



Prevalence of anti-cyclic citrullinated peptide antibodies in juvenile idiopathic arthritis in Benin

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Abstract

Introduction: The diagnosis of Juvenile Idiopathic Arthritis (JIA) is difficult in sub-Saharan countries due to the complexity and polymorphism of the disease. JIA can be accompanied by the presence of Anti-Cyclic Citrullinated Peptide Antibodies (ACPA). This work aims to determine the prevalence of ACPA among children suffering from juvenile idiopathic arthritis in Benin.

Patients and methods: A descriptive cross-sectional study over 5 years was conducted in the rheumatology and pediatric departments of National Hospital University Hubert Koutoukou Maga of Cotonou among children suffering from osteoarticular disorders. ACPA were checked by an Enzyme Linked Immunosorbent Assay (ELISA) in serum samples from patients with JIA. Which had been retained using ILAR criteria. The data collected was analyzed using SPSS 20.0 software.

Results: Among 179 children treated for osteo-articular disorders, 32 (17.8%) had JIA. There were 19 girls and 13 boys. The teenagers' group (range from 13 to 16 years old) was the most represented age group (53.1%). Polyarthritism was the most common symptom for reasons of consultation or hospitalization (63%). The most common form of JIA in our series was enthesitis-related arthritis (9 i.e. 28.1%) that affected female teenagers (sex ratio=0.8), followed by Rheumatoid Factor (RF)-positive polyarthritism (8 i.e. 25%) which were frequent in the female child (7-12 years old). Biological inflammatory syndrome was present in all children. ACPA were present in 28.1% of JIA cases, including 55.6% of RF positive polyarthritism.

Conclusion: Prevalence of ACPA remains relatively high among children suffering from JIA in the Beninese population. Its high presence in teenagers probably suggests that it is early juvenile rheumatoid arthritis. It is important to conduct further studies to better clarify the role of antibodies in the course of the disease.



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Introduction

Epidemiological studies of rheumatic diseases in children are well known in the Maghreb and developed countries, where available data have focused on infections and chronic inflammatory rheumatism [1-6]. On the other hand, in sub-Saharan African countries, chronic inflammatory rheumatism is not well known to non-specialist practitioners and deserves the interest and collaboration of many specialists involved with children [6-9]. Difficulties related to the complexity and polymorphism of Juvenile Idiopathic Arthritis (JIA), sometimes confused with sickle cell disease and rheumatic fever, make early diagnosis difficult [8,9]. Juvenile Idiopathic Arthritis (JIA) is a clinically heterogeneous group of arthritis subtypes that occur in children under 16 years old with arthritis persisting for at least 6 weeks for which the cause is unknown [10]. In sub-Saharan Africa, the prevalence of the disease is unknown, but the hospital frequency varies among countries: Zambia (126 cases in 9 years), Senegal (30 cases in 7 years), Nigeria (23 cases in 9 years), [7,11-14]. The diagnosis of JIA depends primarily on clinical manifestations of the disease, with little in terms of serological support. A wide variety of auto-antibodies have been described in patients with this syndrome, but none are specific to JIA [15]. A number of auto-antibodies, including antiperinuclear factor, antikeratin antibodies, and anticyclic citrullinated peptide antibodies (ACPA), are now known to be specifically associated with rheumatoid arthritis (RA). Although ACPA do not have diagnostic or screening value, JIA can be accompanied by the presence of ACPA. However, the prevalence of ACPA are very little explored in children [16]. The aim of this study was to determine the prevalence of anti-cyclic citrullinated peptide antibodies in juvenile idiopathic arthritis (JIA) in Benin.

Patients and methods

This was a cross-sectional retrospective and descriptive study from January 2012 to December 2017 on children followed in rheumatology and paediatric departments of National Hospital University Hubert Koutoukou Maga of Cotonou among children who met the following criteria:

- Less than 18 years old and age 16 or younger when diagnosed with JIA
- Have consulted in one of the 2 departments during the study period
- Have suffered from juvenile idiopathic arthritis selected on the basis of International League Against Rheumatism (ILAR) classification criteria [17].
- To have achieved ACPA checked by an Enzyme Linked Immunosorbent Assay (ELISA) in serum samples from patients.

Children with another form of rheumatic disease such as osteoarticular infections, bone tumors, osteoarticular manifestations of general pathologies (Sickle cell disease or other blood disease, tumors), mechanical and degenerative osteoarticular disorders were not included in the study.

Data was analyzed using SPSS 18.0 software

Children were classified according to WHO categories:

- Baby: 0- 30 months
- Toddler: 1-30 months
- Preschooler: 30 months to 5 years old

- Grade schooler: 5-13 years old
- Teenagers: 13-16 years old (limited to 16 years old for our study)

All patients had had the following blood tests: Rheumatoid factor, CBC, Erythrocyte Sedimentation Rate, ACPA.

This work was approved by the ethics committee of the National Hospital University of Cotonou and all patients or their parents consented for analysis.

Results

Sociodemographic data

Among 179 children treated for osteoarticular disorders, 32 (17,8%) had JIA. There were 19 girls and 13 boys (sex ratio=0.7). The mean age of the patients was 7 ± 5.8 years with extremes of 0 and 16 years. The most represented age group was the teenagers (17 i.e 53.1%). Figure 1 shows all osteoarticular disorders which the children suffered from.

Clinical features

The most common symptom was polyarthritis. Figure 1 shows the different reasons for consultation. The mean delay of consultation time between the JIA patients was 6 months and 15 days. Half of the population (50.6%) was consulted within 30 days as shown in Table 1.

The most common form of JIA in this series was enthesitis-related arthritis (9 i.e. 28.1%) affecting female teenagers (sex ratio=0.8), followed by Rheumatoid Factor (RF)-positive polyarthritis (8 i.e. 25%), which was most frequent in female child (range from 7 to 12 years old) (0.14). The different forms of JIA and their distribution by age and sex have been summarized in Table 2.

Biological data

Biological inflammatory syndrome was present in all children. Inflammatory anemia was noted in 1/3 of children with an average hemoglobin level of 10.1 g/dL.

ACPA was present in 7 children and rheumatoid factors were identified in 9 children. The biological data as well as the prevalence of ACPA in the different JIA are summarized in Tables 3 and 4.

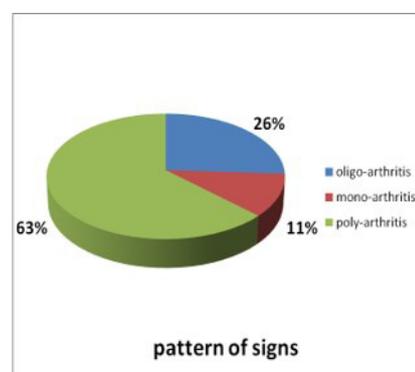


Figure 1: Reasons for consultation.

Table 1: Time to consult.

Time (in days)	number (n=179)	Percentage (%)
<30	91	50.8
30-90	27	15.1
>90	61	34.1

Table 2: JIA subtypes.

	Ages				Sex-ratio (H/F)
	baby	Toddler, preschooler	Grade schooler	teenagers	
Oligoarthritis	1	1	3	0	0.6 (2/3)
RF-positive polyarthritis	0	1	4	3	0.14 (1/7)
RF-negative polyarthritis	0	1	1	4	1(3/3)
psoriatic arthritis	0	0	0	1	0
Systemic arthritis	0	1	2	0	0.5 (1/2)
Enthesitis-related arthritis	0	0	0	9	0.8 (4/5)

RF: Rheumatoid Factor

Table 3: Biological data.

Time (in days)	Number (%)	Mean	Normal (or negative)
Hemoglobin(G/dl)			
Anemia	12	10 ±3	12
Any anemia	20		
Leukocytosis (G/L)			
Yes	19	12 ±7	10-May
No	13		
ESR (MM)			
Normal	5	53±19	5/20/2019
High	27		
Rheumatoid factor (UI/L)			
Positive	9	604±145	<20
Negative	23		
ACPA (UI/L)			
Positive	7(25)	381±19	<5
Negative	25		

ESR: Erythrocyte Sedimentation Rate; ACPA: Anticyclic Citrullinated Peptide Antibodies; UI: International Unit; MM: Millimeter

Table 4: Distribution of ACPA in JIA.

	Presence of ACPA	
	Yes	No
RF-positive polyarthritis	5 (62.5)	3 (37.5)
RF-negative arthritis	2 (18.2)	9 (81.8)
psoriatic arthritis	0 (0)	1 (100)
Systemic arthritis	0 (0)	3 (100)
Enthesitis-related arthritis	1 (11.1)	8 (80.9)

RF: Rheumatoid Factor; ACPA: Anticyclic Citrullinated Peptide Antibodies

Discussion

Juvenile idiopathic arthritis was common (16%) with a predominance of females. This finding was also made in other African countries [7-9,11-14,18]. The most represented age group was teenagers (66.7%), as described by other authors [3-6]. Enthesitis related arthritis and RF-positive polyarthritis are the most clinical forms of JIA in Benin. In Senegal, the clinical forms found were the polyarticular form (70%); spondyloarthropathies (11%); the systemic form (8%); the oligo-articular form (8%) and psoriatic arthritis (3%) [11]. In Morocco, several studies have been conducted on JIA with diversified results. Mawani et al reported a predominance of polyarticular forms [19], while El Magrahoui described the oligo-articular form as most common with a clear predominance of women [20].

The mono or oligo-articular forms were serologically negative to RF. RF-Positive polyarthritis was very common in this series, as in the case of Western and Maghreb works [3-6]. They are often accompanied by the presence of ACPA, which were present in 29% of JIA [21-24]. Various works showed low levels of ACPA in children. Aziza and al. found a rate of 12% in children with JIA [22]. Although the sensitivity and specificity of ACPA is well established in adult rheumatoid arthritis, research of such antibodies remains to be evaluated during childhood rheumatism. ACPA were identified in 75% of young patients with rheumatoid arthritis, compared to 25% of children with oligoarthritis or rheumatoid arthritis, and no children with a systemic form of the disease (Still) [23]. For Syed and al, ACPA were found in 50% of young patients with rheumatoid arthritis, no children with oligoarthritis or seronegative polyarthritis, and 6% of children with systemic disease [24]. Avcin et al. found ACPA in 20.5% of children with polyarthritis, mostly in children with late-onset polyarthritis and rheumatoid factor, in only 1.2% of children with oligoarthritis and none of the children with a systemic form [25].

Conclusion

The prevalence of ACPA remains relatively high among children suffering from JIA in the Beninese population. Its high presence in teenagers suggests that it is juvenile rheumatoid arthritis. It can be a perform test for early diagnosis of JIA and can have an outstanding prognostic value in JIA .It is important to conduct further studies to better clarify the role of antibodies in the course of the disease.

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