ORIGINAL RESEARCH article

Juvenile psoriatic arthritis patients at Tripoli Children's Hospital

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Abstract: Juvenile psoriatic arthritis (JPsA) is a relatively rare condition in childhood, as it represents about 5.0% of the whole Juvenile Idiopathic Arthritis (JIA). There are fewer reports describing the characteristics and outcome of patients with JPsA. The purpose of this study is to determine characteristic features, treatment, and patients' outcomes of JPsA among Libyan children and to compare the findings with other populations worldwide. Medical records of all the patients who met the Vancouver criteria (definite or probable) or ILAR criteria for JPsA, and who were followed up at the Pediatric Rheumatology Clinic in Tripoli Children's Hospital between 2001 and 2020, were retrospectively reviewed, and data were analyzed. The study included a total of 12 cases of JPsA over the study period; all were met Vancouver criteria for juvenile PsA: 42.0% not fulfill ILAR criteria. JPsA represents 4.8% of total JIA cases with a male-to-female ratio of 1: 1, and a mean age of 10.2±6.5 years. The mean age of disease onset was 5.8±5.3 years. Polyarticular pattern was the predominant (58.3%), ANA and HLAB27 were positive among 33.3% and 12.5% of the studied cases, psoriasis in 33.3% of cases, Uveitis in 30.0%, uveitis complications were occurred in one patient. Biologic drugs were used in 25.0% of the patients. The study concludes that the characteristics of JPsA in Libyan children are different from those of other countries regarding a higher frequency of uveitis, equal sex-related distribution, and absence of nail changes. This difference may be attributed to different classification criteria used.

Introduction

The most common rheumatic disease among children is Juvenile idiopathic arthritis (JIA), which includes all arthritis forms that last for six weeks and onset before the age of 16 years [1]. Depending upon the geographical area, the incidence and prevalence vary between 1.6 to 23 for 100,000 children [2-9]. The categorization suggested by ILAR encompasses seven different, mutually exclusive classes, determined by clinical and laboratory measures [10]. Undifferentiated arthritis, not fit for criteria in any subtype, or fit for two or more subtypes [11]. Polyarticular JIA involves five or more joints during the first six months, occurs at any time before the age of 16 years [12, 13]. Systemic JIA (SJIA) is associated with a daily quotidian fever of 39°C persisting for more than two weeks. SJIA onset in adolescents is rare and adult onset is reported in a few cases [14]. Enthesitis-related arthritis (ERA) is arthritis and enthesitis of at least six weeks' duration [15]. The sacroiliacs, knees, ankles, and hips are the commonly affected joints at diagnosis, small joints of the feet and toes are involved [16]. Evidence for the heritability has shown that JIA has a sibling relative risk ranging from

15 to 30, similar to that of type 1 diabetes [17]. Although autoreactive B cells have other important pathogenic functions in JIA as antigen presenting cells within the synovium [18]. The pathetiologic role of infections in causing JIA, and the mediating role of genetic factors, remain unclear [19]. There are no laboratory test or combination of studies to confirm the diagnosis but they can be used to offer evidence of inflammation, support the clinical diagnosis [20].

Rheumatoid factor serology is shown to likely be positive in children with JIA and diseases other than JIA [21]. In individuals with oligoarticular onset disease, ANA deliberates risk for the development of asymptomatic uveitis [22]. Anti-cyclic citrullinated peptide antibodies can indicate severe patterns of disease, and not a diagnostic marker for JIA [23]. Magnetic Resonance Imaging is able to evaluate the manifestations of JIA [24]. Bone scans using technetium-99m are beneficial for detecting the early stage of inflammatory arthritis [25]. A multidisciplinary team approach to the management is important to improve the care of children with arthritis [26]. Intraarticular corticosteroid is effective treatment for synovitis with JIA [27, 28]. Methotrexate (MTX) is the usual first-line systemic immunosuppressive agent in children with JIA-associated uveitis, and in those who are refractory to, or dependent on topical glucocorticoids [29, 30]. Etanercept is used in JIA [31], which has been demonstrated to improve ability and quality of life [32, 33], and is potentially capable of reducing the progression of radiographic joint damage [34]. Infliximab with MTX has been shown to produce an important, rapid, and durable clinical effect with JIA [35]. Tocilizumab has proven useful even in patients whose JIA has been refractory and appears quite effective as monotherapy [36]. Systemic glucocorticoids are used for severe JIA-associated complications [37, 38]. Rapid and accurate diagnosis and therapy are essential to prevent permanent damage of the joint and preserve joint functionality [39].

The prevalence of psoriasis of varies according to regions, but worldwide it is 2.0-11.0% [40]. The psoriasis location can increase the risk of psoriatic arthritis (PsA) with intergluteal and perianal lesions [41]. PsA is a differing inflammatory disorder marked by various clinical manifestations [42]. The American Rheumatism Association recognizes PsA as a separate disease [43]. Spondylitis presented in 40.0% [44]. The prevalence in Europe and other countries varies from 0.02 to 0.42% [45, 46]. There was a difference between PsA and psoriasis alone at three loci (*HLA-C, IL-12B* and *IL-23R*) [47]. Presence of two minor criteria is considered probable JPsA [48]. Two JPsA clinical subtypes are identified and is associated with HLA-B27; antinuclear antibodies are usually absent [49]. In PsA, especially the axial pattern, uveitis may initiate as unilateral and become bilateral in the course of the disease [50]. In peripheral arthritis, NSAID monotherapy without DMARDs should not exceed one, and other treatment possibilities should be considered. While when axial or entheseal involvement dominates the clinical picture, the duration of NSAID therapy might be prolonged up to 12 weeks, provided they have already induced relief for weeks [51]. Systemic glucocorticoids may be used with caution at the lowest effective dose, and MTX has proven efficacy in skin psoriasis and has become the standard DMARD for skin psoriasis [51]. Several other TNFi are approved in adult PsA for juvenile psoriasis; however, specific data on their effectiveness in JPsA remain scarce [52]. Despite this, identification and treatment are still not optimal, and the diagnosis was significantly delayed in the majority of patients. Delays in diagnoses of six and 12 months have been shown to impact long-term joint damage and functional disability [43]. Thus, the aim of this study was to determine all cases of psoriatic arthritis in terms of demographic data, diagnosis, treatment, and prognosis.

Materials and methods

Study design and period: This study was carried as cross-sectional study of the medical records of all the patients diagnosed with psoriatic arthritis who are referred to the Rheumatology Clinic.

Study setting: This study carried out in Tripoli Children's Hospital which is one of teaching hospital providing tertiary health care services, with a number of pediatric subspecialty clinic including: cardiology, endocrine, respiratory, neurology, gastroenterology, metabolic, neonatology, nephrology, and rheumatology clinic, the

rheumatology clinic is the only government clinic offer pediatric rheumatology services covering all western and south area of Libya.

Study population: The study was carried out by reviewing the medical records of children with a diagnosis of psoriatic arthritis according to the international League of Associations for Rheumatology Classification (ILAR) or Vancouver criteria (definite or probable). Patients with active disease as well as those in clinical remission were included in the period of 2001-2020.

Inclusion criteria: Any child diagnosed with psoriatic arthritis.

*Exclusion criteri*a: Other types of juvenile idiopathic arthritis patients.

Study tool: A performed case sheet was used to obtain the relevant data from the medical records including the following: Age, sex, diagnosis, treatment and prognosis in the patients.

Study measurements: The following measurements were used in this study in the purpose of comparison: treatment regimens, disease activity which is represented by JADAS score in the form of inactive disease on treatment, active disease on treatment, inactive disease off treatment, active disease off treatment and disease outcome which was evaluated by JADI score.

Ethical consideration and consent process: Ethical approval was obtained from the scientific committee and the head of Tripoli Children's Hospital before starting the study.

Statistical analysis: The collected data was coded and SPSS software was used for analysis. Frequency, percentage, mean, and SD were used for descriptive statistics.

Results

In this study, out of 12 children meeting the Vancouver criteria for juvenile PsA, five cases (42.0%) did not fulfill ILAR criteria. Grounds for exclusion were family history of psoriasis limited to second-degree relatives (25.0%), presence of systemic JIA (8.3%), RF not done (8.3%) and HLA-B27 in a male with arthritis onset after age six (8.3%). In addition, JPsA represents 4.8% of total JIA cases.

Demographic data: Among the 12 patients, 50.0% were females, male: female ratio was 1: 1. The mean age of patients was 10.2±6.5 years, disease onset above four years of age was observed in 50.0%, mean age of JPsA onset was 5.8±5.3 years. 33.3% of the patients were diagnosed with psoriasis: Two had psoriasis before the onset of arthritis (median 10.0 months). Family history of psoriasis was found in 83.3% patients: 60.0% had a first-degree relative and 40.0% had a second-degree relative. One patient did not attend follow-up. The duration of follow up in the rest of the patients was 45.4%, less than two years, and 54.6% more than two years.

Clinical feature: Arthritis was presented in all cases; arthritis onset pattern is shown in **Table 1**. Polyarticular pattern was the predominant (58.3%). Hips were affected in one patient (8.3%), while no axial involvement, no nail changes were observed; dactylitis was observed in 66.7% of the cases. Enthesitis was seen in 8.3%. Systemic manifestations were observed in 8.3%. Uveitis was observed in 30.0% of cases, of which all were females, as shown in **Table 2**. Uveitis complications occurred in one, four-year-old-girl, who had psoriasis, early disease onset, ANA titer >1: 320 and negative HLAB27.

With regard to the serology result, rheumatoid factor, it was negative in all the patients. HLAB27 (missing values in four patients), it was positive in one patient (12.5%). The ANA was present in four patients accounting for 33.3%. ANA titer and pattern are shown in **Table 3**. ANA was more frequently seen in oligoarticular pattern (P=0.098), and the youngest age group at disease onset (P=0.221) Anti-CCP test (missing values in eight patients), negative in four patients.

Table 1: Comparison between arthritis patterns concerning JPsA general and clinical features

Variables	Polyarticular pattern N, (%)	Oligoarticular pattern N, (%)	P value
Gender			
Female	3 (42.9)	3 (60.0)	0.558
Male	4 (57.1)	2 (40.0)	
Age at disease onset			
≤ 4 yrs.	4 (57.1)	2 (40.0)	0.558
> 4yrs.	3 (42.9)	3 (60.0)	
Patients with psoriasis	3 (42.9)	1 (20.0)	0.408
Family history of psoriasis	5 (71.4)	5 (100)	0.190
Peripheral joints	7 (100)	5 (100)	
Axial joints	0.0 (0.0)	0.0 (0)	
Hip joints	1 (14.3)	0.0 (0)	0.377
Dactylitis	4 (57.1)	4 (80)	0.408
Enthesitis	1 (14.3)	0.0 (0)	0.377

Table 2: General characteristics and treatment of JPsA-associated uveitis

Variables	JPsA uveitis N, (%)	P value
Gender		
Female	3 (100)	0.038
Male	0 (0.0)	
Age at disease onset		
≤ 4 years	2 (66.7)	0.490
> 4 years	1 (33.3)	
Patients with psoriasis	2 (66.7)	0.098
Family history of psoriasis	2 (66.7)	0.571
Arthritis onset pattern		
Oligoarticular onset	2 (66.7)	0.260
Polyarticular onset	1 (33.3)	
Positive ANA	2 (66.7)	0.260
Positive HLAB27	0 (0.0)	0.408
Treatment		
NSAIDs	3 (100)	--
Methotrexate	3 (100)	0.301
Intra-articular injection	1 (33.3)	0.490
Biologics	2 (66.7)	0.098
Follow up duration		
≤ 2 years	0 (0.0)	0.161
> 2 years	3 (100)	

Table 3: ANA titer and pattern in JPsA children

ANA titer	JPsA patients N, (%) [ANA pattern]
> 1: 320	2 (16.7) [Mixed, homogenous]
1:160-320	2 (16.7) [Nucleolar, homogenous]
< 1: 80	8 (66.6)

With respect to the treatment, all JPsA were treated with NSAIDs at presentation and/or during follow-up. Methotrexate was used in 66.7% of the patients, as shown in **Table 4**; it was more frequently used in polyarticular than oligoarticular pattern disease (P=0.679). Biologics were used in 25.0% of the patients, were more used in females and in younger age patients at disease onset (P=0.083). Intra-articular injection was used in 16.7% of the patients. **Table 5** shows the disease outcome concerning clinical, laboratory data and treatment used.

Table 4: Medications used during the course of the disease

Treatment	Polyarticular pattern N, (%)	Oligoarticular pattern N, (%)	P value
NSAIDs	7 (100)	5 (100)	
Methotrexate	5 (71.4)	3 (60)	0.679
Intra-articular injection	1 (14.3)	1 (20)	0.793
Biologics	2 (28.6)	1 (20)	0.735

Table 5: Disease outcome concerning clinical, laboratory data, and treatment used

Variable	Articular damage only N, (%)	Both articular and extra-articular damage N, (%)	P value
Gender			
Female	1 (33.3)	1 (100)	0.248
Male	2 (66.7)	0 (0.0)	
Age at disease onset			
≤ 4 years	1 (33.3)	1 (100)	0.248
> 4 years	2 (66.7)	0 (0.0)	
Psoriasis in patient	0 (0.0)	1 (100)	0.046
Arthritis onset pattern			
Oligoarticular	1 (33.3)	0 (0.0)	0.505
Polyarticular	2 (66.7)	1 (100)	
Positive ANA	1 (33.3)	1 (100)	0.248
Positive HLAB27	1 (50) *	0 (0.0)	0.386
treatment regimens:			
NSAIDs & Methotrexate	2 (66.7)	1 (100)	0.505
NSAIDs, Methotrexate & biologics	0 (0.0)	1 (100)	0.083
Drug compliance			
Good	1 (33.3)	0 (0.0)	0.505
Poor	2 (66.7)	1 (100)	
Follow up duration			
≤ 2 years	2 (66.7)	0 (0)	0.248
> 2 years	1 (33.3)	1 (100)	

*One case is missing

Discussion

In the current study, medical records of 12 children at the Pediatric Rheumatology Clinic were retrospectively analyzed. This does not represent all cases seen in Libya during this period, but represents the referral pattern at Tripoli Children's Hospital. JPA was represents 4.8% of total JIA cases; it was 1.5% of JIA in Egyptian [53], 4.87% in the Saudi Arabia study [54], while in the Jordanian study, it was 8.5% [55]. There was no sex-related difference, on contrary to female predominance reported by Al-Hemair and others [54] and Stoll et al. [56]. Meanwhile, male predominance was reported by Alzyoud et al. [55] and Zisman et al. [57]. The mean age of disease onset was 5.8±5.3 year, which was lower than that reported in Canada (8.0±4.4 year) by Butbul et al [58] and by Al-Hemairi et al. [54] (8.47±3.09 years). The present results regarding psoriasis were higher than that reported by Stoll et al. [56], was 25.0%, but lower than that reported by Zisman et al. [57], who found psoriasis in 66.8% of the cases. Family history of psoriasis showed high frequency among patients as reported by Hamilton et al. [59] and Butbul et al. [58]. Similar to a previous study in Turkey by Kalyoncu et al. [60], polyarticular-onset was found to be the most common clinical pattern. In contrast to the results of Butbul et al. [58], who reported oligoarticular-onset predominance.

Concerning dactylitis, the current results were much higher than that reported by Butbul et al. [61] was 30.0%, while no nail changes were reported in the patients of this study, in contrast to 53.0% in the same study [61]. Being higher than the Saudi study [54], the frequency of ANA positivity in the children of the present study

was 33.3%, although a higher frequency was reported in Taiwan by Shen et al. [62] was 66.7%. Absence of ANA positivity was reported in other studies [9, 53, 55]. As found by Butbul et al. [60], it's more frequently seen in oligoarticular onset disease. HLAB27 was found in 12.5%, while higher results were reported by Flatøb et al. [63] by 19.0%. Previous studies in Taiwan [62] and America [56] reported by 33.3% and 46.0%, respectively. Uveitis was manifested among 33.3% of the cases, which was higher than that reported in Germany by 6.6% [64]. In contrast to the results of Abdwani et al. [9], Al-Hemairi et al. [54] and Hamilton et al. [59], who reported absent cases of uveitis. The present results were similar to the German study by Baquet-Walscheid [65] who found that JPsA-uveitis patients more frequently female, antinuclear antibody positive and younger at PsJA onset as well as in Libya [66]. As found by Butbul et al. [61], JPsA-uveitis occurred more occurred in oligoarticular onset disease. All patients in the current study were started on NSAIDs either alone or combined with DMARDs, but they were the only agent used in 33.3% of the patients [65]. In another study, NSAIDs were only used in combination with DMARDs [54]. MXT was used more in polyarticular onset disease, as reported in the other study [29].

Conclusions: This is the first study describing the pattern of juvenile psoriatic arthritis in Libyan children. The characteristics of JPsA in Libyan children are different from those of European, North American, and Arab countries regarding a higher frequency of uveitis, equal sex-related distribution, and absence of nail changes. This difference could be attributed to different classification criteria used.

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