Serum Interleukin 23 in Psoriatic Arthritis Patients: Relation to disease activity, physical function and health related quality of life

Serum-Interleukin-23 bei Patienten mit Psoriasis-Arthritis: Zusammenhang mit Krankheitsaktivität, körperlicher Funktion und gesundheitsbezogener Lebensqualität

Authors

Noha Abdelhalim Elsawy[1], Abdelmoniem Helal[1], Mohamed El Shafei[2], Neveen Lewis Mikhael[3], Nesrin Ahmed Aboeladl[4]

Affiliations

1 Physical medicine, Rheumatology and Rehabilitation Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt
2 Radiodiagnosis Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt
3 Clinical and Chemical Pathology Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt
4 Rheumatology and Rehabilitation Department, Faculty of Medicine, Helwan University, Cairo, Egypt

Key words

PsA, IL-23, DAPSA, SF-36, PsAQoL

Schlüsselwörter

PsA, IL-23, DAPSA, SF-36, PsAQoL

Online publiziert: 12.12.2019

Bibliografie

Akt Rheumatol 2020; 45: 460–466

DOI 10.1055/a-1059-9475

ISSN 0341-051X

Georg Thieme Verlag KG, Rüdigerstraße 14,
70469 Stuttgart, Germany

Correspondence

Dr. Nesrin Ahmed Aboeladl
Rheumatology and Rehabilitation Department, Faculty of Medicine, Helwan University
Helwan Al sika Al Hadid Al Gharbia Al Masaken Al Iktsadayah
11795 Cairo
Egypt
Tel.: + 00201001995765, Fax: + 20225555021
nesrin.ahmed@med.helwan.edu.eg

ABSTRACT

Objective To assess interleukin 23 (IL-23) levels in the sera of psoriatic arthritis (PsA) patients and to determine the relationship of IL-23 with different disease activity indices, physical function and quality of life (QoL).

Methods Fifty PsA patients and 46 matched healthy controls were included in this study. Data including a detailed history, a thorough clinical examination, skin severity based on the Psoriasis Area and Severity Index (PASI), the Disease Activity index for Psoriatic Arthritis (DAPSA) and the Composite Psoriatic Disease Activity Index (CPDAI) were obtained for all patients. Physical function was assessed by the Health Assessment Questionnaire Disability Index (HAQ-DI) and health-related QoL was assessed using the Short Form Health Survey (SF-36), Psoriatic Arthritis Quality of Life (PsAQoL) and the Dermatology Life Quality Index (DLQI) were also assessed. Serum IL-23 levels were measured in the studied groups.

Results The study included 23(46 %) females and 27 (54 %) males with a mean age of 42.78 ± 12.33 years. The mean serum IL-23 level was significantly higher in PsA patients (50.89 ± 13.86 pg/ml) than in controls (43.88 ± 6.34 pg/ml) ($p = 0.006$). There were significant correlations between serum IL-23 levels and different grades of DAPSA activity ($p = 0.007$) and PASI ($p = 0.015$). No significant correlations could be detected between serum IL-23 levels and (HAQ-DI, DLQI, SF-36 or PsAQoL). CPDAI and DAPSA were significantly correlated with DLQI, SF-36 and PsAQoL.

Conclusion IL-23 is a useful biomarker for identifying joint activity or skin severity but not QoL or physical function.

ZUSAMMENFASSUNG

Ziel Beurteilung des Serumspiegels von Interleukin-23 (IL-23) bei Patienten mit Psoriasis-Arthritis (PsA) und Ermittlung des Zusammenhangs zwischen IL-23 und verschiedenen Krankheitsaktivitätsindizes, körperlicher Funktion und Lebensqualität (QoL).

Methoden In diese Studie wurden 50 PsA-Patienten und 46 vergleichbare gesunde Kontrollprobanden aufgenommen. Die bei allen Patienten durchgeführte Datenerhebung umfasste eine detaillierte Anamnese, eine sorgfältige klinische Untersu-

chung, Ermittlung des Schweregrads der Hautläsionen basierend auf dem Psoriasis Area and Severity Index (PASI), dem Disease Activity Index for Psoriatic Arthritis (DAPSA) und dem Composite Psoriatic Disease Activity Index (CPDAI). Die körperliche Funktion wurde anhand des Health Assessment Questionnaire Disability Index (HAQ-DI) und die gesundheitsbezogene Lebensqualität anhand des Short Form Health Survey (SF-36), des Psoriatic Arthritis Quality of Life (PsAQoL) und des Dermatology Life Quality Index (DLQI) beurteilt. In den untersuchten Gruppen wurden die Serumspiegel von IL-23 gemessen.

Ergebnisse Die Studie umfasste 23 (46 %) Frauen und 27 (54 %) Männer mit einem mittleren Alter von 42,78 ± 12,33 Jahren. Der mittlere Serumspiegel von IL-23 war bei den PsA-Patienten (50,89 ± 13,86 pg/ml) signifikant höher als bei den Kontrollprobanden (43,88 ± 6,34 pg/ml) (p = 0,006). Die Serumspiegel von IL-23 korrelierten signifikant mit verschiedenen Graden der mithilfe des DAPSA (p = 0,007) und des PASI (p = 0,015) ermittelten Krankheitsaktivität. Keine signifikanten Korrelationen fanden sich zwischen den IL-23-Serumspiegeln und HAQ-DI, DLQI, SF-36 oder PsAQoL. CPDAI und DAPSA korrelierten signifikant mit DLQI, SF-36 und PsAQoL.

Schlussfolgerung IL-23 ist ein nützlicher Biomarker zur Identifikation der Krankheitsaktivität oder des Schweregrads von Hautläsionen, aber nicht zur Ermittlung von Lebensqualität oder körperlicher Funktion.

Introduction

Psoriatic arthritis (PsA) is a multiplex chronic inflammatory seronegative enthesoarthro-osteopathy from the group of spondyloarthropathy (SpA), associated with extra-articular manifestations and several comorbidities and occurs in up to 42 % of patients with psoriasis (PsO) [1–3].

The spectrum of PsA disease includes polyarticular or oligoarticular forms, mild to very severe mutilating forms of arthritis, axial spondylitis [4], dactylitis and/or enthesitis [5–8].

Manifestations of active PsA include pain, swelling, morning stiffness and decreased range of motion of the affected joints, and PsA can lead to cartilage and bone damage. Thus, controlling disease activity is an indispensable goal for the treating physician to prevent joint damage and minimize disability [9–11].

Cytokines play a crucial role in the pathogenesis of arthritis [12]. In PsA in addition to tumour necrosis factor α, interleukin 6 and interferon γ; the interleukin 23(IL-23)/interleukin 17 (IL-17) axis plays a prevailing role in the inflammatory sequences, clinical course and response to treatment [13–15].

Recently, it was suggested that IL-23 stimulates T helper 17 cells to secrete IL-17 A-F, which acts on target tissues leading to the activation of synovial fibroblasts, endothelial cell angiogenesis and osteoclast activation thus; promoting enthesitis, synovitis, bone erosion and bone proliferation [16–17].

Owing to the diverse nature of the presentation of PsA, limitations of physical function and diminished QoL are experienced by PsA patients, particularly those with increased disease activity [11, 18].

Because of the emerging pivotal role of IL-23 in PsA, [13] it is important to determine its relation to PsA disease activity and its impact on physical function and QoL.

Aim of the work

To assess IL-23 levels in the sera of PsA patients and determine the relationship of IL-23 with different disease activity indices and its impact on physical function and QoL.

Patients and methods

This cross sectional study included 50 PsA patients fulfilling the Classification Criteria for Psoriatic Arthritis (CASPAR) for the classification of PsA [19] and 46 age, sex and body mass index (BMI)-matched normal healthy subjects. An informed consent was obtained from all participants. The study was approved by the local ethics committee.

The recorded data included: personal data (age and sex), history of the PsA and BMI [20]. Clinical examinations of the studied patients were performed with a focus on the musculoskeletal system: 68 joints for tenderness and 66 joints for swelling [21], peri-articular structures (Leeds enthesitis index (LEI) for enthesitis. [22] and Leeds dactylitis index (LDI) for dactylitis) [23]. The severity of skin symptoms was assessed by the Psoriasis Area and Severity Index (PASI) and classified as mild, moderate or severe skin affection (< 7, 7–12 or > 12 respectively) [24]. The Dermatology Life Quality Index (DLQI) was recorded [25, 26]. PsA disease activity was assessed using the Disease Activity index for Psoriatic Arthritis (DAPSA) and the Composite Psoriatic Disease Activity Index (CPDAI) [27, 28]. The DAPSA was interpreted as DAPSA remission (REM, ≤ 4); or low, moderate or high disease activity (LDA, ≤ 14; MDA, ≤ 28; HDA, > 28 respectively) [9, 10]. Physical function was assessed by the Health Assessment Questionnaire Standard Disability Index (HAQ-DI). [11]. Patients' health-related QoL was assessed by using 2 validated questionnaires: a general measure; the Short Form Health Survey (SF-36) [11] and a PsA-specific measure: Psoriatic Arthritis QoL (PsAQoL) [11, 18]. Laboratory tests were also performed, including: the measurement of CRP [29], rheumatoid factor (RF) [30] and serum IL-23 levels using ELISA [31]. Statistical analysis was performed using SPSS version 20.0. For normally distributed data, comparative studies were performed using independent t-tests and for abnormally distributed data, the Mann-Whitney test and Kruskal Wallis test were used. To assess correlations, the Spearman coefficient was used. A receiver operator characteristic (ROC) curve was used to evaluate the performance of serum IL-23 to differentiate PsA patients from controls: sensitivity, specificity and diagnostic accuracy of different cut-off points were calculated. A probability (p) value ≤ 0.05 was considered significant.

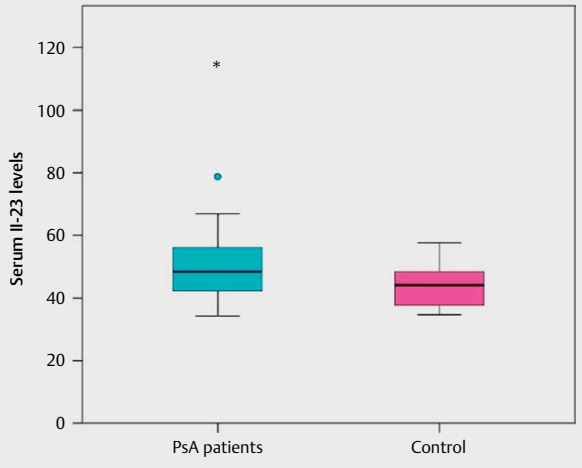
Results

- Twenty-three females (46 %)and 27 males (54 %) constituted the patient group with a mean age of 42.78 ± 12.33 years

▶ **Table 1** Disease characteristics of the PsA patients:

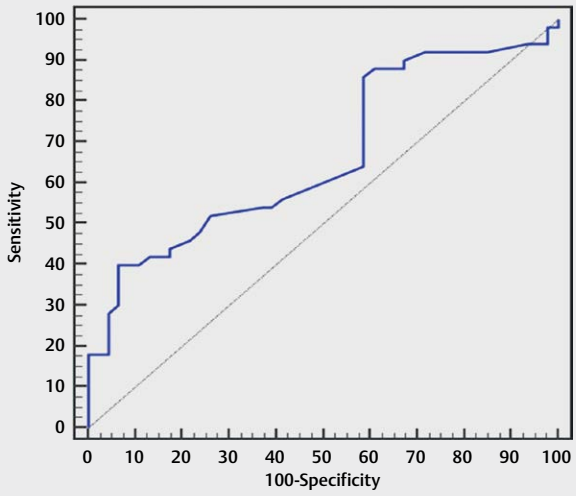
Psoriatic arthritis patients (n = 50)	Mean ± SD	Range
Duration of PsO (years)	11.79 ± 8.96	1–42
Duration of PsA (years)	5.97 ± 6.96	0.3–40
TJC	14.32 ± 9.76	3–38
SJC	6.08 ± 6.75	0–35
LEI	1.94 ± 1.58	0–6
LDI Basics	0.5 ± 0.53	0–1
PASI	9.68 ± 9.41	0–43
CPDAI	11.2 ± 2.66	5–15
DAPSA	40.03 ± 17.83	10.11–81
HAQ-DI	1.09 ± 0.58	0.25–2.63
PsAQoL	10.72 ± 3.13	7–20
SF-36	34.58 ± 11.18	0–52.64
DLQI	11.78 ± 6.68	0–30
RF (n = 4)	29.60 ± 12	19.20–40
CRP	7.57 ± 7.26	0.8–33.9

PsO: Psoriasis, PsA: Psoriatic arthritis, TJC: tender joint count, SJC: swollen joint count, LEI: Leeds enthesits index, LDI: Leeds dactylitis index, PASI: Psoriasis Area and Severity Index, DAPSA: Disease Activity index for Psoriatic Arthritis, CPDAI :Composite Psoriatic Disease Activity Index, HAQ-DI: Health Assessment Questionnaire Standard Disability Index, PsAQoL: Psoriatic Arthritis QoL, SF-36:Short Form Health Survey, DLQI: Dermatology Life Quality Index, RF: Rheumatoid Factor, CRP: C-reactive protein.



▶ **Fig. 1** Serum IL-23 levels in PsA and control groups.

(16–65 years), while 22 females (47.8 %) and 24 males (54 %) with a mean age of 42.15 ± 10.50 years (22–69 years) constituted the control group. There were no significant differences with regards to age ($p = 0.790$) or sex ($p = 0.858$).



▶ **Fig. 2** ROC curve demonstrating the sensitivity and specificity of IL-23 in differentiation between patients and controls.

▶ **Table 2** Correlation between serum IL-23 and activity indices, physical function and QoL of the studied PsA patients.

	Serum IL-23	
	r_s	*p*
CPDAI	0.317 *	0.025 *
DAPSA	0.458 *	0.001 *
PASI	0.103	0.476
HAQ-DI	0.234	0.103
SF-36	0.094	0.515
PsAQoL	0.009	0.949
DLQI	0.175	0.225

rs: Spearman coefficient * : Statistically significant at p ≤ 0.05 IL-23: Interleukin 23, CPDAI: Composite Psoriatic Disease Activity Index, DAPSA: Disease Activity index for Psoriatic Arthritis, PASI: Psoriasis Area and Severity Index HAQ-DI: Health Assessment Questionnaire Standard Disability Index, SF-36: Short Form Health Survey, PsAQoL: Psoriatic Arthritis QoL, DLQI: Dermatology Life Quality Index

- The mean BMI of the patients and the control participants were 29.19 ± 4.96 and 28.14 ± 3.16 kg/m^2 respectively, with no statistically significant difference *(p = 0.220)*.
- ▶ **Table 1** demonstrates the disease characteristics of PsA patients.
- Regarding medications, 40 PsA patients (80 %) were on methotrexate, 2 patients (4 %) were treated with biologic agents (TNF-α inhibitor: adalimumab and IL-17 inhibitor: secukinumab), 14 patients (30.4 %) were on sulphasalazine and one patient (2.3 %) was on leflunamide 20 mg.

- The IL-23 serum level was significantly higher in PsA patients: (median (min-max) (48.41 (34.17–114.5) pg/ml) than the controls (44.08 (34.68–57.63) pg/ml) ($p = 0.006$ *) (U = 773.000) based on the Mann-Whitney test (▶ **Fig. 1**).
- The serum IL-23 level cut-off value was 47.39 pg/ml. IL-23 showed a specificity of 73.91 % and a sensitivity of 52 %, as demonstrated by ROC curve analysis. The number of IL-23-positive PsA patients was 26 (52 %) (▶ **Fig. 2**).
- There was no significant difference in the mean level of IL-23 between both sexes (males (51.23 ± 16.08) and females (50.49 ± 11.04) ($p = 0.697$).
- There were significant positive correlations of serum IL-23 levels with both CPDAI and DAPSA, while no significant correlations were detected with PASI, DLQI, HAQ-DI, SF-36 and PsAQoL (▶ **Table 2**).
- There was a significant difference in IL-23 levels between PsA patients with different categories of DAPSA (p = 0.007). The highest level was detected in patients with HDA (54.40 ± 15.05 pg/ml). Additionally, IL-23 serum levels showed a significant difference with skin severity grades presented by the PASI score ($p = 0.015$). The highest level was detected in patients with severe skin affection (60.87 ± 20.41) (▶ **Table 3**).
- Correlations between skin disease severity (PASI), PsA disease activity (DAPSA and CPDAI) and both HAQ-DI and QoL indices (DLQI, PsAQoL and SF-36) revealed significant correlations between the parameters in both categories except between HAQ-DI and DAPSA ($p = 0.055$) (▶ **Table 4**).

▶ **Table 3** Comparison of IL-23 serum level among the different categories of PsA disease activity and grades of PsO skin severity.

	N	Serum IL-23	H	*P*
		Mean ± SD		
DAPSA				
LDA (≤ 14)	**2**	41.53 ± 1.80		
MDA (≤ 28)	**14**	43.69 ± 6.87	9.967 *	0.007 *
HDA (> 28)	**34**	54.40 ± 15.05		
PASI				
Mild (< 7)	**25**	49.52 ± 9.96		
Moderate (7–12)	**13**	44.31 ± 7.36	8.459 *	0.015 *
Severe (> 12)	**12**	60.87 ± 20.41		

H: for Kruskal Wallis test * : Statistically significant at p ≤ 0.05 IL-23:Interleukin, PASI: Psoriasis Area and Severity Index, DAPSA: Disease Activity index for Psoriatic Arthritis, LDA: low disease activity, MDA: medium disease activity, HDA: high disease activity

Discussion

The demographic and clinical characteristics of the PsA patients in the current study were comparable to those of the participants in a previous study of Egyptian SpA patients [32]. In agreement with our findings, a sex ratio of SpA in favour of males was reported in Japanese and Greek studies [33–34].

The increased serum level of IL-23 in PsA patients compared to the levels in controls probably reflects the contribution of IL-23 to the pathogenesis of PsA via the IL-23/IL-17 axis, which ultimately leads to psoriatic plaques, pannus formation, joint erosion and new bone formation [2, 35, 36]. In this context several studies have found elevated serum IL-23 levels in patients with SpA, PsO and PsA [37–42]. Therefore, close control of inflammation by anti-IL-23 drugs may turn off the disease activity and consequently the structural damage [5, 9, 10, 43].

In contrast to previous results, many researchers found no elevation in the serum level of IL-23 in SpA patients, including patients with PsA [44–45].

Moreover, serum IL-23 showed a significant positive correlation with PsA disease activity indices (DAPSA and CPDAI) and an increase in the IL-23 level with increased DAPSA grades (concerned mainly with articular involvement). These findings suggest the involvement of IL-23 in articular inflammation. Increased IL-23 serum levels with increased PASI grades (mild, moderate and severe) without a significant correlation with PASI score suggest that this elevation might be an epiphenomenon associated with increased skin inflammation.

The epiphenomenon hypothesis in SpA was suggested by McGonagle et al. as an explanation for synovitis in the context of SpA, as it may be secondary to entheseal inflammation due to growth factors

▶ **Table 4** Correlations between PsO disease activity indices and both physical function and QoL.

	HAQ-DI		DLQI		PsAQoL		SF-36	
	r_s	*p*	r_s	*p*	r_s	*p*	r_s	*p*
PASI	0.401 *	0.004 *	0.728 *	< 0.001 *	0.615 *	< 0.001 *	− 0.379 *	0.007 *
CPDAI	0.457 *	0.001 *	0.754 *	< 0.001 *	0.718 *	< 0.001 *	− 0.515 *	< 0.001 *
DAPSA	0.274	0.055	0.410 *	0.003 *	0.438 *	0.001 *	− 0.287 *	0.043 *

r_s: Spearman coefficient * : Statistically significant at p ≤ 0.05 PASI: Psoriasis Area and Severity Index, CPDAI: Composite Psoriatic Disease Activity Index, DAPSA: Disease Activity index for Psoriatic Arthritis, HAQ-DI: Health Assessment Questionnaire Standard Disability Index, DLQI: Dermatology Life Quality Index PsAQoL: Psoriatic Arthritis QoL, SF-36: Short Form Health Survey.

and proinflammatory cytokines from the enthesitis [46, 47]. In contrast to our results, many studies have shown a significant positive correlation between serum IL-23 level and PASI score [48–49].

However, apart from DAPSA, the psoriatic disease activity indices were positively correlated with the HAQ-DI score. Although these indices reflect the current inflammatory state of PsA, the representation of the involved tissues differs among them. DAPSA reflects mainly the state of articular involvement while CPDAI reflects articular, skin and periarticular structure involvement, i. e., the latter is more comprehensive in representing the tissues needed for task performance (HAQ-DI) than the former (only articular). This difference may be a possible explanation of our results. In this context, Kerschbaumer et al. adopted the uni-dimensional (concerned with articular involvement only) versus multi-dimensional disease activity assessment (peripheral joints, skin, enthesitis, dactylitis, and spinal disease) [50].

Moreover, an increase in the extent and severity of skin involvement (PASI) might have a negative impact on activities of daily living (ADLs) (HAQ-DI) because it might limit the activity of patients especially outdoors, thus influencing some ADLs. Furthermore, the patients might refrain from performing many daily tasks due to depression and/or anxiety resulting from disfigurement and discomfort due to skin inflammation.

On the other hand, all QoL indices were found to be negatively influenced by increased psoriatic disease activity including DAPSA. This finding may be explained by the fact that QoL indices reflect the standard QoL the patient is looking forward to attaining or achieving according to his or her cultural and/or personal characteristics [51–52].

In this context, health related QoL (HR-QoL) indices are designed to reflect the influence of a given disease on a patient's QoL. Thus, it is conceivable that the high disease activity indices can lead to decreased QoL. This process may occur irrespective of the functional status of patients, which may be influenced (in addition to disease activity) by the nature of the task, socioeconomic status and the extent of family/caregiver support or even the inherent nature of the instrument used to assess functional status. In this context, a specific version of the HAQ-DI designed for use in PsA patients was found to not be suitable for determining disability associated with the disease [53]. Taylor further observed that the HAQ-DI was not a fair measure of the activities affected in all subsets of PsA patients [54].

Our findings generally agree with those of Borman et al. who demonstrated the negative impact of arthritis and inflammation on QoL [51]. Likewise, PsA patients had a poorer QoL and worse functional status due to joint inflammation and high disease activity than those with the skin disease only [55–56].

In our study, there were no correlations between the serum IL-23 level and either the QoL indices or the HAQ-DI score, despite being positively correlated with disease activity indices. This lack of correlation may be because psoriatic disease (skin and joints) results from an interplay between several pathogenetic mechanisms involving several cytokines, including IL-23 [57–59]. All of the cytokines contribute to the disease activity in different degrees. Thus, IL-23 is just one contributor and it is plausible that it shares its role in disease activity, while the disease activity (combined effects of all pathogenetic mechanisms) was correlated with HAQ-DI and QoL.

In accordance with our results, Duruöz et al. found no significant correlation between serum levels of either IL-17 and IL-23 and PsAQoL [60].

Moreover, it was mentioned in a clinical study that DLQI is a patient-reported outcome and is subjected to personal variation [61]. However, a reduction in the mean DLQI and a PASI score of 75 or 90 were observed with treatment with anti-IL-23 biologics such as ustekinumab [24, 36].

Finally, in view of the current results, it can be assumed that IL-23 may be considered a biomarker of psoriatic disease activity and not a biomarker for disability or QoL.

Conclusions

Serum IL-23 levels were elevated in PsA patients. Serum IL-23 can be a useful marker of joint activity or skin severity but not a marker of QoL or functional status. In the studied PsA patients, increased disease activity (articular and/or dermal) was associated with low physical functioning and worse QoL; thus, controlling psoriatic disease activity is mandatory to improve QoL and physical function.

Acknowledgments

I gratefully appreciate all patients who participated and cooperated in this study, without them, this work would not have been possible.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors declare that they have no conflict of interest.

References

[1] Farrag DA, Asaad MK, Ghobrial CK. Evaluation of IL-34 in psoriasis and psoriatic arthritis patients: Correlation with disease activity and severity. Egypt Rheumatol 2017; 39: 25–31

[2] McInnes IB, Sieper J, Braun J et al. Efficacy and safety of secukinumab, a fully human anti-interleukin-17A monoclonal antibody, in patients with moderate-to-severe psoriatic arthritis: a 24-week, randomised, double-blind, placebo-controlled, phase II proof-of-concept trial. Ann Rheum Dis 2014; 73: 349–356

[3] Piaserico S, Gisondi P, Amerio P et al. Validation and field performance of the Italian version of the psoriatic arthritis screening and evaluation (PASE) questionnaire. Acta Derm Venereol 2016; 96: 96–101

[4] Gheita TA, Azkalany GS, Kenawy SA et al. Bone scintigraphy in axial seronegative spondyloarthritis patients: role in detection of subclinical peripheral arthritis and disease activity. Int J Rheum Dis 2015; 18: 553–559

[5] Mumtaz A, Gallagher P, Kirby B et al. Development of a preliminary composite disease activity index in psoriatic arthritis. Ann Rheum Dis 2011; 70: 272–277

[6] Orbai AM, De Wit M, Mease P et al. International patient and physician consensus on a psoriatic arthritis core outcome set for clinical trials. Ann Rheum Dis 2017; 76: 673–680

[7] Rudwaleit Mv, Van Der Heijde D, Landewé R et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis 2011; 70: 25–31

[8] van der Heijde D, Sieper J, Maksymowych WP et al. 2010 Update of the international ASAS recommendations for the use of anti-TNF agents in patients with axial spondyloarthritis. Ann Rheum Dis 2011; 70: 905–908

[9] Aletaha D, Alasti F, Smolen J. Disease activity states of the DAPSA, a psoriatic arthritis specific instrument, are valid against functional status and structural progression. Ann Rheum Dis 2017; 76: 418–421

[10] Schoels MM, Aletaha D, Alasti F et al. Disease activity in psoriatic arthritis (PsA): defining remission and treatment success using the DAPSA score. Ann Rheum Dis 2016; 75: 811–818

[11] Mease P, Antoni C, Gladman D et al. Psoriatic arthritis assessment tools in clinical trials. Ann Rheum Dis 2005; 64 (suppl 2): ii49–ii54

[12] Alsheikh MM, El-Shafey AM, Gawish HH et al. Serum interleukin-23 level in rheumatoid arthritis patients: Relation to disease activity and severity. Egypt Rheumatol 2018; 41: 99–103

[13] Reinhardt A, Yevsa T, Worbs T et al. Interleukin-23–dependent γ/δ T cells produce interleukin-17 and accumulate in the enthesis, aortic valve, and ciliary body in mice. Arthritis Rheumatol 2016; 68: 2476–2486

[14] Selim ZI, Rashad SM, Abdelaziz MM et al. Interleukin-34 in the Serum and Synovial Fluid of Rheumatoid Arthritis Patients: Relation to Disease Activity and Radiographic Damage. Aktuelle Rheumatol 2019; 58: 65–70

[15] Hadidi HE, Bahaa G, Gheita T et al. Involvement of IL-23 in psoriasis and psoriatic arthritis patients: possible role in pathogenesis. J Egypt wom Dermatol soc 2008; 5: 70–76

[16] Gómez-García F, Epstein D, Isla-Tejera B et al. Short-term efficacy and safety of new biological agents targeting the interleukin-23–T helper 17 pathway for moderate-to-severe plaque psoriasis: a systematic review and network meta-analysis. Br J Dermatol 2017; 176: 594–603

[17] Raychaudhuri SP, Raychaudhuri SK. IL-23/IL-17 axis in spondyloarthritis-bench to bedside. Clin Rheumatol 2016; 35: 1437–1441

[18] McKenna SP, Doward LC, Whalley D et al. Development of the PsAQoL: a quality of life instrument specific to psoriatic arthritis. Ann Rheum Dis 2004; 63: 162–169

[19] Taylor W, Gladman D, Helliwell P et al. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 2006; 54: 2665–2673

[20] Turconi G, Guarcello M, Maccarini L et al. BMI values and other anthropometric and functional measurements as predictors of obesity in a selected group of adolescents. Eur J Nutr 2006; 45: 136–143

[21] Faustini F, Simon D, Oliveira I et al. Subclinical joint inflammation in patients with psoriasis without concomitant psoriatic arthritis: a cross-sectional and longitudinal analysis. Ann Rheum Dis 2016; 75: 2068–2074

[22] Heuft-Dorenbosch L, Spoorenberg A, Van Tubergen A et al. Assessment of enthesitis in ankylosing spondylitis. Ann Rheum Dis 2003; 62: 127–132

[23] Mease PJ. Measures of psoriatic arthritis: Tender and Swollen Joint Assessment, Psoriasis Area and Severity Index (PASI), Nail Psoriasis Severity Index (NAPSI), Modified Nail Psoriasis Severity Index (mNAPSI), Mander/Newcastle Enthesitis Index (MEI), Leeds Enthesitis Index (LEI), Spondyloarthritis Research Consortium of Canada (SPARCC), Maastricht Ankylosing Spondylitis Enthesis Score (MASES), Leeds Dactylitis Index (LDI), Patient Global for Psoriatic Arthritis, Dermatology Life Quality Index (DLQI), Psoriatic Arthritis Quality of Life (PsAQOL), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Psoriatic Arthritis Response Criteria (PsARC), Psoriatic Arthritis Joint Activity Index (PsAJAI), Disease Activity in Psoriatic Arthritis (DAPSA), and Composite Psoriatic Disease Activity Index (CPDAI). Arthritis Care Res (Hoboken) 2011; 63 (Suppl 11): S64–S85

[24] Mattei PL, Corey KC, Kimball AB. Psoriasis Area Severity Index (PASI) and the Dermatology Life Quality Index (DLQI): the correlation between disease severity and psychological burden in patients treated with biological therapies. J Eur Acad Dermatol Venereol 2014; 28: 333–337

[25] Ibrahim SE, Helmi A, Yousef TM et al. Association of asymptomatic hyperuricemia and endothelial dysfunction in psoriatic arthritis. Egypt Rheumatol 2012; 34: 83–89

[26] Ibrahim SE, Morshedy NA, Farouk N et al. Anti-carbamylated protein antibodies in psoriatic arthritis patients: relation to disease activity, severity and ultrasonographic scores. Egypt Rheumatol 2018; 40: 17–21

[27] Helliwell PS, FitzGerald O, Fransen J et al. The development of candidate composite disease activity and responder indices for psoriatic arthritis (GRACE project). Ann Rheum Dis 2013; 72: 986–991

[28] Michelsen B, Diamantopoulos AP, Hammer HB et al. Ultrasonographic evaluation in psoriatic arthritis is of major importance in evaluating disease activity. Ann Rheum Dis 2016; 75: 2108–2113

[29] Poole CD, Conway P, Currie CJ. An evaluation of the association between C-reactive protein, the change in C-reactive protein over one year, and all-cause mortality in chronic immune-mediated inflammatory disease managed in UK general practice. Rheumatology (Oxford) 2009; 48: 78–82

[30] Bogliolo L, Alpini C, Caporali R et al. Antibodies to cyclic citrullinated peptides in psoriatic arthritis. J Rheumatol 2005; 32: 511–515

[31] ThermoFisher SCIENTIFIC. IL-23 Human ELISA Kit. Available from https://www.thermofisher.com/elisa/product/IL-23-Human-ELISA-Kit/BMS2023-3 [Accessed in: May, 2019].

[32] Abdelsalam A, Tharwat S, Almauty MA et al. Demographic, clinical and radiological characteristics of seronegative spondyloarthritis Egyptian patients: a rheumatology clinic experience in Mansoura. Egypt Rheumatol 2017; 39: 109–114

[33] Hukuda S, Minami M, Saito T et al. Spondyloarthropathies in Japan: nationwide questionnaire survey performed by the Japan Ankylosing Spondylitis Society. J Rheumatol 2001; 28: 554–559

[34] Trontzas P, Andrianakos A, Miyakis S et al. Seronegative spondyloarthropathies in Greece: a population-based study of prevalence, clinical pattern, and management. The ESORDIG study. Clin Rheumatol 2005; 24: 583–589

[35] Kavanaugh A, Puig L, Gottlieb AB et al. Efficacy and safety of ustekinumab in psoriatic arthritis patients with peripheral arthritis and physician-reported spondylitis: post-hoc analyses from two phase III, multicentre, double-blind, placebo-controlled studies (PSUMMIT-1/PSUMMIT-2). Ann Rheum Dis 2016; 75: 1984–1988

[36] Gottlieb A, Menter A, Mendelsohn A et al. Ustekinumab, a human interleukin 12/23 monoclonal antibody, for psoriatic arthritis: randomised, double-blind, placebo-controlled, crossover trial. Lancet. 2009; 373: 633–640

[37] Przepiera-Bedzak H, Fischer K, Brzosko M. Serum IL-6 and IL-23 Levels and Their Correlation with Angiogenic Cytokines and Disease Activity in Ankylosing Spondylitis, Psoriatic Arthritis, and SAPHO Syndrome. Mediators Inflamm 2015; 2015: 785705

[38] Chen WS, Chang YS, Lin KC et al. Association of serum interleukin-17 and interleukin-23 levels with disease activity in Chinese patients with ankylosing spondylitis. J Chin Med Assoc 2012; 75: 303–308

[39] Gheita TA, El G II, El-Fishawy HS et al. Involvement of IL-23 in enteropathic arthritis patients with inflammatory bowel disease: preliminary results. Clin Rheumatol 2014; 33: 713–717

[40] Wendling D, Cedoz JP, Racadot E. Serum and synovial fluid levels of p40 IL12/23 in spondyloarthropathy patients. Clin Rheumatol 2009; 28: 187–190

[41] Elghandour TM, Youssef Sel S, Aly DG et al. Effect of Narrow Band Ultraviolet B Therapy versus Methotrexate on Serum Levels of Interleukin-17 and Interleukin-23 in Egyptian Patients with Severe Psoriasis. Dermatol Res Pract 2013; 2013: 618269

[42] Toussirot E. The IL23/Th17 pathway as a therapeutic target in chronic inflammatory diseases. Inflamm Allergy Drug Targets 2012; 11: 159–168

[43] Iannone F, Santo L, Bucci R et al. Drug survival and effectiveness of ustekinumab in patients with psoriatic arthritis. Real-life data from the biologic Apulian registry (BIOPURE). Clin Rheumatol 2018; 37: 667–675

[44] Melis L, Vandooren B, Kruithof E et al. Systemic levels of IL-23 are strongly associated with disease activity in rheumatoid arthritis but not spondyloarthritis. Ann Rheum Dis 2010; 69: 618–623

[45] Mrabet D, Laadhar L, Sahli H et al. Synovial fluid and serum levels of IL-17, IL-23, and CCL-20 in rheumatoid arthritis and psoriatic arthritis: a Tunisian cross-sectional study. Rheumatol Int 2013; 33: 265–266

[46] Kerschbaumer A, Fenzl KH, Erlacher L et al. An overview of psoriatic arthritis – epidemiology, clinical features, pathophysiology and novel treatment targets. Wiener klinische Wochenschrift 2016; 128: 791–795

[47] McGonagle D, Gibbon W, Emery P. Classification of inflammatory arthritis by enthesitis. Lancet 1998; 352: 1137–1140

[48] Coimbra S, Oliveira H, Reis F et al. Interleukin (IL)-22, IL-17, IL-23, IL-8, vascular endothelial growth factor and tumour necrosis factor-alpha levels in patients with psoriasis before, during and after psoralen-ultraviolet A and narrowband ultraviolet B therapy. Br J Dermatol 2010; 163: 1282–1290

[49] Sofen H, Smith S, Matheson RT et al. Guselkumab (an IL-23-specific mAb) demonstrates clinical and molecular response in patients with moderate-to-severe psoriasis. J Allergy Clin Immunol 2014; 133: 1032–1040

[50] Kerschbaumer A, Smolen JS, Aletaha D. Disease activity assessment in patients with psoriatic arthritis. Best Pract Res Clin Rheumatol 2018; 32: 401–414

[51] Borman P, Toy GG, Babaoğlu S et al. A comparative evaluation of quality of life and life satisfaction in patients with psoriatic and rheumatoid arthritis. Clin Rheumatol 2007; 26: 330–334

[52] Husted JA, Gladman DD, Farewell VT et al. Health-related quality of life of patients with psoriatic arthritis: a comparison with patients with rheumatoid arthritis. Arthritis Rheum 2001; 45: 151–158

[53] Husted J, Gladman D, Long J et al. A modified version of the Health Assessment Questionnaire (HAQ) for psoriatic arthritis. Clin Exp Rheumatol 1995; 13: 439–443

[54] Taylor WJ. Assessment of outcome in psoriatic arthritis. Curr Opin Rheumatol 2004; 16: 350–356

[55] Tezel N, Yilmaz Tasdelen O, Bodur H et al. Is the health-related quality of life and functional status of patients with psoriatic arthritis worse than that of patients with psoriasis alone? Int J Rheum Dis 2015; 18: 63–69

[56] Rosen CF, Mussani F, Chandran V et al. Patients with psoriatic arthritis have worse quality of life than those with psoriasis alone. Rheumatology (Oxford) 2012; 51: 571–576

[57] FitzGerald O, Winchester R. Psoriatic arthritis: from pathogenesis to therapy. Arthritis Res Ther 2009; 11: 214

[58] Chimenti MS, Triggianese P, De Martino E et al. An update on pathogenesis of psoriatic arthritis and potential therapeutic targets. Expert Rev Clin Immunol 2019; 1–14

[59] Arican O, Aral M, Sasmaz S et al. Serum levels of TNF-alpha, IFN-gamma, IL-6, IL-8, IL-12, IL-17, and IL-18 in patients with active psoriasis and correlation with disease severity. Mediators Inflamm 2005; 2005: 273–279

[60] Duruöz M, Uçar Ü, Guvenç Y et al. AB0117 Evaluation of serum levels of interleukin (il)-17a, il-17b, il-17c, il-17f and il-23 levels in psoriatic arthritis. Ann Rheum Dis 2013; 72 (Suppl 3): A821–A821

[61] Blauvelt A, Papp KA, Griffiths CE et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. J Am Acad Dermatol 2017; 76: 405–417