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JUVENILE IDIOPATHIC ARTHRITIS IN A NEW RHEUMATOLOGY CLINIC IN NIGERIA

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ABSTRACT

Objectives: To describe the frequency, clinico-laboratory characteristics and treatment outcomes of patients with juvenile idiopathic arthritis (JIA) in Lagos State University Teaching Hospital (LASUTH), Lagos, Nigeria.

Methods: This is a retrospective review of patients with JIA seen over a five-year period at the rheumatology clinic and children ward of LASUTH. We reviewed the folders of 28 patients from our unit records. The demographics, baseline clinical and laboratory characteristics, treatment given and patient outcomes were extracted and analyzed.

Results: A total of 28 patients with JIA were managed over the study period. Twenty one (75%) patients among our JIA cases were female and the mean age at presentation was 9.8±3.9 years. The mean duration of symptoms before diagnosis was 21.8±5.7 months. Polyarticular JIA (PJIA) constituted 14 (50%) cases, while oligoarticular and systemic-onset JIA (SoJIA) constituted 9 (39.3%) and 5 (17.9%) of the JIA cases respectively. Anaemia was present in 20 (71.4%) patients, leucocytosis in 16 (57.1%) and thrombocytosis in 11 (39.2%). Twenty five (89.2%) patients had elevated erythrocyte sedimentation rates (ESRs), 21 (75%) had elevated C-reactive protein levels and 23 (82.1%) patients had hyperferritinaemia. Positive antinuclear antibody (ANA) was found in 5 (17.8%) patients. Mortality was documented in 2 (7.1%) patients both of whom were SoJIA cases. Eleven (39.3%) patients were lost to follow up.

Conclusion: Unlike the common report of oligoarticular JIA (OJIA) being the most frequent subtype of JIA in various series from North America and Europe, PJIA was the most frequent subtype seen among our patients and this variant accounted for half of all JIA cases seen. There were no cases of psoriatic, enthesitis-related or undifferentiated JIA and most patients had haematological abnormalities and high levels of inflammatory markers at presentation.

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INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the most common cause of chronic arthritis in children and it is a cause of considerable morbidity and disability. According to the International League of Associations for Rheumatology (ILAR) definition of JIA, any arthritis lasting at least 6 weeks and developing before the 16th birthday in the absence of a known cause is classified as JIA (1). While the burden and impact of JIA are known across the developed world (2), the topic is still evolving in Africa where more emphasis is on communicable than non-communicable diseases. This double burden of diseases is mounting in Africa and it has been projected that non-communicable diseases will cause more than 60% of all mortalities by the year 2030 (3). A systematic review of studies outside Africa reported a prevalence of JIA ranging from 0.000038% to 0.004% (4). The prevalence among European and North American children populations ranges from 16 to 150 per 100,000 (5). The few reports of JIA in sub-Saharan Africa have been hospital based (6-11), while there are scanty population-based studies from North Africa (12, 13). The prevalence of JIA in Egypt ranges from 0.00343% to 0.33% (12, 13) while the largest JIA series from West Africa is of 23 cases reported from a private rheumatology clinic in Nigeria in an 8-year retrospective study (6). The dearth of published data on JIA in West Africa may in part explain the traditional belief that arthritides are diseases of the elderly. However, the increasing reports of JIA across Africa in the last decade may form an impetus for a change of conviction (6-9, 11, 12). The aim of this study is to describe the attributes of the various forms of JIA encountered by an adult rheumatology team in a retrospective audit of a six-year period in a public tertiary hospital in Nigeria.

SUBJECTS AND METHODS

This is a retrospective review of case records of JIA managed from June 2010 to April 2016 at the adult rheumatology unit of Lagos State University Teaching Hospital (LASUTH). LASUTH is one of the two tertiary teaching hospitals in the cosmopolitan city of Lagos and it has one of the two rheumatology clinics in the city. There is no pediatric rheumatologist in Nigeria and as such JIA and other paediatric rheumatic diseases are managed by adult rheumatologists in conjunction with paediatricians. The paediatric patients with either musculoskeletal complaints or systemic symptoms suspicious of a rheumatic disease were referred for rheumatology review from the paediatric clinic, peripheral hospitals or paediatric wards. The diagnosis of JIA and its sub-groups were based on the ILAR classification criteria. The entry criterion for case selection was the diagnosis of JIA in the patient's record before 16 years of age. The hospital records were retrieved for each patient and details of biodata, baseline clinical parameters, baseline laboratory indices, drug treatments and patient outcomes were extracted. The duration of illness was taken as the onset from the first symptoms to clinical diagnosis at our facility. The full blood count, haematocrit, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum ferritin, and antinuclear antibody (ANA) were recorded in all patients. Rheumatoid factor (RF) was tested in 7 patients who had the diagnosis of polyarticular JIA (PJIA). ANA and RF were analyzed by Enzyme-linked immunosorbent assay (ELISA) and nephelometry methods respectively.

Statistical methods

Descriptive statistics was used to analyze categorical and continuous variables. The categorical variables were presented as frequencies and percentages while continuous variables were presented as mean and standard deviation. Ethical approval was granted by the research and ethics committee of LASUTH.

RESULTS

A total of 28 patients with JIA, which included 25 cases referred from the general paediatric clinic, 2 cases diagnosed in paediatric ward and 1 case referred from a peripheral hospital were managed at the rheumatology unit. These accounted for 1.2% of the 2330 rheumatic disease cases managed over the study period. As shown in Table 1, 21 (75%) of our JIA cases were female and the mean age at presentation was 9.8 years. The mean duration of symptoms before diagnosis was 21.8 months. Constitutional symptoms such as intermittent fever, fatigue, weight loss and night sweat were documented in 15 patients. These 15 cases were made up of 7 with PJIA, 5 with systemic-onset JIA (SoJIA) and 3 with oligoarticular JIA (OJIA). PJIA constituted 14 (50%); OJIA, 9 (32.1%); and SoJIA, 5 (17.9%) of the JIA cases. Extended and persistent variants of OJIA were documented in 6 and 3 OJIA cases respectively. Extra-articular features were observed in 7 JIA patients

(anterior uveitis in 2, pleural effusion in 1, generalized lymphadenopathy in 2, and hepatosplenomegaly in 2). Mortality was documented in 2 cases while 11 patients were lost to follow up.

Laboratory features

As shown in Table 2, anaemia and leucocytosis were observed in more than half of the cases while less than 50% had thrombocytosis. Inflammatory markers such as ESR, CRP and ferritin were elevated in majority of patients with each JIA subtype. ANA was positive in 5 cases (3 OJIA, 1 SoJIA and 1 PJIA). RF was positive in 2 out of 7 PJIA patients that had the test. Table 3 shows the treatment administered and the outcomes of the 3 subtypes of JIA found.

Treatment and outcome patterns in Nigerians with JIA

All patients were treated with non-steroidal anti-inflammatory drugs (NSAIDs) and methotrexate. Many of these patients had been on self-prescribed NSAIDs before diagnosis. Etanercept was administered in one refractory RF-positive PJIA case. There were 2 mortalities accounting for 7.14% of the JIA cases while 11 patients were lost to follow up. Both deaths were in patients with SoJIA. While one patient died from overwhelming sepsis, the other died from suspected macrophage activating syndrome (MAS).

4. DISCUSSION

We studied 28 cases of JIA which constituted 1.2% of the 2330 rheumatic cases diagnosed and managed in a public rheumatology unit over a 6-year period. The scarcity of paediatric rheumatologists in Africa is a challenge for the early detection and appropriate management of childhood-onset rheumatic diseases. There is currently no paediatric rheumatologist in Nigeria and suspected and confirmed cases of paediatric rheumatic diseases are managed by other paediatricians and adult-patient rheumatologists. Accordingly, the awareness and indices of suspicion for paediatric rheumatic diseases are very low among Nigerian clinicians. It is unknown, how large the annual number of missed paediatric rheumatic diseases is and what burden this might be contributing to the morbidity and mortality due to childhood non-communicable diseases.

The high mean age of onset of JIA observed in this study is similar to findings recorded in other African studies (6-9, 11). This finding contrasts with the lower age of onset documented among children from North America and Western Europe (14). Although, there is

Table 1: Baseline clinical characteristics of 28 Nigerian children with JIA

	Number (%)	Range	Mean (SD)
Female	21 (75)		
Male	7 (25)		
Age at presentation (years)		1.5-15	9.8 (±3.9)
Age at onset (years)		1.3-14.3	8.1 (±4.0)
Duration of illness (months)		Mar-60	21.8 (±5.7)
Constitutional symptoms	15 (53.6)		
Only small-joint involvement (number of patients)	3 (10.8)		
Large and small-joint involvement (number of patients)	9 (32.1)		
Only large-joint involvement (number of patients)	16 (57.1)		
Extra-articular features	7 (25)		
Polyarticular JIA	14 (50)		
Oligoarticular JIA	9 (32.1)		
Systemic-onset JIA	5 (17.9)		
Lost to follow up	11 (39.3)		
Mortality	2 (7.14)		

JIA=Juvenile idiopathic arthritis

Table 2: Clinical and laboratory characteristics of the subtypes of JIA

	Polyarticular JIA(N-14)	Oligoarticular JIA(N-9)	Systemic JIA (N-5)
Patient's Age (Mean±SD)	9.9±3.4	8.3±2.8	12±2.4
Age of onset in years (Mean±SD)	7.9±3.6	6.9±4.9	10.2±3.2
Duration of illness at diagnosis in months (Mean±SD)	22.9±16.7	12.5±13.9	21.6±10.0
Number of Female/ Male	12/2	7/2	2/3
Fever [n (%)]	7(50)	3(33.3)	5(100)
History of typical rash [n (%)]	0(0)	0(0)	3(60)
Weight loss [n (%)]	6(42.9)	4(44.4)	3(60)
Chronic anterior uveitis [n (%)]	1(7.1)	1(11.1)	0(0)
Growth disturbance [n (%)]	2(14.3)	1(11.1)	1(20)
Joints deformity [n (%)]	3(21.4)	2(28.6)	0(0)
Anaemia [n (%)]	10(71.4)	5(55.6)	5(100)
Leucocytosis [n (%)]	9(64.3)	3(33.3)	4(80)
Thrombocytosis [n (%)]	6(42.9)	2(28.6)	3(60)
Elevated ESR [n (%)]	12(85.7)	8(88.9)	5(100)
Elevated CRP [n (%)]	11(78.6)	5(55.6)	5(100)
Positive ANA [n (%)]	1(7.1)	3(33.3)	1(20)
Elevated ferritin [n (%)]	10(71.4)	8(88.9)	5(100)
Rheumatoid Factor [n (%)]	2(14.3)	0(0)	0(0)

JIA=juvenile idiopathic arthritis, SD=standard deviation, ESR=erythrocyte sedimentation rate, CRP=C-reactive protein, ANA=anti-nuclear antibody, NSAID=Non-steroidal anti-inflammatory drug.

Table 3: Treatment and Outcome

	Polyarticular JIA(N-14)	Oligoarticular JIA(N-9)	Systemic JIA (N-5)
Intra-articularsteroid treatment [n (%)]	3(21.4)	6(66.7)	1(20)
NSAID treatment [n (%)]	14(100)	9(100)	5(100)
Methotrexate treatment [n (%)]	14(100)	9(100)	5(100)
Biologic treatment [n (%)]	1(7.1)	0(0)	0(0)
Lost to follow up [n (%)]	5(35.7)	4(44.4)	2(40)
Mortality [n (%)]	0(0)	0(0)7	2(40)

JIA=juvenile idiopathic arthritis, NSAID=Non-steroidal anti-inflammatory drug.

currently insufficient information to conclude that disease onset is generally delayed in the African patient; however, the complex interplay of genetics and environmental factors in the aetiology of JIA leaves this possibility open. In a study comparing phenotypic features of JIA between African American and non-Hispanic white, the median age of onset and median age of presentation were significantly higher among African American than the non-Hispanic whites (15). It is likely that a longer mean period since disease onset to diagnosis coupled with poor recall in many illiterate patients may be compounding this detail. The long road to diagnosis which is due to less assess to rheumatology care in our environment often takes the patient through several over-the-counter drug use and alternative medicine patronage.

The female-male ratio of 3:1 found in our study is larger than the range of 1-2.3:1 found in most other studies (6-9, 11, 16-18). Furthermore, the closest ratio to ours of 2.3:1 was found in the only previous Nigerian study (6). The reasons for this may include the fact that polyarticular variant which is known to show female preponderance was the most important category identified in both Nigerian studies. Also, enthesitis-related JIA, a subtype that is more frequent in males was not found (19). Juvenile psoriatic arthritis and undifferentiated JIA were also absent. There is a recognized variation in the geographical, gender and age distributions of the seven ILAR JIA subcategories across the world. In developing countries, polyarthritis is the most common subtype while in Western countries, oligoarthritis is most frequently observed (2). SoJIA is the most predominant subtype recorded among Asian children (2). The distribution of juvenile enthesitis-related arthritis possibly reflects the patterns of occurrence of HLA-B27 around the world. As the prevalence of HLA-B27 is low in Africa (20), the enthesitis related arthritis is less commonly observed among black African children (9, 11). Studies from across Africa have also shown the dominance of PJIA among the cases of JIA on the continent (6, 8-11). The patterns observed among Africans have been demonstrated among African Americans. In a comparative study, Fitzpatrick et al (15) observed that African American children are more likely to have polyarticular subtypes compared with non-Hispanic white children. It was suggested that these racial variations in the distributions of the JIA subtypes may reflect vital roles of genetics in the pathogenesis of JIA (15).

A high proportion of our patients, irrespective of subtype, had prominent constitutional symptoms and elevated inflammatory markers. This finding is in agreement with the observation of Oyoo et al (9) who found that fever and elevated ESR were present in 73.5 % and 100% respectively of Kenyan patients. Similarly, in a multi-ethnic study of JIA by Consolaro et al (14), they observed that African patients with JIA had higher levels of disease activity and low frequencies of inactive diseases compared with North American and Western European patients. Although, we were unable to assess disease activity in the cases studied using validated composite tools, our patients might have had high baseline disease activities based on the levels of the inflammatory markers. Autoantibodies are not necessary for the diagnosis of JIA but they can be useful for excluding differential diagnoses of chronic arthritis in children. They are also important for sub-categorisation of PJIA into RF-positive and RF-negative subtypes as well as determining the risks of chronic anterior uveitis in those with ANA-positive OJIA (1).

Many of our patients had been on NSAIDs and in a few cases oral prednisolone before presentation. Suitable adjustments were made in these drugs and all patients were commenced on subcutaneous or oral methotrexate according to our local policy. Intra-articular steroids were administered in few cases. The only JIA-suitable biologic available in Nigeria is etanercept and only one in six patients eligible for it were able to afford it. Affordability of biologics and other emerging treatment modalities for JIA is a huge barrier to the optimal treatment of Nigerian patients. The only other biologic currently available in Nigeria, rituximab, has not been approved for JIA but anecdotal reports have documented its efficacy in refractory SoJIA (21).

Mortality in JIA has been shown to be higher than in the general population, and especially, higher among individuals with SoJIA than other subtypes (22). Davies et al (22) observed that the standardized mortality rate among 693 JIA cases was 7.3 (95% CI: 2.9-15) while the standardized mortality rate among 99 systemic JIA cases was 21.7 (95% CI: 5.9-55.4). The mortalities in our study were attributable to infection and suspected MAS. Previous studies have documented infection, MAS,

and renal failure from amyloidosis as the major causes of death (22, 23). The Limitations of this study include the fact that the actual outcomes of these cases are likely to have been poorly appreciated due to the high proportion of patients lost to follow up. Also, our findings will have limited generalizability due to the few cases involved and the retrospective nature of the study.

CONCLUSIONS

JIA may not be so rare in Nigeria and the complete absence of paediatric rheumatologists in the country may have contributed to the low awareness and detection of these diseases among clinicians. Similar to many other reports from across Africa, PJIA constitutes the largest proportion of JIA among Nigerian patients. The care of these patients is plagued with several challenges including the often late presentation, high disease activities, lack of adequate healthcare financing and resources and the scarcity of specialists. Prospective studies on the subject will be helpful to determine the true burden and course of JIA among Nigerians.

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