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Application of the 2019 PRINTO Classification Criteria for Juvenile Idiopathic Arthritis at a Tertiary Hospital in Senegal, West Africa

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Abstract

Background: In 2019, PRINTO proposed new classification criteria for Juvenile idiopathic arthritis (JIA) that make the classification more homogeneous than ILAR criteria. **Objectives:** We aimed to describe the profile of JIA in Senegal according to these new classification criteria and compare the findings to other populations. **Methods:** We conducted a mixed cohort study by reviewing the medical records of patients diagnosed with JIA with an age of symptom onset <18 years according to the 2019 PRINTO classification criteria for JIA from January 2012 to December 2023. We collected demographic, clinical, and paraclinical data. **Results:** A total of one hundred seventeen patients with JIA were included. Seventy-two (61.5%) were females. The mean age at symptom onset and at diagnosis was 12.3 years and 14.2 years, respectively. The most common JIA subtypes were Enthesitis/spondylitis-related arthritis (ERA) and Rheumatoid Facteur-positive JIA (50.4% and 37.6%, respectively). The frequencies of the other JIA subtypes were as follows: Systemic-JIA (7.7%), Early-onset antinuclear antibody-positive JIA (2.6%); Unclassified JIA (1.7%). ERA was characterized by peripheral arthritis, hell enthesitis and radiographic sacroiliitis with a high prevalence of positive HLA-B27. Among patients with RF-positive JIA; Anti-CCP and RF were positive in 83.8% and 79.4% of cases. ANA was positive in 56.8% and 20.5% had negative RF, but positive anti-CCP. All patients with Systemic JIA had fever and arthritis. Seven of 9 patients had skin eruption, lymphadenopathy was present in 4 patients and 2 patients had hepatomegaly. Three patients had Early-onset antinuclear antibody–positive JIA. Among them, 2 had uveitis. Unclassified JIA was characterized by association of ERA and RF/CCP-positive JIA. **Conclusion:** Enthesitis/spondylitis-related arthritis and RF/CCP-positive JIA were the most common JIA subtypes in our Senegalese cohort. They represent a continuum with ankylosing spondylitis and rheumatoid arthritis in adulthood.

Subject Areas

Rheumatology

Keywords

Juvenile Idiopathic Arthritis, PRINTO Classification Criteria, Senegal

1. Introduction

Juvenile idiopathic arthritis (JIA) comprises a group of inflammatory disorders that begin before the 18th birthday, persist for at least six weeks, and are of unknown origins [1]. Studies on juvenile idiopathic arthritis usually use the International League of Associations of Rheumatology (ILAR) classification criteria [2]; these criteria have limitations and cannot be used to identify homogenous JIA subtypes. To make the classification criteria more homogeneous, a new provisional classification was adopted by consensus in 2019 under the aegis of PRINTO (Paediatric Rheumatology International Trials Organisation) making it possible to define four main subgroups classified according to more specific clinical and biological criteria [1]: a) systemic JIA; b) rheumatoid factor-positive JIA; c) enthesitis/spondylitis-related JIA; and d) early-onset antinuclear antibody-positive JIA. The other forms were gathered under the terms "others JIA" and "unclassified JIA".

To our knowledge, application of PRINTO classification criteria for JIA has never been used in Africa. Thus, this study aims to describe the profile of JIA according to PRINTO 2019 classification criteria in Senegal (West Africa).

2. Patients and Methods

This mixed cohort (retrospective and prospective) study was carried out at the rheumatology department of Aristide Le Dantec Hospital in Dakar, from January 2012 to December 2023. All patients who fulfilled the 2019 PRINTO classification criteria of JIA were enrolled in the study [1]. Exclusion criteria were: arthritis related to infection (acute rheumatic fever, septic arthritis, reactive arthritis), connective tissue diseases (Primary Sjögren syndrome, systemic lupus, dermatomyositis, systemic scleroderma, vasculitis, sarcoidosis), Bone dysplasia (progressive pseudorheumatoid dysplasia), Malignancy (leukemic arthritis), juvenile primary fibromyalgia syndrome. The following data were collected: – Age at symptom onset and at diagnosis (at presentation in rheumatology department), sex (female, male). – Clinical features: arthritis (defined as swelling within a joint or limitation in the range of joint movement with joint pain or tenderness), enthesitis (defined as tenderness on palpation of entheseal sites; Heel enthesitis is defined as past or present spontaneous pain or tenderness at the examination of the site of the insertion of the Achilles tendon or plantar fascia at the calcaneus), Sacroiliac tenderness (defined as tenderness on palpation of the SI joints and/or pain on SI

manoeuvres) and Uveitis (defined as past or present uveitis anterior, confirmed by an ophthalmologist). – Laboratory investigations: erythrocyte sedimentation rate (ESR, first hour; raised if >20 mm/hour), C-reactive protein (CRP; positive if >6 mg/l). Rheumatoid factor (RF; positive if >30 IU/ml by Waaler-Rose test), anticyclic citrullinated peptide (anti-CCP; positive if >5 U/ml by chemiluminescence immunoassay test), antinuclear antibody (ANA; positive if >1/100 by indirect immunofluorescence test) and HLA-B27. – Subtypes of JIA: **A) Systemic JIA (known as pediatric-onset Still's disease):** Fever of unknown origin (excluding infectious, neoplastic, autoimmune, or monogenic autoinflammatory diseases) that is documented to be daily (quotidian; fever that rises to ≥39˚C once a day and returns to ≤37˚C between fever peaks) for at least 3 consecutive days and reoccurring over a duration of at least 2 weeks and accompanied by 2 major criteria OR 1 major criterion and 2 minor criteria. Major criteria are 1) evanescent (nonfixed) erythematous rash; and 2) arthritis. Minor criteria are 1) generalized lymph node enlargement and/or hepatomegaly and/or splenomegaly; 2) serositis; 3) arthralgia lasting 2 weeks or longer (in the absence of arthritis); and 4) leucocytosis (≥15,000/mm^3) with neutrophilia. **B) Rheumatoid factor-positive JIA (known as childhood-onset rheumatoid arthritis):** Arthritis for ≥6 weeks, and association with 2 positive tests for RF at least 3 months apart or at least 1 positive test for antibodies to Cyclic Citrullinated Peptide (CCP). **C) Enthesitis/spondylitis-related JIA:** Peripheral arthritis ≥6 weeks and enthesitis, or • Arthritis or enthesitis, plus ≥3 months of inflammatory back pain and sacroiliitis on imaging, or: • Arthritis or enthesitis plus 2 of the following: 1) sacroiliac joint tenderness; 2) inflammatory back pain; 3) presence of HLA-B27 antigen; 4) acute (symptomatic) anterior uveitis; and 5) history of a SpA in a first-degree relative. **D) Early-onset antinuclear antibody-positive JIA:** Arthritis for ≥6 weeks, and early-onset (≤6 years), and presence of 2 positive ANA tests with a titer ≥1/160 (tested by immunofluorescence) at least 3 months apart (In our context, we performed only one ANA test due to lack of resources). Exclusions are systemic JIA, RF-positive arthritis, and enthesitis/spondylitis-related JIA. **E) Other JIA:** Arthritis for ≥6 weeks and does not fit criteria for disorders A to D. **F) Unclassified JIA:** Arthritis for ≥6 weeks and fits >1 disorder A-D.

Given the nature of this study, informed consent for participation was not required. Confidentiality was ensured for all participants.

Data analysis

Statistical analysis of data was done using Statistical Package for Social Sciences (SPSS) version 21.0 for Windows. Descriptive analysis was done and statistics were presented as numbers and percentages for categorical data and mean and standard deviation (SD) for continuous data.

3. Results

A total of 144 patients were enrolled in the study. 27 patients were excluded (9 Sjögren Syndrome, 9 acute rheumatic fever, 4 systemic lupus, 2 dermatomyositis, 1 tuberculosis arthritis, 1 progressive pseudorheumatoid dysplasia, 1 calcaneal apo-

physitis) leaving a total of 117 patients. The 117 JIA patients comprised 72 females and 45 males giving a female to male ratio of 1.6:1. The mean age at symptom onset and at diagnosis was 12.3 years and 14.2 years, respectively. All met the 2019 PRINTO classification criteria for JIA. Descriptive data for all patients are presented in Table 1. Enthesitis/spondylitis-related arthritis (ERA) was the single largest subtype (n: 59, 50.4%), followed by RF-positive JIA (n: 44, 37.6%), systemic-JIA (n: 9, 7.7%), early onset (n: 3, 2.6%) and unclassified JIA (n: 2, 1.7%). We don't find "other JIA".

Systemic-JIA (SJIA)

A total of 9 patients (5 Female, 4 Male) had SJIA. The mean age at diagnosis was 10 years (range: 4 - 16 years). All patients had fever and arthritis at diagnosis. Seven of 9 patients had skin eruption. Lymphadenopathy was present in 4 patients. Two patients had hepatomegaly. All patients had elevated inflammatory biomarkers (CRP, ESR). Seven of 9 patients had anemia, 4 patients had thrombocytosis, and 3 patients had neutrophilic leucocytosis.

RF/CCP-positive JIA (RF/CCP-JIA)

A total of 44 patients had RF/CCP-positive JIA. The female-to-male ratio was 10 (40F:4M). The mean age at symptom onset and at the time of diagnosis was 12.7 ± 2.7 (median: 12 years) and 16.8 ± 4.0 years (median: 17 years), respectively. Peripheral arthritis was present in all patients. Extra-articular manifestations were represented by rheumatoid nodules in 5 patients and two patients with interstitial lung disease. The mean ESR was 46.1 mm/h, while the average CRP was 55.9 mg/l. Anti-CCP was positive among 26 of 31 (83.8%) patients, while 31/39 (79.4%) had positive RF. Eight (20.5%) of 39 patients had negative RF, but positive anti-CCP. ANA was positive in 9 of 16 (56.2%) patients.

Enthesitis/spondylitis-related arthritis (ERA)

Fifty-nine patients had ERA. The male-to-female ratio was 1.46 (35M:24F). The mean age at symptom onset and at the time of diagnosis was 12.2 ± 2.9 (median: 13 years) and 20.8 ± 8.4 years (median: 20 years), respectively. Peripheral arthritis was present in 53 (89.8%) of 59 patients. Axial involvement was dominated by low back pain in 52 (96.2%) of 54 patients followed by sacroiliac tenderness in 44 (81.5%) of 54 patients, dorsal pain in 14 (24.5%) and cervical pain in 13 (24%) of 54 patients. Entheseal involvement was dominated by heel enthesitis in 40 of 59 cases, followed by the anterior chest wall in 13 of 44 patients. Among 59 patients with ERA, 46 underwent HLA-B27 testing. HLA-B27 was positive in 37 (80.4%) patients. The ESR was accelerated in 29 (63%) of 46 patients, with an average of 39.4 mm/h. While CRP was elevated in 26 (56.5%) of 46 patients, with an average of 24.8 mg/l. Among 54 patients with axial involvement, 38 underwent radiography and/or computed tomography of the sacroiliac joints. Sacroiliitis was found in 35 (88%) of 38 patients. These patients with radiographic sacroiliitis represented the advanced form known as ankylosing spondylitis. Seven patients had anterior uveitis.

Early-onset antinuclear antibody-positive JIA (EoANA-JIA)

Three patients (2F:1M) had EoANA-JIA. The mean age at diagnosis was 7 years.

All patients had peripheral arthritis and two patients of 3 had uveitis.

Unclassified JIA

Two patients had an association of Enthesitis/spondylitis related arthritis (sacroiliitis, heel enthesitis with positive HLA-B27) and RF/CCP-positive JIA (polyarthritis with positive Ac-CCP and RF).

Table 1. Demographic and patient characteristics of JIA subtypes.

Variable	S-JIA	RF-JIA	ERA	EO-ANA	Unclassified JIA	Total
Patient (%)	9 (7.7)	44 (37.6)	59 (50.4)	3 (2.6)	2 (1.7)	117 (100)
Female/Male	5/4	40/4	24/35	2/1	1/1	72/45
Age at symptom onset (years)	NA	12.7	12.2	NA	12	12.3
Age at presentation (years)	10	16.8	20.8	7	16.5	14.2
Arthritis (%)	9 (100)	44 (100)	53 (89.8)	3 (100)	2 (100)	111 (94.9)
Enthesitis (%)	0	0	40/59 (67.8)		2 (100)	42 (35.9)
Uveitis (%)	0	0	7/31 (22.5)	2/3	0	9 (26.5)
Positive RF (%)	0	31/39 (79.4)	0	0	1	32 (80)
Positive anti-CCP (%)	0	26/31 (83.8)	0	0	2	28 (85)
Positive ANA (%)	0	9/16 (56.2)	0	3/3 (100)		12 (63)
Positive HLA-B27 (%)	1	0	37/46 (80.4)	0	2/2	40 (83.3)

NA: Not available.

4. Discussion

To our knowledge, this study is the first in Africa to describe the profile of JIA using PRINTO 2019 classification criteria. Only two previous studies from Korea and Portugal have described juvenile idiopathic arthritis using these criteria [3] [4]. In our cohort, we describe four main subtypes of JIA according to PRINTO 2019 classification criteria.

The most frequent JIA subtype was Enthesitis/spondylitis-related arthritis, distinguished by peripheral arthritis, sacroiliitis, inflammatory low back pain, heel enthesitis, and high prevalence of HLA-B27 and affects mainly adolescents of the Fula (Peulh) ethnic group [5]. In the Indian study, ERA was also the most common JIA subtype (35.3%) [6]. However, lower prevalence was reported in Swedish (8.8%) and German (10.7%) studies [7] [8]. The second largest frequent JIA subtype was RF/CCP-positive JIA. This subtype of JIA shares the same clinical features and genetic risk factors as adult-onset rheumatoid arthritis, representing childhood-onset rheumatoid arthritis [9] [10]. Previous studies showed that RF-positive polyarthritis is more common among children of African ancestry than European ancestry [11] [12]. Our study showed a high frequency of RF/CCP-positive JIA compared to the Korean and Portuguese studies (11.8% and 3.8% respectively) [3] [4]. In this cohort, Rheumatoid Factor appears to be less effective than anti-CCP in the diagnosis of childhood-onset rheumatoid arthritis. Indeed, eight

(20.5%) patients had negative rheumatoid factors, but positive anti-CCP, suggesting a systematic search for anti-CCP in children with RF-negative JIA, to avoid missing childhood-onset rheumatoid arthritis.

Regarding Systemic JIA, the frequency was in agreement with the Portuguese study (7.7%) and Indian study (8%) [4] [6]. However, a higher prevalence was reported in Korean (27.1%) and Turkish (15.3%) studies [3] [13].

Early-onset ANA-positive JIA constitutes a new JIA subtype, and its definition is based on previous work which supported the identification of a homogeneous form of arthritis, characterized by early onset (80% under 6 years), female predominance, asymmetric arthritis, high incidence of chronic uveitis, and ANA positivity. This form seems to exist only in children, and has no equivalent in adult patients [1] [14] [15].

We found a low frequency (2.6%) of Early-onset ANA-positive JIA. However, a higher prevalence was reported in the Portugal study (34.6%) [4]. In Korea, Kwon *et al.* [3] found a low prevalence (8.4%) of Early-onset ANA-positive JIA.

Unclassified JIA comprises patients with features of more than one of the four main subtypes (SJIA, RF/CCP-JIA, ERA, EoANA-JIA). In this study, only two patients (1.7%) presented an association of ERA and RF/CCP-positive JIA. In the Korean and Portuguese studies, which also used PRINTO classification criteria, the frequency of the Unclassified JIA was low (3.8% and 0%, respectively) [3] [4].

Our cohort found a predominance of enthesitis/spondylitis-related arthritis and RF/CCP-positive JIA subtypes. This predominance is probably linked to genetic and environmental factors.

Several limitations of our study should be noted. This cohort was mixed with some retrospective data, and other extra-articular manifestations such as cardiovascular and ocular involvement were not systematically studied. Despite the study's limitations, this research is relevant to future studies on JIA in sub-Saharan African populations.

5. Conclusion

In summary, according to PRINTO 2019 classification criteria, the clinical profile of JIA in Senegal is characterized by a predominance of enthesitis/spondylitis-related arthritis and RF/CCP-positive arthritis subtypes. They represent a continuum with ankylosing spondylitis and rheumatoid arthritis in adulthood. However, further prospective studies are needed, including research into genetic factors, to obtain reliable subtypes of JIA, particularly in sub-Saharan Africa.

Conflicts of Interest

The authors declare no conflicts of interest.

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