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ORIGINAL RESEARCH

Juvenile Idiopathic Arthritis in a Tertiary Rheumatology Clinic

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Abstract

Background: Juvenile Idiopathic Arthritis (JIA) is one of the common chronic diseases in childhood. The inflammatory process in the joint is triggered by pro-inflammatory cytokines. The treatment is directed at alleviation of pain, inhibition of disease activity and preservation of range of motion.
Objectives: To describe the spectrum of clinical presentations, laboratory parameters and drug therapy among patients with Juvenile Idiopathic Arthritis seen at a Tertiary Health Centre.
Methods: All the patients who fulfilled the classification criteria of the International League of Associations for Rheumatology for JIA between July 2012 and June 2016 were included in the study. The clinical features, results of laboratory investigations and the treatment received were recorded.
Results: A total of 1910 patients was seen at the Out-Patient Rheumatology Clinic over the 4-year period, but only 18 case files of patients with JIA (0.95% of total) were retrieved. There were 13 females and 5 males with a female-to-male ratio of 2.6:1. The age range was 8-15 years with a mean of 10.3 ± 2.1 years. The duration of symptoms prior to presentation ranged between 2 years and 7 years with a mean of 4.2 ± 1.3 years. Polyarticular presentation was observed among 61.1% (11/18), pauciarticular in 27.8% (5/18) and systemic in 11.1% (2/18). Fever was uniformly seen among the patients with systemic onset, while fever and joint swelling were the common presentations in the other groups. Knee and ankle joints were most commonly affected. Erythrocyte Sedimentation Rate was elevated in 88.9% of the patients. Methotrexate was used in 61.1% and combination therapy was used as necessary.
Conclusion: JIA is relatively uncommon in the setting of the study. Polyarthritis form of JIA was the commonest type and response to steroid was uniformly good. Early recognition of the subtypes of JIA will enhance effective management of cases.

Key words: Juvenile Idiopathic Arthritis, Pattern and management, Rheumatology Clinic, Rheumatic disease.

Introduction

Juvenile idiopathic arthritis (JIA) is characterized by chronic synovitis of peripheral joints, manifesting as soft tissue swelling and effusion. It, almost certainly, comprises of a number of entities, characterized principally by arthritis of appendicular joints. [1] Several changes in the terminology of juvenile arthritis have been used. The older terms such as juvenile rheumatoid arthritis and juvenile chronic arthritis were replaced by the term juvenile idiopathic arthritis (JIA) at a meeting of the International League of Associations for Rheumatology (ILAR) in the late 1990s. [2] JIA incorporates all of what was called JRA in the past, and also includes all other forms of idiopathic arthritis in childhood. [2] Juvenile idiopathic arthritis is the most common inflammatory arthritis of childhood. Chronic inflammation of the joints markedly limits the

patient's mobility and productivity in daily life. [3] The ongoing inflammatory process is the usual cause of the changes in the joints and that makes it difficult to control. [3] The inflammatory process is secondary to excessive release of pro-inflammatory cytokines such as tumour necrosis factor (TNF) alpha, interleukin-1 and interleukin-6. [4]

The incidence of JIA is approximately 13.9/100,000 children/year among children 15 years or younger, with an overall prevalence of approximately 113/100,000 children. [5] Different racial and ethnic groups appear to have varying frequencies of the subtypes of JIA. One study reported that black American children with JIA were older at presentation and less likely to have elevated antinuclear antibody (ANA) titers or uveitis. [6]
There are seven distinct subtypes of JIA. Sub-typing is based on the number of affected joints at presentation, serological features including the presence of antinuclear antibodies, rheumatoid factor and human leucocyte antigen B27 (HLA-B27), family history (of spondyloarthropathy and psoriasis) and associated features. [6] The ILAR subset classifications include systemic onset JIA, polyarticular rheumatoid factor positive, polyarticular rheumatoid factor negative, oligoarticular (persistent and extended subtypes), psoriatic arthritis JIA, enthesitis-related arthritis and others (undifferentiated). [2]
Non-recognition of disease and long diagnostic delays are common, while early recognition and prompt treatment improves the outcome. [7] Approximately 10% of children with systemic JIA develop overt clinical features of macrophage activation syndrome (MAS), a life-threatening condition characterized by fever, organomegaly, cytopaenias, hyperferritinaemia, hypertriglycaeridemia, hypofibrinogenaemia and coagulopathy among other findings. [8] The mortality rate for children hospitalized with systemic JIA and MAS is estimated to be as high as 6%. [9]

Severe growth retardation, significant leg length discrepancy and mandibular asymmetries, micrognathia and malocclusion are common sequelae of JIA. Inflammatory eye disease, especially uveitis, occurs with increased frequency in children with arthritis. The known risk factors include age less than six years at disease onset, pauciarticular pattern of disease, and antinuclear antibody (ANA) positivity. Osteoporosis is a recognized complication of JIA. Some epidemiological studies concluded associated risks for psychosocial and educational related problems in JIA patients. [10]

Local studies on JIA are rather few. Adelowo *et al*. reported 23 cases over eight and a half years with polyarticular predominance (56.5%). [11] In a study of the spectrum of paediatric rheumatic diseases in Nigeria conducted by Olaosebikan *et al*., there were 14 (50%) polyarticular cases out of twenty eight cases of JIA. [12] Chipeta *et al*. in the study of cohorts of patients with juvenile idiopathic arthritis in Zambia recorded polyarticular rheumatoid factor negative subtype as the most frequent type of chronic arthritis encountered. [13]

The goals of therapy for JIA focus on the prompt control of active inflammation and symptoms and the prevention of a number of disease and treatment-related morbidities such as growth disturbances, joint damage, and functional limitations. [14] The present retrospective study was conducted to describe the spectrum of clinical presentations, laboratory parameters and drug therapy among patients with JIA seen at a Tertiary Health Centre.

Methods

Subjects and Methods

A retrospective study of the hospital records of all 1910 patients with rheumatic disorders seen at the Medical Out-Patient Clinic of the Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, Nigeria between July 2012 and June 2016 was carried out. Ethical clearance was obtained from the

Research Ethics Committee of the hospital. The diagnosis of JIA was ascertained using established classification criteria for all the patients and the disease onset and duration were recorded. The socio-demographic parameters were obtained and the following clinical features were also searched for and retrieved from the case records: arthritis, fever, rash, lymphadenopathy, parotid gland enlargement, xerostomia, xerophthalmia, pulmonary symptoms, renal symptoms, and nervous symptoms.

Laboratory and radiological investigations

All the patients with the diagnosis of JIA had serological evaluations, including antinuclear antibody and rheumatoid factor (RF). Full blood count and erythrocyte sedimentation rates were also recorded; (definition of terms included: anaemia - Haemoglobin concentration <10 g/dl, leucopaenia -white blood cell count <4000/µl, thrombocytopaenia - platelet count <100, 000/µl)). Chest X-Ray and joint radiographs were done where necessary to detect the presence of peri-articular erosion and osteopaenia. Serum ferritin level was not determined routinely because of non-availability of facilities.

The patients were treated with non-steroidal anti-inflammatory drugs (NSAIDs), steroids and methotrexate as per unit treatment protocol and the clinical course was followed up at the Out-Patient Rheumatology Clinic.

Disease definition

The disease was defined according to the criteria adopted by the International League of Associations for Rheumatology for Juvenile Idiopathic Arthritis to include the following: [6]

(1) age less than 16 years (2) signs of arthritis in one or more joints (3) disease duration 6 weeks or longer.

Onset type defined in first 6 months as: (1) Polyarticular - when five or more inflamed joints are involved (2) Pauciarticular - when less than five joints are involved and, (3) Systemic onset disease - arthritis of any number of joints with rash and characteristic fever.

Data management:

The data were analysed using simple descriptive statistics.

Results

The total number of Rheumatology cases seen over a four-year period was 1910. There were 18 cases of juvenile idiopathic arthritis constituting 0.9% of the total cases seen. These cases of JIA comprised 13 (72.2%) females and 5 (27.8%) males with a female-to-male ratio of 2.6: 1. Table I shows the socio-demographic characteristics of the patients The age patients ranged between 8 years and 15 years with a mean age of 10.3 ± 2.1 years. The duration of disease prior to presentation ranged between 2 years and 7 years with a mean of 4.2 ± 1.3 years.

Table II shows the pattern of clinical presentations of the patients. The leading constitutional symptom was fever, which cuts across all the subtypes of JIA. Large joint involvement was seen in all the subtypes; polyarticular subtype was identified in 11 (61.1%), oligoarticular in 5 (27.8%) and systemic onset disease in 2 (11.1%) cases.

Knee and ankle were most commonly affected. Small joint involvement was also seen in all cases; this was found in 44.0% (8/18) of all subjects and 72.7% (8/11) of patients with polyarticular subtype. Spinal (lumbo-sacral region) and temporal-mandibular involvement was observed only in polyarticular subtypes. Abdominal organ involvement (liver or splenic enlargement) was seen only in the systemic onset subtype.

Table III shows the laboratory parameters recorded in the patients with JIA. Anaemia was the leading blood count abnormality noted while thrombocytopaenia was only found in 3 patients. Rheumatoid factor was positive (with a titre of 1/80) in only 2 patients belonging to the polyarticular subtype while Anti-nuclear antibody was not significantly positive in all the cases.

Table I: Socio-demographic characteristics of the patients with Juvenile Idiopathic Arthritis

Characteristics	*Polyarticular (n=11)*	*Pauciarticular (n= 5)*	*Systemic (n=2)*
Age range	8-15	8-13	8-9
Mean age at presentation	10.1	9.0	8.5
Sex	F-9 M-2	F-3 M-2	F-1 M1
Female: Male ratio	1.2:1	1.5:1	1;1
Occupation	Students-8 Artisan - 3	Students-5 Artisan - 0	Students- 2 Artisan - 0

Table II: Clinical features of Juvenile Idiopathic Arthritis

Features	*Polyarticular (n=11)*	*Pauciarticular (n=5)*	*Systemic onset (n=2)*	*Total (n=18)*
Morning stiffness	8	1	0	9
Fever	5	3	2	10
Large joint involvement	11	5	2	18
Small joint involvement	8	2	2	12
Spine (Lumbo-sacral)	2	0	0	2
Temporo-mandibular	3	0	0	3
Skin rash	0	0	2	2
Hepatomegaly	0	0	1	1
Splenomegaly	0	0	1	1
Lymphadenopathy	0	0	2	2
Leg length disparity	0	1	0	1

Treatment protocol and outcome

All the patients were treated with a combination of non-steroidal anti-inflammatory drugs (NSAIDS) and steroids, while polyarticular subtype were treated with NSAIDS, steroid and methotrexate. Intra-articular steroid was given to patients with severe articular pain. Table IV shows the treatment regimen for the patients. Seven patients defaulted from follow-up care while three patients died from sepsis syndrome.

Discussion

The subdivision of Juvenile Idiopathic Arthritis into three main subtypes helps both in diagnosis and follow-up of treatment plans for the patients. We chose to use the current International League of Associations for Rheumatology (ILAR) JIA classification criteria in the present study because it enables a more uniform nomenclature and thus guarantee, improved comparative disease diagnosis and epidemiology across countries and

Table III: Laboratory features of Juvenile Idiopathic Arthritis

Features	*Polyarticular (n=11)*	*Pauciarticular (n=5)*	*Systemic onset (n=2)*	*Total (n= 18)*
Anaemia (<10mg/dl)	8	3	2	13
Total white count >10,000/cumm	3	1	2	6
Platelets >400,000/cumm	0	1	2	3
Rheumatoid factor positivity	2	0	2	4
Erythrocyte sedimentation rate>20 mm/hr	9	5	2	16

ethnic populations.

Polyarticular subtype of JIA was the commonest type observed in the present study. Various other studies conducted in Nigeria by Adelowo *et al.*, and Olaosebikan *et al*. also reported the polyarticular subtype to be the commonest form of JIA encountered in clinical practice. [11,12] A study conducted in Zambia by Chipeta *et al.* found the polyarticular rheumatoid factor negative JIA, as the most frequent type of chronic arthritis encountered. [13] The studies in Sri Lanka.[15] and in Lahore. [16] also reported that polyarticular subtype was the commonly encountered subtype of JIA. Similar disease patterns were found in various studies in India. [17 18] The predominance of the polyarticular subtype in the third world countries is, however, in variance with what obtains in the developed countries.

Studies from the Kingdom of Saudi Arabia and Japan showed the predominance of systemic onset JIA. [19,, 20] In the Western countries, oligoarthritis and systemic onset subtypes were more prevalent as compared to polyarthritis. [21, 22]

The observed differences in the distribution of the subtypes in different regions may be attributed to differences in the settings where the studies were conducted. Tertiary hospital-based studies are likely to have polyarticular predominance because

Table IV: Drug treatment of patients with juvenile idiopathic arthritis

	Polyarticular (n=11)	*Pauciarticular (n=5)*	*Systemic onset (n=2)*	*Total (n= 18)*
NSAIDS alone	0	2	0	2
NSAIDS + Methotrexate	11	0	0	11
NSAIDS + steroid	11	5	2	18
NSAIDS+ Methotrexate + steroid	11	0	0	11

of the likelihood of affected patients attending specialized centres for treatment due to obviously worse severity of the disease.

It is also possible that the differences in prevalence rates of oligoarthritis JIA in Africa distinct from those reported in the industrialized western countries may simply be the result of selection bias as a result of the dearth of pediatric rheumatologists in sub-Saharan African. Another plausible explanation is that some children who were classified as polyarticular JIA, may in fact be oligoarticular extended. The explanation for this could be the delay in presentation to the hospital, which is a common finding in the resource-poor parts of the world such as the Sub-Saharan Africa.

The mean duration of disease prior to presentation in the specialist clinic as recorded in the present study was comparable to that reported by Adelowo *et al* (4.2 years versus 3.7 years). The joints most commonly affected in the two Nigerian studies were the ankles and the knees. However, Chipeta *et al*, reported that both upper and lower limbs were equally affected and the knee was not involved in patients with symmetric polyarticular disease. The mean age of the affected children at presentation was 10.3 years in the present study and females were predominantly affected. The high age at presentation was similarly observed in other Nigerian studies and the Zambian study by Chipeta *et al*. Some Indian and Pakistani studies [17, 23] also reported late presentation in patients with JIA. On the other hand, studies from the western parts of the world frequently reported age at onset ranging from one to three years and females were also commonly affected. [24, 25] Though the female preponderance was reported in the present study in agreement with reports from the Western World, the mean ages at presentation differ. The reason for the different age at presentation may in part be due to the late presentation of cases commonly seen in

the developing countries. Some studies have also reported no sex predilection in JIA. [17, 26] The reason for this observation may be the biological characteristics of the disease in those regions of the world.

Fever and early morning joint stiffness were the leading presenting symptoms in the present study. The study by Samia *et al*. in Pakistan also showed the predominance of fever and morning stiffness as presenting complaints in JIA. [27] Some studies from India also agreed with these findings. [28] Fever was a regular feature in patients with systemic onset disease followed by skin rash, hepatosplenomegaly and lymphadenopathy. Anaemia, leukocytosis and thrombocytosis were significant findings in systemic onset disease. Erythrocyte sedimentation rate was uniformly elevated. These findings were consistent with various findings in India and parts of the western world. [26, 28]

All the three subsets of JIA had both large and small joints involvement in the present study. In this study, 11.1% of cases were polyarticular rheumatoid factor positive. Rheumatoid factor positivity was recorded in 11.5% of cases in Chipeta's study, whereas, rheumatoid factor was invariably negative in Adelowo's study. Rheumatoid factor positivity rate of 15% was reported in India by Seth *et al,* and 9.7% by Parkodi *et al*. [26,29] while Selvaag *et al*. reported 4.1% seropositivity in Norway. [30] The percentage of rheumatoid factor positivity in this study was comparable with those reported by Chipeta *et al.* and Parkodi *et al*. The two patients that were seropositive for rheumatoid factor presented with polyarticular disease with higher number of joints involvement. Similar findings were reported in India and some parts of the western world. [17, 31] The reason for this pattern may be the predominance of polyarticular subtype in this study.

All the patients were treated with non-steroidal anti-inflammatory drugs (NSAIIDS), mainly naproxen and ibuprofen. The NSAIDS are commonly used medications in all types of JIA as suggested by a previous study. [32] Systemic steroid (initially in high dose for patients with systemic subtype of JIA) in the form of prednisolone was used for short course therapy in our patients to prevent the complications of long term use in children. Disease modifying anti-rheumatic drug, mainly methotrexate, was used as steroid sparring agent and in patients who had poor response to NSAIDS, and patients with clinical deformity. Intra-articular steroid injection was used where necessary, especially in the pauciarticular subtype.
The objectives of treatment included the alleviation of pain, inhibition of disease activity, and preservation and recovery of range of motion. Since NSAIDS are mostly not efficient when used alone in the treatment of JIA, other more potent anti-inflammatory drugs are often required. Methotrexate has improved the disease course significantly in JIA. Biologics were not used in our patients because of the high cost which was far beyond the reach of our patients. However, the use of biologics has significantly improved the outcome in JIA. [33]
In conclusion, the polyarticular subtype of JIA was the commonest form of JIA in this study while late presentation in the hospital, coupled with the dearth of paediatric rheumatologists, is a major issue in this clinical setting.

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