Modern Rheumatology, **00**, 2022, 1–5
DOI: https://doi.org/10.1093/mr/roac044
Advance Access Publication Date: 10 May 2022
Original Article

Cluster analysis of paediatric Behçet's disease: Data from The Pediatric Rheumatology Academy-Research Group

Ferhat Demir[a,*,†], Hafize Emine Sönmez[b,†], Esra Bağlan[c], Özlem Akgün[d], Taner Coşkuner[e], Gülçin Otar Yener[f], Kübra Öztürk[g], Mustafa Çakan[e], Şerife G. Karadağ[h], Semanur Özdel[c], Nuray Aktay Ayaz[d] and Betul Sözeri[e], The Pediatric Rheumatology Academy (PeRA)-Research Group (RG)

[a]Department of Pediatric Rheumatology, Acıbadem Healthcare Group, Yurtcan Sokağl No:1, 34662, Üsküdar/İstanbul 34662, Turkey
[b]Department of Pediatric Rheumatology, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey
[c]Department of Pediatric Rheumatology, University of Health Sciences, Sami Ulus Maternity and Children's Diseases Training and Research Hospital, Ankara, Turkey
[d]Department of Pediatric Rheumatology, Faculty of Medicine, Istanbul University, Istanbul, Turkey
[e]Department of Pediatric Rheumatology, University of Health Sciences, Ümraniye Training and Research Hospital, Istanbul, Turkey
[f]Department of Pediatric Rheumatology,Şanlıurfa Training and Research Hospital,Şanlıurfa, Turkey
[g]Department of Pediatric Rheumatology, Istanbul Medeniyet University, Göztepe Prof. Dr. Süleyman Yalçın City Hospital, Istanbul, Turkey
[h]Department of Pediatric Rheumatology, Erzurum Regional Research and Training Hospital, Erzurum, Turkey

[†]These authors contributed equally to this work.
*Correspondence: Ferhat Demir; drferhat@outlook.com; Department of Pediatric Rheumatology, Acıbadem Healthcare Group, Yurtcan Sokağl No:1, Üsküdar/İstanbul 34662, Turkey.

ABSTRACT

Objectives: Behçet's disease (BD) is a systemic vasculitis affecting many organ systems, with the involvement of all-sized arteries and veins. The study aims to determine the main characteristics of paediatric BD patients and also analyse the clustering phenotypes.

Methods: Demographic data, clinical manifestations, laboratory features, treatment schedules, and disease outcomes were achieved from patients' charts retrospectively. A cluster analysis was performed according to the phenotype.

Results: A total of 225 (109 male/116 female) patients with BD were enrolled in the study. The median ages of disease onset and diagnosis were 131 (36–151) and 156 (36–192) months, respectively. According to cluster analysis, 132 (58.6%) patients belonged to the mucocutaneous-only cluster (C1), while 35 (15.6%) patients fitted to articular type (C2), 25 (11.1%) were in the ocular cluster (C3), 26 (11.6%) were in the vascular cluster (C4), and 7(3.1%) belonged to the gastrointestinal cluster (C5). Ocular and vascular clusters were more common in boys ($p < .001$), while girls usually presented with the mucocutaneous-only cluster. The disease activity at the diagnosis and the last control was higher in ocular, vascular, and gastrointestinal clusters.

Conclusions: These identified juvenile BD clusters express different phenotypes with different outcomes Our analysis may help clinicians to identify the disease subtypes accurately and to arrange personalized treatment.

KEYWORDS: Juvenile Behçet's disease; cluster analysis; Behçet's disease

Introduction

Behçet's disease (BD) is a systemic vasculitis affecting many organ systems by the involvement of all-sized arteries and veins [1]. Recurrent oral aphthous and cutaneous lesions are the predominant features during the disease course. However, diverse manifestations of gastrointestinal (GI), ocular, neurologic, cardiovascular, and musculoskeletal involvement may be observed [2]. Albeit the peak age of the disease onset is between the second and fourth decades of life, it is well known that paediatric BD (PEDBD) patients account for 5–15% of all BD cases [2].

Patients with BD present with heterogeneous clinical manifestations varying according to genders, ethnicities, and geographic regions. For instance, GI involvement is widespread in Asians, while the vascular disease is more predominant in patients from the Middle East and the eastern Mediterranean region [3]. Different phenotypic clusters have attracted the attention of adult rheumatologists in terms of organizing the individualized management of patients with BD. While subgroups of the disease are defined in adult BD patients, studies concerning cluster analysis in PEDBD patients are limited. Recently, in a review written by Sag *et al*. [4], five clusters for PEDBD were suggested: (1) mucocutaneous-only cluster, (2) papulopustular lesion–arthritis–enthesopathy cluster, (3) ocular cluster, (4) GI cluster, and (5) vascular cluster. Nevertheless, there is only one study

Received 4 March 2022; Accepted 3 May 2022
© Japan College of Rheumatology 2022. Published by Oxford University Press. All rights reserved.
For permissions, please e-mail: journals.permissions@oup.com

Downloaded from https://academic.oup.com/mr/advance-article/doi/10.1093/mr/roac044/6582903 by Istanbul University Library user on 20 June 2022

focusing on cluster analysis in juvenile BD patients [5]. Zou *et al.* [5] evaluated 69 patients with juvenile BD, and they identified three clusters (C): C1 with mucocutaneous type; C2 with GI type; and C3 with a mixture of uveitis, vascular, and central nervous system involvement.

Herein, we aimed to identify the baseline characteristics of PEDBD patients and also to analyse the clustering phenotype of PEDBD in a large multicentre cohort.

Materials and methods

This is a retrospective observational study that was conducted by eight paediatric rheumatology centres in Turkey. The study protocol was reviewed and approved by the Ethics Committee of the University of Health Sciences, Ümraniye Training and Research Hospital (Approval no. B.10.1.TKH.4.34.H.GP.0.01/251) with the ethical principles laid down in the Declaration of Helsinki.

We included the patients fulfilling at least one of the following classification criteria: (1) the International Study Group criteria (ISG), (2) the Japan revised criteria, and (3) the PEDBD classification criteria [6–8]. The files of children with BD diagnosed between 2015 and 2020 were reviewed retrospectively. Demographic data, clinical manifestations, laboratory features, treatment schedules, and disease outcomes were recorded from patient charts.

The disease activity was assessed by the Iranian BD dynamic activity measure (IBDDAM) [9] and by the physician global assessment (PGA) scale. Patients who were followed for <1 year were excluded from the study.

Statistical analysis

The SPSS version 21.0 (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. The variables were investigated using visual (histogram or probability plots) and analytic methods (Kolmogorov–Smirnov/Shapiro–Wilk test) to determine whether or not they were normally distributed. Descriptive analyses were presented using proportion, mean, SD median, and range (*R*) whichever were appropriate. Cluster analysis was performed by using the two-step cluster analysis method. Initially, variables were selected such as continuous or categorical. The current age, age at disease onset, duration of disease, IBDDAM, and PGA were the continuous variables, while gender, clinical manifestations, major organ involvement, and classification criteria were the categorical variables.

Results

Baseline characteristics of the patients

A total of 225 patients with BD were enrolled in the study. Among them, 109 (48.4%) were male, and 116 (51.6%) were female. Seventy-seven (34.2%) patients had a family history of BD. The median ages of disease onset and diagnosis were 131 (36–151) and 156 (36–192) months, respectively. The median time between the onset of symptoms and diagnosis was 23.5 (0–45) months.

Oral aphthous ulcers (81.7%) were the most common initial symptom. During the course of the disease oral ulcers were also the most frequent symptom (99.1%) followed by genital ulcers (70.2%) and pseudofolliculitis (35.6%). Forty-one (18.2%) patients had a history of erythema nodosum. Uveitis was observed in 34 (15.1%) patients. Of these 34 patients, 14 had anterior uveitis, 14 had panuveitis, and 6 had posterior uveitis. Retinal vasculitis was observed in seven (3.1%) patients. Of 26 (11.6%) patients presented with vascular involvement, 26 patients had venous thrombosis, and 1 patient had additional arterial thrombosis. Thirty-two (14.2%) patients had neurological involvement. Among these 32 patients, 26 had non-parenchymal involvement, 5 had parenchymal involvement, and 1 had both parenchymal and non-parenchymal involvement. Eight (3.6%) patients had GI involvement. Arthralgia was reported in 119 (52.9%) patients, and arthritis was detected in 41 (18.2%) patients. Pathergy test was positive in 63 (28%) patients, and Human Leukocyte Antigen (HLA)-B51 was positive in 100 (44.4%) patients.

Of 225 patients, 137 (60.9%) fulfilled the ISG and 142 (63.1%) satisfied the PEDBD classification criteria. Forty-nine (21.8%) patients completely met the Japan revised criteria, while 133 (59.1%) were classified as incomplete BD according to the Japan revised criteria.

Treatments and outcomes

Almost all ($n = 217$, 96.4%) were receiving colchicine, and 54 (24%) patients were using azathioprine, concomitantly. Five (2.2%) patients were treated with cyclophosphamide. Seven patients, of whom five with uveitis, one with GI involvement, and one with neurologic involvement, were on biological drugs. Eleven (4.8%) patients received corticosteroids.

At the time of diagnosis, the median IBDDAM and PGA scores were 4 (1–24) and 5 (2–9), respectively. At the last visit, both IBDDAM (1 [1–10]) and PGA scores (1 [1–5]) decreased significantly ($p < .001$). At the time of enrolment, 208 (92.4%) patients had inactive disease, while 15 (6.7%) had partial response and two (0.9%) still had active disease.

Cluster analysis

According to the two-step cluster analysis, five clusters had been identified with distinct features (Figure 1). The first cluster (C1) ($n = 132$, 58.6%) had female predominance with

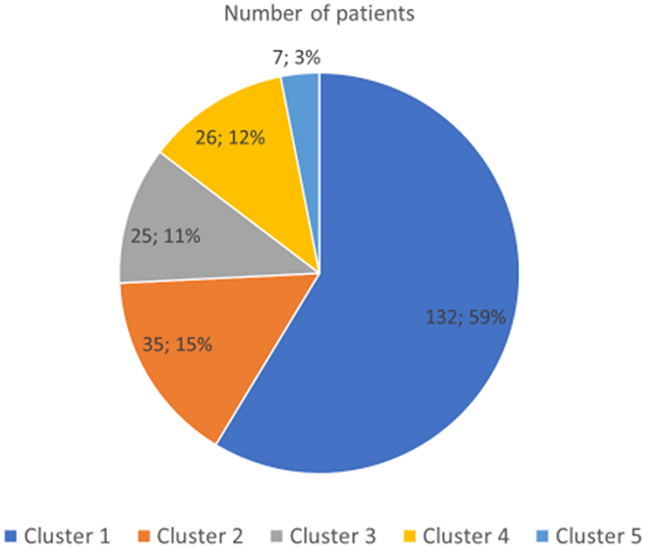


Figure 1. Distribution of clusters in PEDBD.

Downloaded from https://academic.oup.com/mr/advance-article/doi/10.1093/mr/roac044/6582903 by Istanbul University Library user on 20 June 2022

Table 1. Characteristics of the patients according to clusters (C).

	C1 ($n=132$)	C2 ($n=35$)	C3 ($n=25$)	C4 ($n=26$)	C5 ($n=7$)
Family history of BD, *n*	53	12	6	3	3
Clinical features, *n*					
Oral aphthous	132	35	25	24	7
Genital ulcers	100	25	15	13	5
Papulopustular lesions	48	13	10	7	2
Erythema nodosum	23	7	4	5	2
Arthritis	0	35	3	3	0
Uveitis	0	0	25	9	0
GI involvement	0	0	1	0	7
Vascular involvement	0	0	0	26	0
Neurologic involvement	0	4	3	23	2
Laboratory features, *n*					
Positive pathergy test	39	9	9	6	0
HLA-B51 positivity	62	11	13	11	3
Disease activity assessment, median					
IBDDAM, at diagnosis	4	4	5.5	6	10
PGA, at diagnosis	4	4	7	5.5	8
Classification criteria, *n*					
ISG	80	24	17	13	3
PEDBD	85	20	18	16	3
Japan revised criteria					
Complete	26	5	11	6	1
Incomplete	78	23	12	16	4
Treatment, *n*					
Colchicine	129	33	24	25	6
Azathioprine	10	7	9	25	3
Cyclophosphamide	0	0	0	3	2
Biologic drugs	0	0	5	1	1
Outcomes, *n*					
Inactive disease	130	34	18	22	4
Partial response	1	1	6	4	3
Active disease	1	0	1	0	0

mucocutaneous features. In this cluster, the median age at diagnosis was 147 months. All patients had oral ulcers, 100 had genital ulcers, 48 patients had papulopustular lesions, and 23 had erythema nodosum. None of the patients had major organ involvement (Table 1).

Thirty-five (15.6%) patients fitted to C2 with a median age of disease onset of 164 months. In this cluster, joint involvement was predominant. While joint involvement was present in all patients, 22 patients had enthesitis. Thirteen patients had papulopustular lesions and seven had erythema nodosum. Four patients had major organ involvement (Table 1).

Twenty-five (11.1%) patients fitted the ocular cluster (C3). The median age at the diagnosis was 132 months. Of these 25 patients, 11 had anterior uveitis, 8 had panuveitis, and 6 had posterior uveitis. Retinal vasculitis was observed in four patients. Three patients had neurologic involvement and one had GI involvement, concomitantly (Table 1).

Twenty-six patients belonged to the vascular cluster (C4). The median age at the diagnosis was 144 months. Nine patients had uveitis, additionally, and 23 patients had neurologic involvement (Table 1).

Seven patients were in the GI cluster (C5). The median age at the diagnosis was 144 months. Two patients had additional neurologic involvement (Table 1).

Ocular and vascular clusters were more common in boys ($p < .001$), while girls usually presented with mucocutaneous features. The age at the diagnosis was similar among the clusters. The activity scores at the diagnosis were higher in ocular, vascular, and GI clusters ($p = .001$), while at the last control, partial response to the treatment was more common among ocular, vascular, and GI clusters. Therefore, patients belonging to these clusters needed more intensive treatment such as azathioprine, cyclophosphamide, and biologic agents (Table 1).

Discussion

This multicentre cluster analysis showed different clinical features among juvenile BD patients, leading to cluster five different phenotypes: C1, mucocutaneous type; C2, articular type; C3, ocular type; C4, vascular type; and C5, GI type (Figure 1). According to the comprehensive analysis, ocular and vascular clusters were more predominant in boys, while girls usually belonged to C1 with mucocutaneous features (Figure 2). Furthermore, we demonstrated certain differences between clusters in terms of outcomes and treatment requirements.

As Turkey is along the Silk Route, the estimated prevalence of BD was higher in our country [119.8 per 100,000; 95% confidence interval (CI) 59.8, 239.9] compared to countries in the Middle East (31.8 per 100,000; 95% CI 12.9, 78.4) and in Europe (3.3 per 100,000; 95% CI 2.1, 5.2) [10]. The mean age of disease onset varied from 4.8 to 12.3 years [11, 12], and it was reported as 11 years by a recent study from Turkey [13]. It is well known that juvenile BD usually presents as an incomplete form and after some time expresses the full disease phenotype [14]. Therefore, ~3 years of diagnostic delay has been reported in the paediatric cohorts. In the present study, the median age of disease onset was ~11 years and the median time between the onset of symptoms and the diagnosis was ~2 years.

In the paediatric cohorts, the most common feature is oral ulcers which are present in 96–100% of juvenile BD patients followed by other mucocutaneous lesions such as genital ulcers (33.6–82.5%), papulopustular lesions (4.3–69%), and erythema nodosum (4.3–58.6%) [7, 11–18]. Correspondingly, oral ulcers were also the most frequent symptom (99.1%), followed by genital ulcers (70.2%) and pseudofolliculitis (35.6%) in our cohort. Furthermore, the most frequent cluster presented with mucocutaneous findings (C1, 58.6%). Musculoskeletal involvement accounts for 22.7–52.5% of the features among patients with juvenile BD [7, 11–18]. Ocular involvement, which is the most important cause of morbidity, is seen in 8.7–66.2% of patients [7, 11–18]. Neurological involvement is observed in 2.2–59.6% of the paediatric cohorts [7, 11–18]. In juvenile BD, vascular involvement ranges from 1.8 to 21% and GI involvement ranges from 4.8% to 42.7% [7, 11–18]. In the present study, the frequency of musculoskeletal, ocular, neurological, vascular, and GI involvement was 52.9%, 15.1%, 14.2%, 11.6%, and 3.6%, respectively.

Downloaded from https://academic.oup.com/mr/advance-article/doi/10.1093/mr/roac044/6582903 by Istanbul University Library user on 20 June 2022

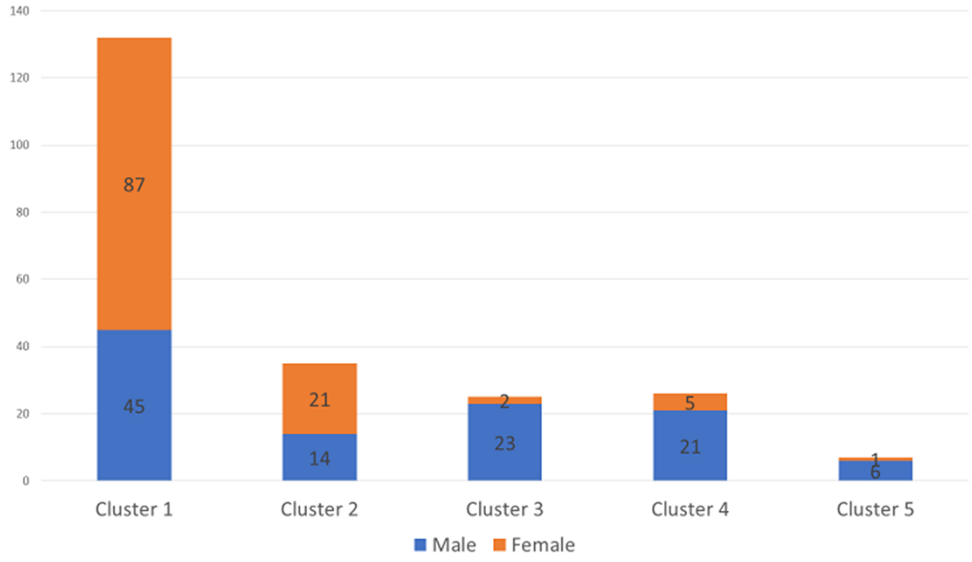


Figure 2. Distribution of gender among clusters.

Adult studies have already shown that clinical manifestations in BD patients differ between patients. As BD follows a heterogeneous and complex course, stratifying patients into subtypes may lead clinicians to individualize treatment. For instance, the mucocutaneous cluster has a mild course, while clusters with organ involvement require more intensive treatment to reduce morbidity and mortality. Predicting outcomes at the initiation of treatment and accurately identifying disease subtypes are crucial for personalized treatment. Several cluster analyses were performed in adult BD patients [19–21]. Kurosawa *et al*. [20] evaluated the database of 2218 patients and reported three distinct clusters: C1 (male, HLA-B51-positive, ocular inflammation, and neurologic involvement); C2 (female, onset age: <30 years, HLA-B51-negative, genital ulcers, no ocular inflammation, and no neurologic involvement); and C3 (onset age: 30–39 years, skin lesions, and arthritis). Both ethnicity and environment may influence the clustering of the disease. Therefore, the phenotype and subtypes of the disease may differ between countries. Two studies from Turkey, done 10 years apart, identified the same four clusters: C1 (oral ulcers, genital ulcers, and erythema nodosum); C2 (superficial and deep vein thrombosis); C3 (uveitis); and C4 (papulopustular skin lesions and joint involvement) [19, 22]. Studies from Turkey also identified a different cluster especially belonging to this geography: papulopustular skin lesions and joint involvement with a family aggregation [22, 23]. In our cohort, 35 patients fitted to the articular type (C2) and 22 had enthesitis, concomitantly. However, we could not show an association between this cluster and papulopustular lesions or family history.

In addition to the fact that the disease varies from person to person, patients with juvenile BD express a quite different phenotype than adults with BD. For instance, the presence of a family history of BD, GI and neurologic involvement, and arthralgia are more common in children, while genital ulcers and vascular involvement are more frequent in adults [13]. Therefore, it is not surprising that different types emerge in cluster analysis. Recently, a study from China showed five subtypes of adult BD [24]. According to this study, C1 (skin and mucosa type) had a milder course; C2 (articular type), which presented with articular involvement, had an association with increased frequency of papulopustular lesions; C3 (GI type) consisted of patients with GI involvement with a lower frequency of ocular involvement; C4 (uveitis type) showed male predominance with a younger age of disease onset; and C5 (cardiovascular type) had an association between cardiac and vascular lesions with an aggregation of parenchymal neurologic involvement [24]. Previous reports also confirmed the relationship between deep vein thrombosis and neurologic involvement in BD patients [25, 26]. A significant relationship between vascular involvement and neurologic involvement was discovered in our cohort. A total of 23 individuals with neurologic impairment in addition to vascular involvement were identified in C4 (vascular type).

The data on disease clusters in juvenile BD patients are scarce. Only one report from China evaluated the clusters in 69 patients with juvenile BD [5]. According to the aforementioned study, three sub-clusters were presented as follows: C1 with mucocutaneous type; C2 with GI type; and C3 with a mixture of uveitis, vascular, and central nervous system involvement. C1 and C2 were compatible with adult studies; however, C3 was quite different. C3 comprised 19 patients: 6 had ocular lesions, 6 had arterial thrombosis or aneurysms, 3 had neurologic involvement, 3 had deep vein thrombosis, and 2 had major vein (vena cava and hepatic) thrombosis [5]. The small size of the study group may not allow the identification of other disease subtypes. Our study's multicentre approach enables us to more precisely characterize the subgroups of juvenile BD patients. We defined five distinct phenotypes with different outcomes. The ocular, vascular, and GI clusters had greater disease activity scores at the time of diagnosis. In addition, partial treatment response was more frequent in these three clusters. Consequently, patients in these clusters required more aggressive treatment. As BD is not a unique disease, understanding its subsets can prevent delay in the diagnosis and also help clinicians to tailor their therapy accordingly.

Our study is restricted by its retrospective design. Furthermore, since the data were collected from a single country and ethnicity may affect the presentation of the illness, we

Downloaded from https://academic.oup.com/mr/advance-article/doi/10.1093/mr/roac044/6582903 by Istanbul University Library user on 20 June 2022

cannot generalize our results. Another limitation of the study is that organ involvement gradually appears during the disease course, so a shorter observation period may influence our results.

In conclusion, our findings revealed that the mucocutaneous-only cluster was the most frequent cluster in PEDBD. While mucocutaneous and articular clusters had a female predominance, ocular, vascular, and GI clusters had a striking male predominance. Furthermore, having ocular, vascular, and GI involvement affected disease activity not only at the diagnosis but also throughout the course of the disease, and more aggressive treatment modalities were required in these clusters.

Conflict of interest

None declared.

Funding

None declared.

References

[1] Jennette JC, Falk RJ, Bacon PA *et al.* 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 2013;**65**:1–11.
[2] Ozen S. Pediatric onset Behçet disease. *Curr Opin Rheumatol* 2020;**22**:585.
[3] Seyahi E. Phenotypes in Behçet's syndrome. *Intern Emerg Med* 2019;**14**:677–89.
[4] Sag E, Demir S, Ozen S. Clusters in pediatric rheumatic diseases. *Curr Rheumatol Rep* 2020;**22**:28.
[5] Zou J, Luo JF, Shen Y *et al.* Distinct clinical characteristics of pediatric Behçet's syndrome: a study from a referral center in China. *Mod Rheumatol* 2021;**16**:1–6.
[6] Criteria for Diagnosis of Behçet's Disease. International study group for Behçet's disease. *Lancet* 1990;**335**:1078–80.
[7] Koné-Paut I, Shahram F, Darce-Bello M *et al.* Consensus classification criteria for paediatric Behçet's disease from a prospective observational cohort: PEDBD. *Ann Rheum Dis* 2016;**75**:958–64.
[8] Mizushima Y. Recent research into Behçet's disease in Japan. *Int J Tissue React* 1988;**10**:59–65.
[9] Davatchi FA, Shahram F, Tebbi M *et al.* Iran Behçet's disease dynamic activity measure. Abstracts of the XIIth European Congress of Rheumatology. *Hungarian Rheumatol* 1991;**32**:134.
[10] Maldini C, Druce K, Basu N *et al.* Exploring the variability in Behçet's disease prevalence: a meta-analytical approach. *Rheumatology (Oxford)* 2018;**57**:185–95.
[11] Karincaoglu Y, Borlu M, Toker SC *et al.* Demographic and clinical properties of juvenile-onset Behçet's disease: a controlled multicenter study. *J Am Acad Dermatol* 2008;**58**:579–84.
[12] Nanthapisal S, Klein N, Ambrose N *et al.* Paediatric Behçet's disease: a UK tertiary centre experience. *Clin Rheumatol* 2016;**35**:2509–16.
[13] Ekici Tekin Z, Çelikel E, Aydin F *et al.* Juvenile Behçet's disease: a tertiary center experience. *Clin Rheumatol* 2022;**41**:187–94.
[14] Yildiz M, Haslak F, Adrovic A *et al.* Pediatric Behçet's disease. *Front Med (Lausanne)* 2021;**3**:627192.
[15] Atmaca L, Boyvat A, Yalçindag F *et al.* Behçet disease in children. *Ocul Immunol Inflamm* 2011;**19**:103–7.
[16] Krause I, Uziel Y, Guedj D *et al.* Childhood Behçet's disease: clinical features and comparison with adult-onset disease. *Rheumatology (Oxford)* 1999;**38**:457–62.
[17] Kim D, Chang S, Bang D *et al.* Clinical analysis of 40 cases of childhood-onset Behçet's disease. *Pediatr Dermatol* 1994;**11**:95–101.
[18] Gallizzi R, Pidone C, Cantarini L *et al.* A national cohort study on pediatric Behçet's disease: cross-sectional data from an Italian registry. *Pediatr Rheumatol Online J* 2017;**15**:84.
[19] Tunc R, Keyman E, Melikoglu M *et al.* Target organ associations in Turkish patients with Behçet's disease: a cross sectional study by exploratory factor analysis. *J Rheumatol* 2002;**29**:2393–6.
[20] Kurosawa M, Takeno Y, Kirino Y *et al.* Subgroup classification of Behçet's disease using clinical information: analysis of a clinical database of patients receiving financial aid for treatment. In: *ISBD Conference*, 2018, Rotterdam.
[21] Arida A, Vaiopoulos G, Markomichelakis N *et al.* Are clusters of patients with distinct clinical expression present in Behçet's disease? *Clin Exp Rheumatol* 2009;**27**:48–51.
[22] Karaca M, Hatemi G, Sut N *et al.* The papulopustular lesion/arthritis cluster of Behcet's syndrome also clusters in families. *Rheumatology (Oxford)* 2012;**51**:1053–60.
[23] Hatemi G, Fresko I, Tascilar K *et al.* Increased enthesopathy among Behcet's syndrome patients with acne and arthritis: an ultrasonography study. *Arthritis Rheum* 2008;**58**:1539–45.
[24] Zou J, Lin C, Wang Y *et al.* Cluster analysis of phenotypes of patients with Behcet's syndrome: a large cohort study from a referral center in China. *Arthritis Res Ther* 2021;**23**:45.
[25] Krause I, Leibovici L, Guedj D *et al.* Disease patterns of patients with Behcet's disease demonstrated by factor analysis. *Clin Exp Rheumatol* 1999;**17**:347–50.
[26] Kidd D, Steuer A, Denman A *et al.* Neurological complications in Behçet's syndrome. *Brain J Neurol* 1999;**122**:2183–94.

Downloaded from https://academic.oup.com/mr/advance-article/doi/10.1093/mr/roac044/6582903 by Istanbul University Library user on 20 June 2022