

Original article

PsART-ID inception cohort: clinical characteristics, treatment choices and outcomes of patients with psoriatic arthritis

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Abstract

Objectives. Our aim is to understand clinical characteristics, real-life treatment strategies, outcomes of early PsA patients and determine the differences between the inception and established PsA cohorts.

Methods. PsArt-ID (*Psoriatic Arthritis- International Database*) is a multicentre registry. From that registry, patients with a diagnosis of PsA up to 6 months were classified as the inception cohort ($n=388$). Two periods were identified for the established cohort: Patients with PsA diagnosis within 5–10 years ($n=328$), ≥ 10 years ($n=326$). Demographic, clinical characteristics, treatment strategies, outcomes were determined for the inception cohort and compared with the established cohorts.

Results. The mean (s.d.) age of the inception cohort was 44.7 (13.3) and 167/388 (43.0%) of the patients were male. Polyarticular and mono-oligoarticular presentations were comparable in the inception and established cohorts. Axial involvement rate was higher in the cohort of patients with PsA ≥ 10 years compared with the inception cohort (34.8% vs 27.7%). As well as dactylitis and nail involvement ($P = 0.004$, $P = 0.001$ respectively). Both enthesitis,

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deformity rates were lower in the inception cohort. Overall, 13% of patients in the inception group had a deformity. MTX was the most commonly prescribed treatment for all cohorts with 10.7% of the early PsA patients were given anti-TNF agents after 16 months.

Conclusion. The real-life experience in PsA patients showed no significant differences in the disease pattern rates except for the axial involvement. The dactylitis, nail involvement rates had increased significantly after 10 years from the diagnosis and the enthesitis, deformity had an increasing trend over time.

Key words: psoriatic arthritis, inception cohort, early disease

Rheumatology key messages

- Characteristics of inception cohort patients indicate that early diagnosis is still an unmet need.
- Compared to the established cohort, inception cohort has important differences in certain disease manifestations.
- Anti-TNF agents are required in 10% of inception cohort patients after 16 months of follow-up.

Introduction

PsA is an inflammatory musculoskeletal disease associated with psoriasis. Initially Moll and Wright described five clinical subtypes (mono or oligoarthritis, polyarthritis, DIP joint predominant disease, psoriatic spondylitis, and/or sacroiliitis, and arthritis mutilans) that emphasize the heterogeneity of the PsA [1]. In addition, it is also characterized by various other manifestations such as, nail involvement, enthesitis, and dactylitis [2, 3]. Some of these manifestations are added over time as well as a change in patterns [4, 5]. As a result of either the use of different classification criteria or the pattern shifts over time; the manifestations and disease phenotypes reported in a wide range.

Our approach to patients may also differ with time. With the advances in the diagnostic tools and treatments, patients diagnosed at different decades may be treated differently. This shift over time may also impact the long terms outcomes, leading to a different patient population (usually with milder disease activity and better-controlled disease at a population level). In this study, we aimed to analyze the characteristics of an inception cohort of PsA population and the treatments in real life and compare with a patient population with the established disease in two different periods; with a disease duration of 5–10 years and ≥ 10 years.

Methods

Patient selection and data collection

PsArt-ID (Psoriatic Arthritis- International Database) is a multicentre registry that was initiated in Turkey in 2014, was extended to Canada in 2015 and Italy in 2018 [6, 7]. Methodology and the details of the registry were explained in detail previously [6]. Briefly, the diagnosis of PsA was based on the decision of the treating rheumatologist. Demographics and disease characteristics of psoriasis and PsA were documented at baseline

visit. Patient and physician-reported outcomes were collected in each visit.

Definition of the inception cohort: Patients with the diagnosis of PsA up to 6 months at recruitment were accepted as the inception cohort [$n=388/1734$ (22.4%)]. Within these, 186 patients had at least one follow-up visit to review the responses to initial treatment strategies. From this group, a subgroup ‘inception cohort with the follow-up’ was determined to contain patients who had not been treated with DMARDs >3 months for their psoriasis at recruitment, not to be confounded with psoriasis treatments that may also affect PsA outcomes ($n=167/186$).

Definition of the established cohort: Two periods were identified for the established cohort: Patients with PsA diagnosis within 5–10 years ($n=328$) and ≥ 10 years ($n=326$) at the time of recruitment.

Assessments and treatment strategies

Baseline demographics, clinical characteristics (psoriasis duration, PsA subtypes, presence and type of nail involvement, dactylitis, enthesitis, and joint deformity) were analyzed, according to the subgroups (inception and established). The Leeds Enthesis Index (LEI) was used to assess enthesitis on the exam [8]. The presence of axial involvement was mainly based on the physician’s assessment and in nearly 40% of the patients, the involvement was radiographically supported.

Treatment strategies were also collected. Overall 338/388 patients in the inception cohort, 285/328 and 308/326 patients from the established cohorts with PsA diagnosis within 5–10 years and ≥ 10 years were included to assess treatment strategies: Baseline medication list of the inception cohort and last visit/ever used medication lists of established cohorts were collected and baseline medication list of the inception cohort and last visit medication list of the established cohorts were compared. For the ‘the inception cohort with the follow-up’ ($n=167$) baseline and last visit

medication lists were collected and medication changes were determined.

ESR, CRP levels, baseline Minimal Disease Activity (MDA) parameters, and the BASDAI were collected. To understand the change in the outcome of the inception cohort patients, both baseline and last visit MDA parameters of the inception cohort were collected and analyzed at follow up [9, 10].

This study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics boards [Hacettepe University Ethics Board, Ankara; Ottawa Health Science Network Research Ethics Board, Ottawa; Sacro Cuore Don Calabria Hospital, Italy] and informed consent was obtained from all patients before data collection.

Statistical analysis

Statistical Package for Social Sciences software (SPSS version 22.0, IBM® corp., Armonk, NY, USA) was used to conduct all statistical analyses. Normal distribution was tested both visually (histogram, probability plots) and analytically (Kolmogorov-Smirnov skewness and kurtosis). Results were presented as mean ((s.d.) or median [interquartile range (IQR)] for continuous variables and as percentages (frequencies) for categorical variables. Independent continuous variables were analyzed using the Student's *t* test or Mann-Whitney *U* test according to the distribution status. Dependent continuous variables were analyzed using the Paired Sample *t* test or Wilcoxon Test according to the distribution status. Categorical variables were compared using either the χ^2 test or Fisher's exact test where appropriate. We also performed logistic regression to determine independent predictors that may be associated with deformities. Age (at the time of registration) and gender-adjusted final regression model included; nail involvement, presence of dactylitis, DIP joint, and axial involvement.

Results

Patient characteristics

Baseline characteristics of the inception cohort

The mean (s.d.) age was 44.7 (13.3) years and 167/388 (43%) patients were male with a mean (s.d.) psoriasis duration of 11.3 (10.5) years. Around half of the patients were non-smokers and the mean (s.d.) of BMI was 28 (4.9) (Table 1). Polyarticular and oligoarticular phenotypes were 41.9% and 38.8%, respectively and 27.7% of patients had axial disease. Twenty patients (5.2%) had monoarticular involvement and DIP arthritis was found in 13.2% of patients. The mean (s.d.) swollen joint count (SJC) and the tender joint counts (TJC) were 2.9 (3.6) and 4.9 (5) respectively. Nail involvement and dactylitis were found in 45.6% and 22.7% of the patients and enthesitis was detected in 17.4% of the patients (Table 1). Baseline demographics and disease

parameters of the inception cohort patients with and without follow-up were also given in [Supplementary Table S1](#), available at *Rheumatology* online.

Joint deformity was observed in 41/314 (13.1%) of patients of the inception cohort. When factors predicting the deformity were analyzed; the analysis revealed that deformity increased with the DIP joint involvement [OR 3.35 (1.45–7.77), *P* = 0.005 and with the presence of dactylitis [OR 3.55 (1.68–7.52), *P* = 0.001] in this group.

The differences in the baseline characteristics of the inception cohort and the established cohorts

As expected, the inception cohort had a younger population with a mean (s.d.) age [44.7 (13.3) vs 48.8 (13.3)/51.9 (12.6)] and less psoriasis duration [11.3 (10.5) years than both established cohorts with PsA diagnosis of 5–10 years (15.6 (10.8)) and ≥ 10 years (22.9 (11.4) (*P* < 0.001 for all). The frequency of male patients was higher in the inception cohort (43.0%) then the diagnosis of 5–10 years (33.2%) and ≥ 10 years 37.4%) (*P* < 0.001) (Table 1).

Regarding disease phenotype, rates of patients with polyarticular (41.9% vs 41.9%/36.6%) and mono-oligoarticular (44.0% vs 37%/35.4%) disease were similar between the inception and established cohorts. However axial involvement rates were higher in the established cohort with a PsA diagnosis ≥ 10 years compared with the inception cohort (34.8% vs 27.7%). Also, DIP involvement showed a trend during the disease course (Table 1, [Supplementary Fig. S1](#), available at *Rheumatology* online).

In terms of other disease manifestations, dactylitis and nail involvement were significantly higher after 10 years from the diagnosis. Moreover, both enthesitis and deformity rates were significantly lower in the inception cohort compared with both established cohorts (Table 1, [Supplementary Fig. S2](#), available at *Rheumatology* online). Most of the parameters showing disease activity indicated higher disease activity in the inception cohort (Table 1).

Treatment strategy

Baseline treatment choices of the inception cohort

MTX (71.3%) was the most commonly prescribed medication followed by corticosteroids (CS) (39.6%) and sulfasalazine (SAZ) (22.2%). In 14.2% of patients no DMARDs were initiated (Table 2).

Differences of treatment choices between the inception and the established cohorts

In each group, MTX was the most commonly prescribed medication. MTX, SAZ, and corticosteroids (CS) were chosen at a significantly higher rate in the inception cohort compared with both established cohorts. However, Leflunomide (LEF) is a less frequent choice for the inception cohort patients (1.5%) compared with both established cohorts with PsA diagnosis of 5–10 years (20.7%) and ≥ 10 years (19.8%) (*P* < 0.001 for all) (Table 2).

TABLE 1 Baseline demographic characteristics of patients in the inception and established cohorts

Variables	Inception Cohort <i>n</i> = 388	Established Cohort with PsA diagnosis ≤ 5–<10 years <i>n</i> = 328	<i>P</i> value ^e	Established Cohort with PsA diagnosis ≥ 10 years <i>n</i> = 326	<i>P</i> value ^e
Age, mean (s.d.)	44.7 (13.3)	48.8 (13.3)	<0.001	51.9 (12.6)	<0.001
Male gender, <i>n</i> (%)	167 (43.0)	109 (33.2)	0.007	122 (37.4)	0.128
Education years, mean (s.d.)	8.93 (4.5)	9.8 (4.7)	0.011	10.1 (4.8)	0.001
Smoking					
Non-smoker, <i>n</i> (%)	211/377 (56)	182/309 (58.9)	0.440 (ever vs never)	164/311 (52.7)	0.396 (ever vs never)
Current smoker, <i>n</i> (%)	100/377 (26.5)	62/309 (20.1)		66/311 (21.2)	
Ex-smoker, <i>n</i> (%)	66/377 (17.5)	65/308 (21)		81/311 (26)	
BMI, mean (s.d.)	28 (4.9)	28.2 (5.7)	0.966	28.4 (5.4)	0.502
Psoriasis duration (years), mean (s.d.)	11.3 (10.5)	15.6 (10.8)	<0.001	22.9 (11.4)	<0.001
Polyarthritis, <i>n</i> (%)	162/386 (41.9)	137/327 (41.9)	0.984	119/325 (36.6)	0.146
Oligoarthritis, <i>n</i> (%)	150/386 (38.8)	118/327 (36.1)	0.446	114/325 (35.1)	0.298
Axial disease, <i>n</i> (%)	107/386 (27.7)	82/327 (25.1)	0.425	113/325 (34.8)	0.043
Monoarthritis, <i>n</i> (%)	20/386 (5.2)	3/325 (0.9)	0.001	1/325 (0.3)	–
DIP involvement, <i>n</i> (%)	51/386 (13.2)	53/327 (16.2)	0.259	60/325 (18.5)	0.055
Nail involvement (ever), <i>n</i> (%)	176/386 (45.6)	150/328 (45.7)	0.971	189/326 (58)	0.001
Dactylitis (ever), <i>n</i> (%)	86/379 (22.7)	77/316 (24.4)	0.604	99/304 (32.6)	0.004
Enthesitis (ever), <i>n</i> (%)	65/373 (17.4)	93/304 (30.6)	<0.001	94/300 (31.4)	<0.001
Joint Deformity, <i>n</i> (%)	41/314 (13.1)	70/274 (25.5)	<0.001	101/269 (37.5)	<0.001
SJC (0–66), mean (s.d.)	2.9 (3.6)	1.7 (2.8)	<0.001	1.7 (3)	<0.001
TJC (0–68), mean (s.d.)	4.9 (5)	3.9 (4.9)	<0.001	3.9 (5.7)	<0.001
BSA, median (IQR)	5 (1–11)	1 (0–5)	<0.001	1 (0–5)	<0.001
ESR (mm/h), mean (s.d.)	28.2 (20.6)	23.7 (20)	0.001	23.7 (19.7)	0.002
CRP (mg/l), median (IQR)	7 (3–16.5)	3.4 (1–9)	<0.001	3 (1–10.5)	<0.001
HAQ (0–3), mean (s.d.)	0.86 (0.67)	0.79 (0.65)	0.251	0.86 (0.78)	0.400
BASDAI (0–100), mean (s.d.)	49.4 (24.4)	41.2 (23.9)	0.001	38.4 (24.9)	<0.001
VAS PGA (0–100), mean (s.d.)	46.9 (29)	33.8 (27.5)	<0.001	33.8 (27.9)	<0.001
VAS Pain (0–100), mean (s.d.)	55.9 (23.9)	41.9 (26.6)	<0.001	40.5 (28.5)	<0.001
Leeds Enthesitis Index, mean (s.d.)	0.13 (0.56)	0.24 (0.70)	0.026	0.24 (0.84)	0.100

SJC= Swollen Joint Count, TJC= Tender Joint Count, BSA= Body Surface Area; VAS PGA= Visual Analogue Scale Patient Global Assessment, VAS Pain= Visual Analogue Scale Pain, IQR=Interquartile range. ^eIn this table, *P* values were determined for continuous variables by using the Student's *t* test or Mann–Whitney *U* test according to the distribution status and for categorical variables by using either the χ^2 test or Fisher's exact test where appropriate.

Treatment strategy of the inception cohort with the follow-up

During a mean (s.d.) follow-up period of 16.4 (13.3) months, baseline and the follow-up treatment choices of this subgroup of the inception cohort were documented (Fig. 1). At baseline, MTX was again the most commonly prescribed medication in this group (*n* = 138/167) with a median (IQR) dose of 15 (3.12) milligrams (mg). In 46/167 (27.5%) of the patients, MTX was given as monotherapy and in 92/167 (55%) of them, MTX was combined either with corticosteroids or with other DMARDs. Overall MTX retention rate was 82.6% and median MTX retention was 40 (36–43) months. During the whole follow-up period, 18 (10.8%) patients were needed Anti-TNF agents. Further details of the treatment changes and the overall treatment

strategy can be found in (Supplementary Table S2, available at *Rheumatology* online).

Outcomes of the inception cohort with the follow-up

After a mean (s.d.) follow-up period of 15.9 (12.9) months, 44.3% of the inception cohort patients achieved MDA. The rate of patients who were in MDA at baseline and the last visit were 3.8% and 44.3% respectively. All measured physician and patient-reported outcomes improved at follow up (Table 3).

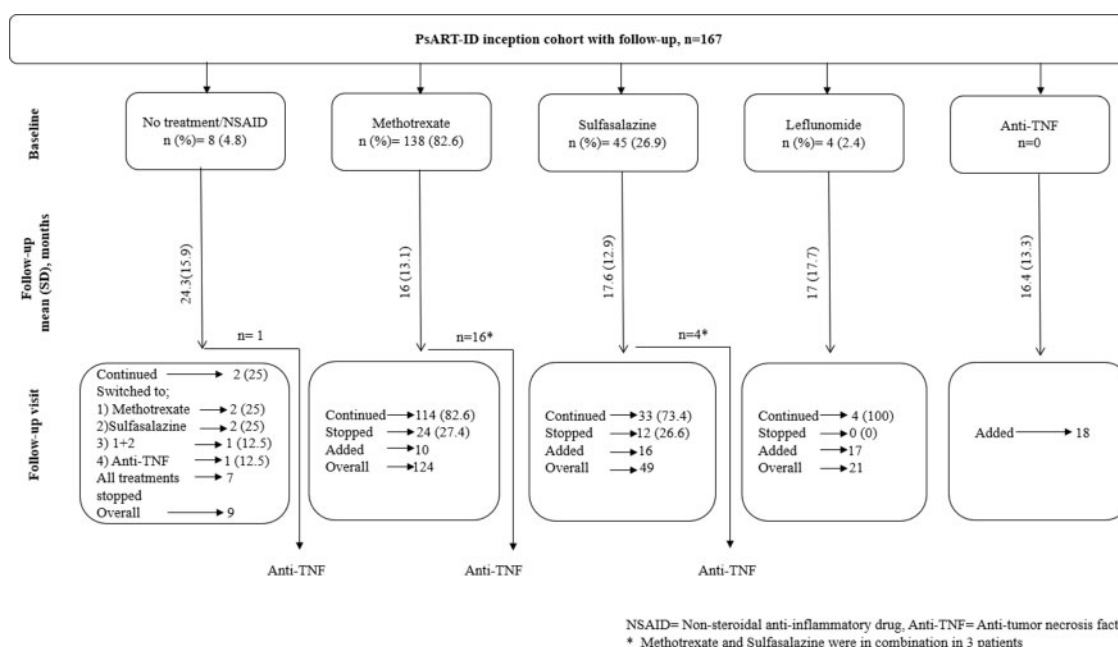
Discussion

To the best of our knowledge, this is the largest study that has shown the clinical characteristics, treatment strategies,

TABLE 2 Treatment choices of patients in inception (baseline) and established cohorts (at last visit and ever)

Treatment	Inception Cohort ⁿ = 338/388	Established Cohort with PsA diagnosis ≤ 5 – <10 years n= 285/328 ^b		P value ^{d,e}	Established Cohort with PsA diagnosis ≥ 10 years n= 308/326 ^b		P value ^{d,e}
		At last visit	Ever		At last visit	Ever	
No treatment/NSAIDs	48 (14.2)	37 (13)	7 (2.5)	0.659	41 (13.3)	12 (3.9)	0.836
MTX	241 (71.3)	165 (57.9)	262 (91.9)	0.001	164 (53.2)	281 (91.2)	<0.001
Sulfasalazine	75 (22.2)	43 (15.1)	121 (42.5)	0.024	44 (14.3)	134 (43.5)	0.010
Hydroxychloroquine	18 (5.3)	25 (8.8)	46 (16.1)	0.125	11 (3.6)	44 (14.3)	0.282
Leflunomide	5 (1.5)	59 (20.7)	112 (39.3)	<0.001	61 (19.8)	109 (35.4)	<0.001
Ciclosporin	4 (1.2)	3 (1.1)	16 (5.6)	^c	3 (1)	19 (6.2)	^c
Corticosteroids	134 (39.6)	50 (17.5)	112 (39.3)	<0.001	48 (15.6)	107 (34.7)	<0.001
Adalimumab	–	42 (14.8)	51 (18.1)	^c	43 (14)	58 (18.8)	^c
Etanercept	–	25 (8.8)	44 (15.4)	^c	41 (13.3)	74 (24)	^c
Infliximab	1 (0.3)	15 (5.3)	36 (12.6)	^c	14 (4.5)	40 (13)	^c
Secukinumab	1 (0.3)	5 (7.5)	5 (7.5)	^c	9 (9.3)	12 (3.9)	^c
Golimumab	1 (0.3)	13 (4.6)	14 (4.9)	^c	18 (5.8)	24 (7.8)	^c
Certolizumab	–	1 (1.5)	1 (1.5)	^c	–	1 (1)	^c

DMARD: Disease-modifying anti-rheumatic drugs. Data was given in number of patients (valid percent). ^aForty-four of the patients had been using DMARD for >3 months for their psoriasis and treatment information was lacking in 6 patients. ^bFrom the established cohort with PsA diagnosis within 5–10 years and ≥10 years, 43 and 18 patients had been using DMARD for >3 months for their psoriasis respectively. ^cThe numbers were small for analysis. ^dThe comparison was made between baseline treatment of the inception cohort and the treatment at last visit in the prevalent cohort. ^eIn this table, *P* values were determined by using either the χ^2 test or Fisher's exact test where appropriate.

Fig. 1 Baseline and the last visit treatment strategies of the inception cohort with follow-up

and outcomes of the early PsA patients in an inception cohort. There is no widely accepted definition of 'early PsA' in literature and there has been a debate whether to rely on the onset of symptoms or to choose the diagnosis date as the starting point. One approach is to accept the diagnosis date

for disease duration, as done in our study, since patients may have difficulties to remember the duration of symptoms as it usually has an insidious onset [11].

PsA can be a highly deforming and disabling condition [12]. Our study also showed that the deformity rate on

TABLE 3 Minimal disease activity parameters at baseline and follow-up

Variables	Baseline	Follow-up visit	P ^a
SJC (0–66), mean (s.d.)	3.1 (3.5)	1.2 (2.4)	<0.001
TJC (0–68), mean (s.d.)	5.1 (4.7)	3.0 (4.7)	<0.001
BSA, median (IQR)	10 (2.5–16)	3 (0–9)	<0.001
HAQ (0–3), mean (s.d.)	0.92 (0.62)	0.53 (0.69)	<0.001
VAS PGA (0–100), mean (s.d.)	52.9 (27.2)	32 (23.5)	<0.001
VAS Pain (0–100), mean (s.d.)	61.4 (21.3)	31.2 (23.3)	<0.001
Leeds Enthesitis Index, mean (s.d.)	0.09 (0.38)	0.03 (0.23)	0.112

SJC= Swollen Joint Count, TJC= Tender Joint Count, BSA= Body Surface Area, VAS PGA= Visual Analogue Scale Patient Global Assessment, VAS Pain= Visual Analogue Scale Pain, IQR=Interquartile range. ^aIn this table, *P* values were determined by using the Paired Sample *t* test or Wilcoxon Test according to the distribution status.

the physical exam was 13.1% in patients within 6 months of diagnosis. Moreover, we showed that DIP joint involvement and dactylitis are linked to deformities, the latter being supported by the literature. Dactylitis is a sign of severe disease and linked to disease progression [13, 14]. DIP involvement may be a reason for late diagnosis while this presentation can be confused with osteoarthritis. A study from an early arthritis clinic found that 27% of the patients had at least 1 joint erosion at presentation showing that the disease seems to be aggressive at an early stage [15]. Moreover, even a 6-month delay from symptom onset to the diagnosis is linked to the development of peripheral joint erosions and worse long-term outcomes [16]. These data support both the aggressive nature of the disease and the early diagnosis being still an unmet need [17].

Several studies have shown a change in clinical patterns in the course of PsA [18, 19]. We compared our early PsA patients with established PsA patients, therefore, indirectly, there was no significant change in disease patterns over time. All the studies that previously showed the pattern change are published between 1991–2003, the new treatment modalities that have come on board in the last decade may have changed this shift as well. Moreover, a study showed a pattern shift across patients, however, overall subtype rates did not show a remarkable difference after 5 years [5]. Therefore, new studies investigating the change in patterns over time within the same patients' follow up may reveal different results than the previous literature.

Although the joint pattern did not change over time in the current study, certain disease manifestations changed during time, such as dactylitis, nail involvement and axial disease. While the axial involvement rates were between 25–70% of patients with longstanding disease in the previous literature, patients with early disease had less axial involvement (5–28%) [19–27]. These suggest that axial disease typically a late disease finding in PsA patients which complies with our finding of significantly higher axial involvement 10 years after diagnosis [28]. We also found that enthesitis is more frequent in established disease, which is in parallel to the data

from University of Toronto Psoriatic Arthritis Program registry where 14.5% of the patients having enthesitis at the registration compared with 35.9% at follow-up [29]. Further studies using imaging modalities can help to clarify the underlying lesions in early vs established disease [17].

EULAR, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and ACR have treatment recommendations for PsA patients [30–32]. In our early PsA arthritis cohort, MTX is still an anchor synthetic DMARD, either as monotherapy or as a combination with other csDMARDs, particularly SAZ. Interestingly, even the LEF is the agent that was shown as effective and safe in a placebo-controlled trial, clinicians are choosing LEF during the disease course instead of using as first-line [33]. When the early PsA patients were followed 16 months, 10% required biologics, which was mostly limited to anti-TNF treatments at the time of the recruitment. Similar to our results, TICOPA trial showed that 6.7% of patients in the standard care arm were on biologic DMARDs by first year [34]. Furthermore, in the established cohorts of PsA diagnosis 5–10 years and ≥10 years, 33.6% and 37.6% of the patients were on Anti-TNF treatments in their last visit respectively.

Our study showed both the clinical characteristics, treatment strategies and outcome in a relatively large inception cohort compared with the previous reports. The limitations of this study include: We did not follow the same patients to see pattern changes over time and the comparison was made between the inception and established cohorts. Also lacking supportive radiological data on clinical categorization in every patient is another limitation. Since our follow up is only 16 months, it is not possible to share the effect of the treatment patterns on responses over time.

In conclusion, the real-life experience of PsA patients showed differences in disease characteristics between the inception and established cohorts. Axial involvement is increasing over time. Nail involvement and dactylitis rates have a significant trend after 10 years of diagnosis and enthesitis is a less frequent finding in the early PsA. As a remarkable finding, the deformity is as high as

13% and still has an increasing rate in the disease course. Moreover, MTX is the most selected first-line agent and in almost 10% of patients an anti-TNF treatment was added during ~16 months of follow-up.

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Supplementary data

Supplementary data are available at *Rheumatology* online.

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