%).

In a study of **Hussien et al. (2018)**, they examined and spotted systemic findings commonly associated with a severe form of ocular Behcet's disease in 249 patients, ocular affection was found in (127 patients) of all patients were found to have some form of ocular involvement by the disease. Of these, 59% anterior uveitis, 74.8% posterior uveitis, and 33.8% from panuveitis. Also, 54.3% of these patients manifested by retinitis, 46.4% vitritis, 66.9% chorioretinitis, 31.4% retinal vasculitis, 7.8% papillitis, 9.4% macular edema, and 7.8% secondary retinal detachment.

In our study, the skin pattern of BD observed in 40 (80 %) of the examined patients. While, the neurological pattern of Behcet's disease was 5 (10 %) of the examined patients. Also, the neurological lesions observed take the form of hemiplegia 3 (6 %), paraplegia 1 (2 %) and Transverse myelitis & encephalitis 1 (2 %).

Meanwhile our results on the vascular pattern cleared that, the number of patients suffering from

vascular form of Behcet's disease were 13 (26 %) of the examined patients, the vascular lesions observed in DVT leg unilateral, DVT on both L.L , DVT recurrent, DVT & atrial thrombosis, DVT & pulmonary embolism, S.V.C thrombosis, Cerebral infarction, Post vasculitis lesions and Recurrent stroke.

This results agreed with those of **(El Menyawi et al.(2009)** where they reported that, ulcers occur in 39.7% in patients with BD in Egypt , orogenital ulcers and deep venous thrombosis occur also but with lower incidence. During the study period, oral ulcers are the commonest manifestations of BD which occur in (100%) of cases, followed by genital ulcers , vascular lesions, cutaneous , ocular , joint , neurological , gastrointestinal and cardiac lesions with an incidence rate (96.8%, 57.1%, 55.5%, 47.6%,36.5%,34.9%,19%,6.3%) respectably. Male affected more than females in Egypt. Vascular and neurological manifestations have high incidence rate in Egypt. Also, they found that venous lesions were 94.6% of vascular Behcet and mostly were deep venous thrombosis. Arterial lesions were less common as it was 16.6% of patients with vascular Behcet. Pulmonary artery aneurysm occurred in 8.3%. While the neurological lesion was brain stem of 27.2% of neurological manifestations, followed by benign intracranial hypertension and hemisphere disturbance, each presented 22.7% of neurological study involvement.

Also, **Elzanaty et al. (2020)** concluded that, Cardiovascular manifestations can be the initial presentation of BD, and the early clinical recognition of BD as a cause of DCM and SVC thrombosis.

Conclusion

Our results concluded that, the BD is a serious disease affecting human and take many forms that includes oral, genital ulcer , skin lesions and ocular lesions which are the predominant forms in upper Egypt while, the vascular and neurological forms are of lower incidences.

References

- **Abu Al-Fadl EM, Al-Aga AR, Ali GM. (2019).** Pattern of Behcet's Disease in Sohag Governorate. Sohag Medical Journal, 23(2): 6-17.
- **Accorinti M, Pesci FR, Pirraglia MP, Abicca I and Pivetti-Pezzi P .(2017).** Ocular Behcet's Disease: Changing Patterns Over Time, Complications and Long-Term Visual Prognosis. Ocul Immunol Inflamm, 25 (1)**:** 29-36.
- **Ait Badi MA, Zyani M, Kaddouri S, Niamane R, Hda A , Algayres JP. (2008).** [Skeletal manifestations in Behcet's disease. A report of 79 cases]. Rev Med Interne,29 (4)**:** 277-82.
- **Al-Araji A , Kidd DP .(2009).** Neuro-Behcet's disease: epidemiology, clinical characteristics, and management. Lancet Neurol, 8 (2)**:** 192-204.
- **Calamia KT, Schirmer M and Melikoglu M . (2011).** Major vessel involvement in Behcet's disease: an update. Curr Opin Rheumatol,23 (1)**:** 24-31.
- **Caruso P , Moretti R. (2018).** Focus on neuro-Behcet's disease: A review. Neurol India, 66 (6)**:** 1619-28.
- **El Menyawi MM, Raslan HM, Edrees A.(2009**). Clinical features of Behcet's disease in Egypt. Rheumatol Int, 29(6):641-6.
- **Elzanaty AM, Awad MT, Acharaya A, Sabbagh E, Elsheikh E, AbdAlamir M.(2020**). Superior vena cava thrombosis and dilated cardiomyopathy as initial presentations of Behcet's disease. Thromb J,6;18:12.
- **Geri G, Wechsler B, Thi Huong du L, Isnard R, Piette JC, Amoura Z, Resche-Rigon M, Cacoub P and Saadoun D. (2012).** Spectrum of cardiac lesions in Behcet disease: a series of 52 patients and review of the literature. Medicine (Baltimore),91 (1)**:** 25-34.
- **Gul A. (2012).** Behcet's disease as an autoinflammatory disorder. Curr Drug Targets Inflamm Allergy, 4 (1)**:** 81-3.
- **Gürgün C, Ercan E, Ceyhan C, Yavuzgil O, Zoghi M, Aksu K, et al. (2002).** Cardiovascular involvement in Behcet's disease. Jpn Heart J ,43:389–98.
- **Gheita TA, El-Latif EA, El-Gazzar II, Samy N, Hammam N, Abdel Noor RA, et al. (2019).**Behçet's disease in Egypt: a multicenter nationwide study on 1526 adult patients and review of the literature. Clin Rheumatol,38(9):2565-2575.

- **Hamuryudan V, Hatemi G, Sut N, Ugurlu S, Yurdakul S and Yazici H (2012):** Frequent oral ulceration during early disease may predict a severe disease course in males with Behcet's syndrome. Clin Exp Rheumatol.; 30 (3 Suppl 72)**:** S32-4.
- **Hatemi G, Christensen R, Bang D, Bodaghi B, Celik AF, Fortune F, Gaudric J, Gul A, Kotter I, Leccese P (2018):** 2018 update of the EULAR recommendations for the management of Behcet's syndrome. Ann Rheum Dis.; 77 (6)**:** 808-18.
- **Hussein MA, Eissa IM, Dahab AA.** Vision-Threatening Behcet's Disease: Severity of Ocular Involvement Predictors. J Ophthalmol. 2018 Apr 26;2018:9518065.
- **ISGBD (1990):** Criteria for diagnosis of Behcet's disease. International Study Group for Behcet's Disease. Lancet.; 335 (8697)**:** 1078-80.
- **Kaklamani VG, Vaiopoulos G and Kaklamanis PG(1998):** Behcet's Disease. Semin Arthritis Rheum.; 27 (4)**:** 197-217.
- **Kaneko F, Togashi A, Nomura E and Nakamura K (2014):** A New Diagnostic Way for Behcet's Disease: Skin Prick with Self-Saliva. Genet Res Int. 2014;**:** 581468.
- **Kim DH and Cheon JH (2016):** Intestinal Behcet's Disease: A True Inflammatory Bowel Disease or Merely an Intestinal Complication of Systemic Vasculitis? Yonsei Med J.; 57 (1)**:** 22-32.
- **Koca SS, Kara M, Özgen M**, **et al** (**2017**):. Low prevalence of obesity in Behçet's disease is associated with high obestatin level. *Eur J Rheumatol*.;4(2):113-117. doi:10.5152/eurjrheum.2017.160095
- **Ksiaa I, Abroug N, Kechida M, Zina S, Jelliti B, Khochtali S, Attia S and Khairallah M (2019):** Eye and Behcet's disease. J Fr Ophtalmol.; 42 (4)**:** e133-e46.
- **Mendes D, Correia M, Barbedo M, Vaio T, Mota M, Goncalves O and Valente J (2009):** Behcet's disease--a contemporary review. J Autoimmun.; 32 (3-4)**:** 178-88.
- **Nair JR and Moots RJ (2017):** Behcet's disease. Clin Med (Lond).; 17 (1)**:** 71-7.
- **Pineton de Chambrun M, Wechsler B, Geri G, Cacoub P, Saadoun D (2012):**. New insights into the pathogenesis of Behçet's disease. Autoimmun Rev. ;11:687–98.
- **Saadoun D, Asli B, Wechsler B, Houman H, Geri G, Desseaux K, Piette JC, Huong du LT, Amoura Z, Salem TB (2012):** Long-term outcome of arterial lesions in Behcet disease: a series of 101 patients. Medicine (Baltimore).; 91 (1)**:** 18-24.
- **Saip S, Akman-Demir G and Siva A (2014):** Neuro-Behcet syndrome. Handb Clin Neurol.; 121**:** 1703-23.
- **Seyahi E (2019):** Phenotypes in Behcet's syndrome. Intern Emerg Med.; 14 (5)**:** 677-89.
- **Skef W, Hamilton MJ and Arayssi T(2015):** Gastrointestinal Behcet's disease: a review. World J Gastroenterol.; 21 (13)**:** 3801-12.
- **Tugal-Tutkun I, Ozdal PC, Oray M and Onal S (2017) :** Review for Diagnostics of the Year: Multimodal Imaging in Behcet Uveitis. Ocul Immunol Inflamm.; 25 (1)**:** 7-19.
- **Uygunoglu U and Siva A (2018):** Behcet's Syndrome and Nervous System Involvement. Curr Neurol Neurosci Rep.; 18 (7)**:** 35.
- **Verity DH, Marr JE, Ohno S, Wallace GR and Stanford MR (1999):** Behcet's disease, the Silk Road and HLA-B51: historical and geographical perspectives. Tissue Antigens.; 54 (3)**:** 213-20.
- **Yazici H, Seyahi E, Hatemi G and Yazici Y (2018):** Behcet syndrome: a contemporary view. Nat Rev Rheumatol.; 14 (2)**:** 119.