Disease characteristics of psoriatic arthritis patients may differ according to age at psoriasis onset: cross-sectional data from the Psoriatic Arthritis-International Database

E. Bilgin[1], S.Z. Aydin[2], I. Tinazzi[3], Ö. Bayindir[4], G. Kimyon[5], C. Özişler[6], A. Doğru[7], E. Dalkiliç[8], K. Aksu[4], G. Yildirim Çetin[9], S. Yılmaz[10], D. Solmaz[11], A. Omma[12], M. Can[13], O. Küçükşahin[14], Ş. Yavuz[13], E.D. Ersözlü[15], L. Kiliç[1], E.F. Tarhan[16], M. Aydin Tufan[17], L. Akyol[18], M. Çinar[19], A. Erden[12], E. Gönüllü[20], F. Yildiz[9], S. Bakirci[2], F. Erbasan[21], S. Ergülü Eşmen[22], A. Küçük[23], A. Tufan[24], A. Balkarli[25], R. Mercan[26], Ş. Erten[12], S. Akar[11], T. Kaşifoğlu[27], T. Duruöz[28], V. Yazisiz[21], U. Kalyoncu[1]

[1]Division of Rheumatology, Dept. of Internal Medicine, Hacettepe University, Ankara, Turkey; [2]Division of Rheumatology, Dept. of Internal Medicine, University of Ottawa School of Medicine, Ottawa Hospital Research Institute, Ottawa, ON, Canada; [3]Division of Rheumatology, IRCCS Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy; [4]Division of Rheumatology, Dept. of Internal Medicine, Ege University, Izmir; [5]Division of Rheumatology, Dept. of Internal Medicine, Hatay Mustafa Kemal University, Turkey; [6]Division of Rheumatology, Dept. of Internal Medicine, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey; [7]Division of Rheumatology, Dept. of Internal Medicine, Süleyman Demiral University, Isparta, Turkey; [8]Division of Rheumatology, Dept. of Internal Medicine, Uludağ University, Bursa, Turkey; [9]Division of Rheumatology, Dept. of Internal Medicine, Kahramanmaraş Sütçü İmam University, Turkey; [10]Division of Rheumatology, Department of Internal Medicine, Selcuk University, Konya, Turkey; [11]Division of Rheumatology, Dept. of Internal Medicine, İzmir Katip Çelebi University, Turkey; [12]Division of Rheumatology, Dept. of Internal Medicine, Ankara City Hospital, Turkey; [13]Division of Rheumatology, Dept. of Internal Medicine, Marmara University, İstanbul, Turkey; [14]Division of Rheumatology, Dept. of Internal Medicine, Yıldırım Beyazıt University, Ankara, Turkey; [15]Adana Numune Training and Research Hospital, Adana, Turkey; [16]Division of Rheumatology, Dept. of Internal Medicine, Muğla Sıtkı Koçman University, Muğla, Turkey; [17]Division of Rheumatology, Dept. of Internal Medicine, Başkent University, Ankara, Turkey; [18]Diyarbakır Training and Research Hospital, Diyarbakır, Turkey; [19]Division of Rheumatology, Dept. of Internal Medicine, Gülhane Training and Research Hospital, Ankara, Turkey; [20]Division of Rheumatology, Dept. of Internal Medicine, Sakarya University, Sakarya, Turkey; [21]Division of Rheumatology, Dept. of Internal Medicine, Akdeniz University, Antalya, Turkey; [22]Division of Rheumatology, Dept. of Internal Medicine, Konya Education and Research Hospital, Turkey; [23]Division of Rheumatology, Dept. of Internal Medicine, Necmettin Erbakan University, Konya, Turkey; [24]Division of Rheumatology, Dept. of Internal Medicine, Gazi University, Ankara, Turkey; [25]Antalya Training and Research Hospital, Antalya, Turkey; [26]Division of Rheumatology, Dept. of Internal Medicine, Namık Kemal University, Tekirdağ, Turkey; [27]Division of Rheumatology, Dept. of Internal Medicine, Eskişehir Osman Gazi University, Konya, Turkey; [28]Department of Physical Medicine and Rehabilitation, Marmara University, Istanbul, Turkey.

Abstract

Objective

To explore the impact of early versus late-onset psoriasis (PsO) on the disease characteristics of psoriatic arthritis (PsA) in a large-multicentre cohort.

Methods

The data from a multicentre psoriatic arthritis database was analysed. Patients were grouped according to age at psoriasis onset (early onset; <40 years of age, late-onset; >40 years of age) and disease characteristics of the groups were compared by adjusting for BMI and PsA duration, where necessary.

Results

At the time of analyses, 1634 patients were recruited [62.8% females; early onset 1108 (67.8%); late-onset, 526 (32.2%)]. The late-onset group was more over-weight [66.8% vs. 86.8%, p<0.001; adjusted for age - aOR 1.55 (1.11-2.20; 95% CI)]. The early onset group had more scalp psoriasis at onset (56.7% vs. 43.0%, p<0.001), whereas extremity lesions were more common in the late-onset group (63.8% vs. 74.2%, p<0.001). Axial disease in males and psoriatic disease family history in females were significantly higher in the early onset group [38.0% vs. 25.4%; p=0.005; adjusted for PsA duration - aOR 1.76 (1.19–2.62; 95% CI) / 39.5% vs. 30.1%; p=0.003; OR 1.51 (1.15–1.99; 95% CI), respectively]. Psoriatic disease activity parameters, patient-physician reported outcomes and HAQ-DI scores were similar in both groups.

Conclusion

Clinical features of PsA may be affected by the age at onset of PsO. Different genetic backgrounds in early and late-onset PsO may be driving the differences in psoriasis and PsA phenotypes.

Key words

psoriasis, psoriatic arthritis, early and late-onset

Emre Bilgin, Sibel Zehra Aydin, Ilaria Tinazzi, Özün Bayindir, Gezmiş Kimyon, Cem Özişler, Atalay Doğru, Ediz Dalkiliç, Kenan Aksu, Gözde Yildirim Çetin, Sema Yilmaz, Dilek Solmaz, Ahmet Omma, Meryem Can, Orhan Küçükşahin, Şule Yavuz, Emine Duygu Ersözlü, Levent Kiliç, Emine Figen Tarhan, Müge Aydin Tufan, Lütfi Akyol, Muhammet Çinar, Abdulsamet Erden, Emel Gönüllü, Fatih Yildiz, Sibel Bakirci, Funda Erbasan, Serpil Ergülü Eşmen, Adem Küçük, Abdurrahman Tufan, Ayşe Balkarli, Ridvan Mercan, Şükran Erten, Servet Akar, Timuçin Kaşifoğlu, Tuncay Duruöz, Veli Yazisiz, Umut Kalyoncu.

Please address correspondence to: Umut Kalyoncu, Hacettepe University Medical School, Department of Internal Medicine, Division of Rheumatology 06100 Sihhiye, Ankara, Turkey. E-mail: umut.kalyoncu@yahoo.com

Received on March 14, 2020; accepted in revised form on May 18, 2020.

Competing interests: D. Solmaz received funding from Union Chimique Belge (UCB) for an axial fellowship. S. Bakirci received funding from the Turkish Rheumatology Association (TRD). The other co-authors have declared no competing interests.

Introductıon

Psoriasis (PsO) is a chronic, multifactorial and inflammatory skin disease that can present with a very broad spectrum of symptoms, including psoriatic arthritis ((PsA) in about 20–30% of patients) (1, 2). In the attempt to explain some of the heterogeneity of the disease, Henseler and Christopher published their pivotal work in 1985, classifying PsO into two main subgroups: PsO beginning at age <40 years: early onset PsO (EOPsO) (type 1); PsO beginning at age >40 years: late-onset psoriasis (LOPsO) (type 2) (3). They described the EOPsO group as having more extensive skin disease, strong family aggregation and HLA-C*06 positivity, whereas LOPsO as being more sporadic, having less family inheritance and unclear genetic background (3). This hypothesis has mostly been tested in PsO cohorts. Other than a relatively smaller study, the role of these subgroups based on the age onset of psoriasis in PsA has not been tested (4). However, the impact of this classification in large PsA cohort has not been studied, to the best of our knowledge, and still needs to be tested in large PsA cohorts.

Our aim was to explore the impact of early and late-onset psoriasis on the disease characteristics of PsA in a large-multicentre PsA cohort.

Methods

Patient selection and data collection

This is a cross-sectional study conducted with patients who were recruited to PsART-ID (Psoriatic Arthritis- International Database) which is a prospective database in PsA, including centres from Turkey (in 2014), Canada (in 2015) and Italy (in 2018). Consecutive patients with PsA are recruited to the database and data are collected using a web-based system (www.trials-network.org). PsA diagnosis is based on the clinical decision of the treating rheumatologist. Details of the database previously have been published (5). Ethics approval was obtained from Hacettepe University Ethics Board, Ankara, Turkey (GO 14/578), Ottawa Health Science Network Research Ethics Board, Ottawa, Canada (20160436-01H) and Italy (Sacro Cuore Don Calabria Hospital, Italy (F8MRG)) All patients gave informed consent prior to recruitment.

Assessments

In summary, the following parameters were recorded; for the demographic profile; sex, age, duration of education, smoking status, and body mass index (BMI); for PsO; onset date, type, initially involved site of skin (scalp, torso, extremity, genital), nail involvement (ever) and family history; for PsA; the fulfilment of the ClASsification criteria for Psoriatic ARthritis (CASPAR) criteria, type of articular involvement (mono-, oligo-, polyarthritis, distal interphalangeal joint involvement, arthritis mutilans), and presence of axial disease (according to treating physician), dactylitis (ever), enthesitis (ever), family history of psoriatic disease, Disease Activity in Psoriatic Arthritis (DAPSA) category (remission (≤4), low (4–14), moderate (15–28) and high (≥29) disease activity), Leeds Enthesitis index, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Fuctional Index (BASFI), patient and physician global assessment, visual analogue scale (VAS, 0–100 mm), Health Assessment Questionnaire Disability index (HAQ-DI) and treatments. For the aim of this analysis, the patients were grouped into 2 according to the onset age of psoriasis: early onset (EOPsO; age <40 years) and late-onset (LOPsO; age >40 years) (3).

Statistical analysis

Descriptive statistics were performed with the frequencies and percentages for categorical variables, mean and SD, or median and range. Categorical variables were compared using Chi-square test. Continuous variables were compared by student's t-test or Mann-Whitney U-test depending on the distribution of the data. Odds ratios were calculated for the comparison of categorical variables. Adjustments for possible confounding factors (*e.g.* BMI adjusted for age, nail involvement adjusted for PsO disease duration, axial PsA adjusted for PsA disease duration) were performed where necessary. Hosmer-Lemeshow test was used to assess

Table I. Comparison of demographic and psoriatic disease features in early- or late-onset psoriasis (Data represented as n, % unless otherwise specified).

Variable	Early-onset (EOPsO)	Late-onset (LOPsO)	Overall	Odds ratio (%95 CI)	*p*-value
Age, mean (SD)	41.5 (11.8)	58.3 (8.3)	46.9 (13.3)	--	<0.001
Female	674 (60.8)	352 (66.9)	1026 (62.8)	0.76 (0.61-0.95)	0.017
Smoking *					
Ever	446 (43.2)	207 (42.3)	653 (42.9)	0.96 (0.77-1.20)	0.75
Never	587 (56.8)	282 (57.7)	869 (57.1)		
BMI, mean (SD)	27.6 (5.2)	29.5 (5.0)	28.2 (5.2)	--	<0.001
≥25	736 (66.8)	454 (86.8)	1190 (73.3)	3.26 (2.46-4.32)	<0.001
				1.55 (1.11-2.20)[α]	0.011
Psoriasis (PsO)					
Age at diagnosis, mean (SD)	23.5 (9.4)	50.4 (7.2)	32.1 (15.3)	--	<0.001
Disease duration, mean (SD) (year)	18.1 (12.2)	7.8 (6.5)	14.7 (11.7)	--	<0.001
Initial scalp inv.°	560 (56.7)	193 (43.0)	753 (52.5)	1.74 (1.32-2.18)	<0.001
Initial torso inv.°	208 (21.1)	84 (18.7)	292 (20.3)	1.16 (0.87-1.54)	0.32
Initial extremity inv. °	629 (63.8)	333 (74.2)	962 (67)	0.61 (0.47-0.78)	<0.001
Initial genital inv.°	73 (7.4)	29 (6.5)	102 (7.1)	1.15 (0.74-1.80)	0.52
Plaque psoriasis (+) °°	649 (80.8)	295 (80.2)	944 (80.6)	0.95 (0.70-1.30)	0.81
Pustuler psoriasis (+)°°	144 (17.9)	69 (18.8)	213 (18.2)	1.05 (0.76-1.45)	0.73
Nail involvement (ever)	552 (50.0)	222 (42.2)	774 (47.5)	1.36 (1.10-1.68)	0.003
				0.99 (0.78-1.25)[†]	0.96
Psoriatic arthritis (PsA)					
Age at diagnosis, mean (SD)	35.8 (11.2)	54.2 (8.4)	41.7 (13.4)	--	<0.001
Disease duration, mean (SD)	5.7 (7.6)	4.2 (5.2)	5.2 (7.0)	--	<0.001
Monoarthritis	30 (2.7)	20 (3.8)	50 (3.1)	1.42 (0.80-2.53)	0.22
Oligoarthritis	344 (31.1)	163 (31.2)	507 (31.1)	1.01 (0.82-1.26)	0.98
Polyarthritis	542 (49.1)	246 (47.0)	789 (48.5)	0.90 (0.72-1.11)	0.42
Arthritis mutilans	3 (0.3)	1 (0.2)	4 (0.2)	0.70 (0.07-6.78)	0.76
Axial disease					
Female	187 (27.8)	78 (22.3)	265 (25.9)	0.76(0.56-1.03)[‡]	0.08
Male	164 (38.0)	44 (25.4)	208 (34.4)	1.76(1.19-2.62)[‡]	0.005[††]
DIP involvement	164 (14.8)	76 (14.5)	240 (14.7)	0.97 (0.72-1.30)	0.86
Dactylitis (ever)	245 (23.4)	123 (24.7)	368 (22.9)	1.07 (0.83-1.38)	0.56
Enthesitis (ever)	255 (25.0)	129 (26.3)	384 (23.5)	1.07 (0.84-1.37)	0.56
CASPAR (+)	959 (86.7)	444 (84.7)	1403 (85.9)	0.85 (0.63-1.14)	0.28
Psoriatic disease					
Family history					
Female	266 (39.5)	106 (30.1)	372 (36.3)	1.51 (1.15-1.99)	0.003[††]
Male	127 (29.3)	52 (29.9)	179 (29.4)	1.03 (0.70-1.51)	0.87

*n=1522, °n=1435, °°n=1171, [α] adjusted for age, [†] adjusted for psoriasis duration, [‡] adjusted for psoriatic arthritis duration, [††] Bonferroni correction.
BMI: body mass index; CASPAR: ClASsification criteria for Psoriatic Arthritis; DIP: distal interphalangeal.

model fit for adjusted variables. SPSS 25.0 (SPSS Inc., Chicago, IL, USA) was used for analyses.

Results

Of 1648 patients registered in the database, 1634 had data of their PsO diagnosis date. A total of 1634 (62.8% females) patients with PsA were recruited, 1108 (67.8%) being in the EOPsO group and 526 (32.2%) being in the LOPsO group. Rate of over-weight patients was higher in LOPsO group. Details of the demographic data of the patients are given in Table I.

Duration of PsO was longer in the EOPsO group (18.1 *vs*. 7.8 years, $p<0.001$). The EOPsO group had scalp involvement as the initial site of skin disease more often than the LOPsO group (56.7% *vs*. 43.0%, $p<0.001$), whereas extremity involvement was more frequent as the initial finding in the LOPsO group (EOPsO *vs*. LOPsO 63.8% *vs*. 74.2%, $p<0.001$) (Table I). Nail involvement (ever) was more common in EOPsO group, however, the significance disappeared when adjusted for psoriasis duration. Duration of PsA was also longer in the EOPsO group (5.7 *vs*. 4.2 years, $p<0.001$). We found gender as a modifier for axial disease and psoriatic disease family history, so we compared axial disease and psoriatic disease family in the EOPsO and LOPsO groups by stratifying them according to gender. This suggested a higher prevalence of axial disease in males in the EOPsO group as well as more frequent family history in females [axial disease in males; EOPsO *vs*. LOPsO; 38.0% *vs*. 25.4%; $p=0.005$; adjusted for PsA duration - aOR 1.76 (1.19–2.62; 95% CI) / psoriatic disease history in females; EOPsO *vs*. LOPsO; 39.5% *vs*. 30.1%; $p=0.003$; OR 1.51 (1.15–1.99; 95% CI), respectively].

Psoriatic disease activity parameters, patient- and physician-reported outcomes and HAQ-DI scores were similar in both groups (Table II). Distribu-

Table II. Comparison of psoriatic arthritis disease activity parameters and distribution of ever-used treatment options.

Variable	Total number of patients (n)	Early-onset (EOPsO)	Late-onset (LOPsO)	Overall	*p*-value
Psoriatic Arthritis Disease Activity Parameters					
DAPSA category**	1126				0.89
Remission		119 (15.6)	51 (14.0)	170 (15.1)	
Low		285 (37.4)	142 (39.1)	427 (37.9)	
Moderate		246 (32.2)	116 (32.0)	362 (32.1)	
High		113 (14.8)	54 (14.9)	167 (14.8)	
Leeds Enthesitis Index**	1242	0.17 (0.62)	0.22 (0.68)	0.19 (0.64)	0.25
BASDAI VAS (0-100 mm)**	960	42.4 (24.5)	42.3 (23.2)	42.4 (24.1)	0.96
BASFI VAS (0-100mm)**	938	33.2 (24.2)	32.9 (23.8)	33.1 (24.1)	0.84
Patient Global Asssessment VAS (0-100 mm)**	1191	44.5 (25.6)	44.6 (25.1)	44.5 (25.5)	0.94
Physician Global Assessment,	1144	36.5 (23.2)	37.1 (23.2)	36.9 (23.2)	0.84
VAS (0-100 mm)** HAQ-DI**	1369	0.80 (0.74)	0.81 (0.72)	0.81 (0.73)	0.98
Ever-used Treatment Options					
Corticosteroids	1612	433 (39.6)	204 (39.4)	637 (39)	
Conventional Synthetic DMARDs					
Methotrexate	1612	941 (86.0)	424 (81.9)	1365 (83.5)	
Sulphasalazine		415 (37.9)	204 (39.4)	619 (37.9)	
Leflunomid		266 (24.2)	117 (22.6)	383 (23.4)	
Biologic DMARDs					
Anti-TNF					
Adalimumab	1612	165 (15.1)	75 (14.5)	240 (14.7)	
Etanercept	1612	134 (12.2)	50 (9.7)	184 (11.3)	
Infliximab	1612	92 (8.4)	47 (9.1)	139 (8.5)	
Golimumab	1612	43 (3.9)	26 (5.0)	69 (4.2)	
Certolizumab	299	1 (0.5)	3 (2.7)	4 (1.4)	
Anti- IL17					
Secukinumab	299	12 (6.4)	9 (8.0)	21 (7.0)	

* n (%), **mean (SD)
BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; DAPSA: Disease activity in Psoriatic Arthritis; HAQ-DI: Health Assessment Questionnaire Disability Index.

tion of treatment options patients ever had is given in Table II.

Discussion

In this study, we found that the psoriasis and PsA phenotypes may differ based on the age onset of psoriasis. More specifically obesity and psoriasis at the extremities as the initial site were more prevalent in patients with LOPsO, while psoriasis in the scalp as the initial site, axial disease in males, psoriatic disease family history in female patients, were seen more often in EOPsO. To the best of our knowledge, this is the largest study investigating the effect of these subgroups.

Historical dichotomy of PsO was first proposed by Henseler *et al*. in 1985 as EOPsO (<40 years) and LOPsO (>40 years) (3). These 2 groups have been found to have some genetic differences. HLA-Cw6 and family history are more frequent in EOPsO patients (3, 4, 6-9). Another important genetic variation is single-nucleotide polymorphisms (SNPs) in the endoplasmic reticulum aminopeptidase 1 (ERAP1) gene (10). Besides, several tumour necrosis factors and interleukin 1 receptor type 1 were linked to EOPsO risk (11, 12). The genetic differences between these 2 subgroups of psoriasis are likely to explain the clinical differences.

We found that patients with LOPsO were more likely to be overweight than EOPsO, even after correcting for age. This is in parallel with previous publications. (4, 13). One possible explanation may be that in the presence of a hereditery risk, the disease onset may be seen earlier whereas enviromental risk factors, such as obesity may require more time to cause disease. Although the LOPsO group was more overweight at the time of analysis, due to our cross-sectional analysis and lack of data retrospectively, we did not have a chance to analyse the onset of obesity and its connection with the disease onset. Although we made the analysis by correcting for age, patients with LOPsO may have functional impairment more often due to their arthritis than a younger population, which may increase the risk of obesity.

Our observation on the differences on the initial involvement sites of PsO were also similar to the previous studies on psoriasis cohorts (13-15). The site of involvement of psoriasis is strongly associated with physical, psychological, social and economic factors (16). As the age of patients were significantly different in our study, their habits, physical and social activities can be divergent, which may explain the differences in psoriatic phenotypes. Also, as we previously discussed, genetic background could have a role in the way first psoriasis lesion presents.

We observed that axial PsA is more common in male patients with EOPsO then male LOPsO patients. Similar to our data, Alonso *et al*. reported the rate

of the axial disease at psoriasis onset in EOPsO patients as 22.3%, whereas it was 6.1% in the LOPsO group and a higher rate of HLA-B27 in the EOPsO group (4). Quiero *et al*. have previously shown that HLA-B27 may be a key player in the disease process of EOPsO and psoriatic arthritis in in this group, but with a lower frequency in psoriatic axSpA than axSpA (9, 17). Unfortunately, our database did not mandate data collection on HLA-B27, however, our observations support the clinical observations that have been raised in a smaller group by Alonso *et al*.

Our study has some limitations. Firstly, lack of genetic information regarding HLA subtypes makes some of our assumptions speculative. However, clinical aspects of earlier studies strongly support our results. We cannot rule out a recall bias as some of the data that are collected from the patients require information from the past. However, we tried to overcome this bias by having a large number of participants and multicentred patient allocation which can be counted as the strongest aspects of our study. Finally, our cross-sectional design for this analysis does not allow us to seek for a causal relationship

In conclusion; clinical features of PsA and psoriasis may be affected by the age at the onset of psoriasis. As the genetic background is different in early and late-onset psoriasis, this may suggest a different pathogenetic mechanism based on the psoriasis phenotype, also affecting the PsA features. Further prospective studies are needed to define whether the classification of PsA also requires including psoriasis phenotypes.

References

1. GLADMAN DD, ANTONI C, MEASE P, CLEGG DO, NASH P: Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* 2005; 64 (Suppl. 2): ii14-17.
2. CARLI L, CALABRESI E, GOVERNATO G, BRAUN J: One year in review 2018: axial spondyloarthritis. *Clin Exp Rheumatol* 2019; 37: 889-98
3. HENSELER T, CHRISTOPHERS E: Psoriasis of early and late onset: characterization of two types of psoriasis vulgaris. *J Am Acad Dermatol* 1985; 13: 450-56.
4. ALONSO S, TEJON P, SARASQUETA C, COTO P, ALPERI M, QUEIRO R: Age at disease onset may help to further characterize the disease phenotype in psoriatic arthritis. *Joint Bone Spine* 2016; 83: 533-37.
5. KALYONCU U, BAYINDIR O, FERHAT OKSUZ M *et al*.; PSORIATIC ARTHRITIS REGISTRY OF TURKEY STUDY GROUP: The Psoriatic Arthritis Registry of Turkey: results of a multicentre registry on 1081 patients. *Rheumatology* (Oxford) 2017; 56: 279-86.
6. SCHMITT-EGENOLF M, EIERMANN TH, BOEHNCKE WH, STANDER M, STERRY W: Familial juvenile onset psoriasis is associated with the human leukocyte antigen (HLA) class I side of the extended haplotype Cw6-B57-DRB1*0701-DQA1*0201-DQB1*0303: a population- and family-based study. *J Invest Dermatol* 1996; 106: 711-14.
7. FERRANDIZ C, PUJOL RM, GARCIA-PATOS V, BORDAS X, SMANDIA JA: Psoriasis of early and late onset: a clinical and epidemiologic study from Spain. *J Am Acad Dermatol* 2002; 46: 867-73.
8. QUEIRO R, ALPERI M, ALONSO-CASTRO S *et al*.: Patients with psoriatic arthritis may show differences in their clinical and genetic profiles depending on their age at psoriasis onset. *Clin Exp Rheumatol* 2012; 30: 476-80
9. QUEIRO R, TORRE JC, GONZALEZ S, LOPEZ-LARREA C, TINTURE T, LOPEZ-LAGUNAS I: HLA antigens may influence the age of onset of psoriasis and psoriatic arthritis. *J Rheumatol* 20003; 30: 505-7
10. FU Y, LI X, CHEN Y, LIU R, WANG R, BAI N: Association of ERAP1 gene polymorphisms with the susceptibility to psoriasis vulgaris: A case-control study. *Medicine* (Baltimore) 2018; 97: e12828.
11. JIA Y, QIN HJ, ZHANG JX, LIU XL, LI LJ: Association of the tumour necrosis factor-alpha polymorphisms rs361525 and rs1800629 with susceptibility to psoriasis: a meta-analysis. *Clin Exp Dermatol* 2013; 38: 836-44.
12. HEBERT HL, BOWES J, SMITH RL *et al*.: Identification of loci associated with late-onset psoriasis using dense genotyping of immune-related regions. *Br J Dermatol* 2015; 172: 933-39.
13. HEREDI E, CSORDAS A, CLEMENS M, ADAM B *et al*.: The prevalence of obesity is increased in patients with late compared with early onset psoriasis. *Ann Epidemiol* 2013; 23: 688-92.
14. KWON HH, KWON IH, YOUN JI: Clinical study of psoriasis occurring over the age of 60 years: is elderly-onset psoriasis a distinct subtype? *Int J Dermatol* 2012; 51: 53-58.
15. CHULAROJANAMONTRI L, KULTHANAN K, SUTHIPINITTHARM P *et al*.: Clinical differences between early- and late-onset psoriasis in Thai patients. *Int J Dermatol* 2015; 54: 290-94.
16. DOPYTALSKA K, SOBOLEWSKI P, BLASZCZAK A, SZYMANSKA E, WALECKA I: Psoriasis in special localizations. *Reumatologia* 2018; 56: 392-98.
17. GENSLER LS, SZUMSKI A, JONES HE, BARALIAKOS X: Does psoriatic axial spondyloarthritis phenotype correlate with imaging morphotype? *Clin Exp Rheumatol* 2020; 38: 329-32.