Research article

Clinical patterns of juvenile idiopathic arthritis: A single tertiary center experience in Kenya

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Abstract

Background: Juvenile Idiopathic Arthritis (JIA) is a heterogeneous group of disorders with different disease manifestations among various populations. There are few reports of JIA among indigenous Africans in sub-Saharan Africa. We present herein the clinical patterns of JIA encountered at a rheumatology clinic, Nairobi, Kenya.

Method: Medical records of patients with a diagnosis of chronic arthritis with onset at the age of 16 years or less presenting to the Nairobi Arthritis Clinic were reviewed between January 2009 and January 2016. They were retrospectively reviewed and reclassified as Juvenile Idiopathic Arthritis (JIA) based on the International League of Associations for Rheumatology (ILA R) JIA diagnostic criteria.

Results: A total of 68 patients were recruited, the females gender was predominant in all categories of JIA apart from Enthesitis related arthritis. The overall female to male ratio was 2.4:1. The range of age at onset of symptoms was between 2 years and 15 years and the mean age at JIA onset was 8.45 ± 4.37 years. The mean age of presentation at the clinic was 10.22± 3.79 years. Polyarticular rheumatoid factor negative arthritis was most common at 38.2%, followed by oligoarticular 23.5%, polyarticular rheumatoid factor positive 17.6%, systemic JIA at 14.7% and enthesitis associated arthritis at 5.9%. Large joints were affected in 85.2%, small joints 44% and fever was present in 73.5% of patients. One patient had the typical rash of systemic onset JIA (Still's) and another had uveitis. The ESR was raised in all categories of JIA with a mean of 44.35mm/hr while the haemoglobin was reduced with a mean of 10.82mg/dl. Positive Rheumatoid Factor (RF) was found only in RF positive polyarticular JIA. NSAIDs were used in all the patients. NSAIDS were combined with corticosteroids in 38/68 (55.9%) patients while NSAIDs, corticosteroids and methotrexate were used in 16/68 (23.5%) patients and biologics were received by 6/68 (8.8%) patients at different and varying length of time.

Conclusion: This is the first study of JIA undertaken in Kenya. Our patients had a delayed presentation, were predominantly female and sero negative polyarticular arthritis. Challenges experienced in this setting include late presentation to rheumatologists and inadequate resources (personnel, finances, equipment and drugs).

Key words: Juvenile idiopathic arthritis, ILAR, Kenya, Clinical patterns, Treatment

Introduction

Juvenile Idiopathic Arthritis (JIA) is a poorly described disease in Kenyan children. JIA is defined by International League of Associations for Rheumatology (ILAR) as arthritis that begins before the 16th birthday and persists for at least 6 weeks, other conditions being excluded[1]. Literature on the prevalence and incidence of JIA suggest that the rates differ depending on different ethnic and geographically distinct populations[2]. JIA is the most common chronic rheumatic disease amongst children and is an important cause of both short and long term disability in children resulting in decreased quality of life[3]. Kenya has a high burden of infectious diseases (HIV, TB) as well as social diseases (poverty, malnutrition) which demand for a great amount of attention and resources. This has left rheumatic diseases such as JIA with limited amount of resources, education, and research. This is compounded by the fact that Kenya has very few trained paediatric subspecialists caring for children with rheumatic diseases and educating medical students and paediatric trainees. Recently Kenya appointed its first paediatric rheumatologist. There are few reports on JIA in sub-Saharan Africa. In this study, we present the spectrum and epidemiological subtypes of JIA among children seen at a rheumatology clinic in Nairobi.

Materials and Methods

This was a retrospective study carried out in the Nairobi Arthritis Clinic. The study site is situated in Nairobi, the capital city of Kenya and serves as a tertiary referral centre. It not only serves the two million inhabitants of Nairobi but also patients from all over Kenya and the greater East and Central African Region.

Following ethical approval, we reviewed the case records of all patients with a diagnosis of Juvenile Idiopathic Arthritis (arthritis in one or more joints lasting 2 weeks or more with no identifiable cause in those who are less than 16 years of age) attending the Nairobi Arthritis Clinic between January 2009 and January 2016.

Medical records of patients who met the International League of Associations for Rheumatology (ILAR) JIA diagnostic criteria of Juvenile Idiopathic Arthritis (JIA) and had been on follow up for at least 6 months were recruited into the study. This retrospective review of the JIA case records involved reclassifying each of the patients by the ILAR diagnostic JIA criteria and then compiling respective clinical data of each patient. Clinical, haematological, immunological and other relevant findings from the history were obtained from the available records. Patients were thus categorized as systemic arthritis (Stills disease), persistent oligoarthritis (4 joints or less), polyarthritis (RF negative), polyarthritis (RF positive), psoriatic arthritis and Enthesitis Related Arthritis (ERA). The remaining two subgroups within the ILAR classification system, Extended Oligoarthritis and Undifferentiated Arthritis rely on a period of observation which for many of our patients was not possible.

Patients excluded from the study were those who had signs and symptoms of other arthritis such as acute rheumatic fever, septic arthritis, systemic inflammatory disorders (systemic lupus erythematosus, vasculitis, or dermatomyositis), malignancy, human immune deficiency virus type 1 (HIV-1) infection, or metabolic diseases were excluded from the study after careful scrutiny of the respective case records. Data were collected about number of patients of each JIA subtype, gender, age at disease onset, joints involved, presence of fever, rash and pharmacological agent used. The percentage of each JIA subtype was calculated and the age of disease onset was expressed as the mean ± standard deviation (SD); as shown in Tables 1 and 2.

The major clinical data collected were large joints involvement (knee, ankle, elbow, shoulder, and wrist) or small joints involvement and presence of uveitis during the course of the disease. The presence of fever and skin rash at diagnosis was also recorded. These clinical findings were diagnosed by a rheumatologist while uveitis was diagnosed using slit lamp examination by an ophthalmologist. Initial data at diagnosis included haemoglobin level (anaemia defined as Hb < 12mg/dL), ESR > 20 mm/hr, and positivity of Anti-Nuclear Antibodies (ANA) and Rheumatoid Factor (RF) as shown in Table 2.

Review of anti-rheumatic pharmacologic treatments used during the study period included (Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), corticosteroids (intra-articular/ systemic), methotrexate (MTX), and biologic agents) was done. Number and percentage of those who were treated with NSAIDs alone, NSAIDs and corticosteroids, NSAIDs, corticosteroids and MTX, NSAIDs and NSAIDS, corticosteroids, MTX and biologics in each JIA subtype were calculated and presented in Figure 1.

Results

The records of 73 patients were reviewed of which 5 patients were excluded due to insufficient data. Table 1 shows general characteristics of the patients: Of the total 68 patients recruited, female gender was predominant in all categories of JIA apart from enthesitis related arthritis. The overall female to male ratio was 2.4:1. The range of age at onset of symptoms was between 2 years and 15 years with a mean age of 8.45 ± 4.37 years. The mean age of presentation at the clinic was 10.22 ± 3.79 years. Polyarticular rheumatoid factor negative arthritis was most common at 38.2%, followed by oligoarticular 23.5%, polyarticular rheumatoid factor positive 17.6%, systemic JIA at 14.7% and enthesitis associated arthritis at 5.9%.

Table 2 shows main clinical features of our patients; The main symptoms were in the large joints (85.2%) and fever (73.5%). The numbers of affected patients' small joints were lower at 44%. One patient had the Still's rash and another had uveitis. The ESR was raised in all categories of JIA with a mean of 44.35mm/hr while the haemoglobin was reduced with a mean of 10.82mg/dl. Ferritin levels were elevated in 11.8% of the total population (systemic JIA at 40%, oligoarticular arthritis at 40%). Positive Rheumatoid Factor was found only in RF positive polyarticular JIA. ANA was positive in 5 out of the 46 (10.9%) samples tested (oligoarticular arthritis 2, polyarticular arthritis RF positive at 3).

Figure 1 shows the anti- rheumatic pharmacologic treatment received by our patients during the course of the disease. NSAIDs were used in all the patients. NSAIDS were combined with corticosteroids in 38/68 (55.9%) patients while NSAIDs, corticosteroids and methotrexate were used in 16/68 (23.5%) patients and biologics were received by 6/68 (8.8%) patients at different and varying length of time. Biologics used included etanercept (Enbrel), rituximab (Mabthera), and tocilizumab (Actemra).

Table 1: Profiles of JIA patients presenting at the Nairobi Arthritis Clinic

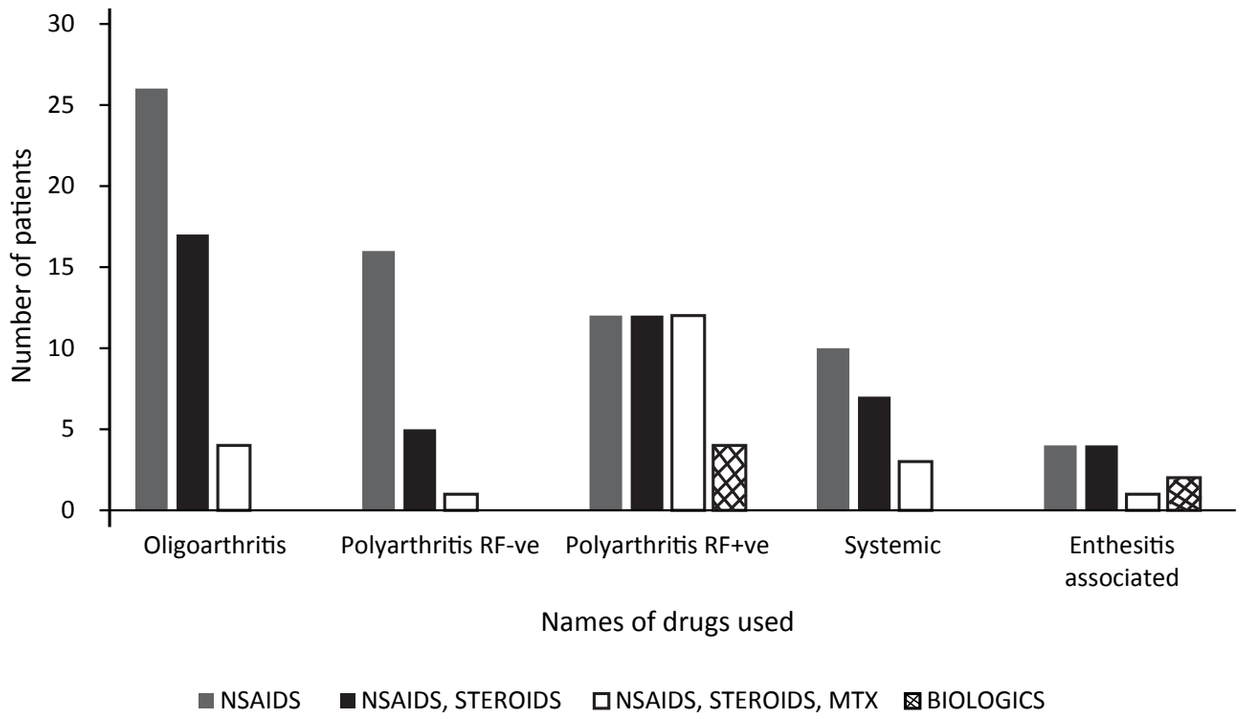
JIA subtypes	Total number	Gender M:F ratio	Age range at presentation (years)	Mean age of onset of disease (years)
Overall	68	1:2.4	2-15	8.45 ± 4.37
Systemic JIA	10 (14.7%)	3:7	3-15	8.5 ± 3.98
Oligoarticular arthritis	16 (23.5%)	1:3	2-15	6.46 ± 4.46
Polyarticular RF (−) JIA	26 (38.2%)	5:8	6-15	10.7 ± 2.57
Polyarticular RF (+) JIA	12 (17.6%)	0:12	6-15	10.41 ± 3.02
Psoriatic arthritis JIA	0	N/A	N/A	N/A
Enthesitis related arthritis	4 (5.9%)	3:1	10-15	12 ± 2.16
Other	0	N/A	N/A	N/A

Table 2: Clinical features related to disease categories in children with JIA

Features	Systemic JIA (n=10)	Polyarticular RF(−) JIA (n=26)	Polyarticular RF(+) JIA (n=12)	Oligoarticular arthritis (n=16)	Psoriatic arthritis JIA	Enthesitis related arthritis (n=4)	Total
ESR (mean)mm/hr	40.6±13.8	49.92±13.17	58.44±15.8	35.5±12.37	0	46.75±6.38	44.35
Percentage with elevated Ferritin	40%	0%	0%	40%	0	0	8(11.8%)
HB (mean in mg/dl)	11.0±1.86	10.01±2.01	11,54±1.2	11.3±1.46	0	11.89±1.76	10.82
Fever(n)	8	9	12	17	0	4	50(73.5%)
Large joint(n)	6	16	11	21	0	4	58(85.2%)
Small joints (n)	3	9	8	10	0	2	30(44%)
Eye involvement(n)	0	0	2	0	0	1	3 (4.1%)
Still's rash(n)	1	0	0	0	0	0	1 (1.5%)

ESR = Erythrocyte Sedimentation Rate
Large joint = knee, hip, sacroiliac, lumbar
Small joint = elbow, finger, ankles, toe, wrist

Figure 1: Pharmacologic therapy used in JIA patients



NSAIDS = Non-steroidal anti-inflammatory drugs; MTX = methotrexate; Biologics = Biologic Disease-modifying antirheumatic drugs

Discussion

This study covered a total period of 8 years and has yielded 68 cases of JIA. Table 3 is a summary of other studies that have used the ILAR classification criteria. It highlights similarities and differences between various populations worldwide in particular developed and developing countries. Similarities include a female predominance over all the JIA subtypes apart from ERA. This is in keeping with known literature that JIA is more common in females than males[4 - 7]. However the gender ratios also show a relative paucity of females in developing nations compared to studies in industrialized nations where the FM ratio is around of 5.1.

The mean age at onset of JIA was 8.45 ± 4.37 years which is largely similar to studies from Zambia and South Africa and higher than most studies from Europe, some Asian and Latin America countries[8-12]. The study noted a delay in presentation of the patients as the mean age at presentation was 10.22 years. Similar observations have been noted in other studies around Africa and Asia. This differs from data in the western world where time between age of onset to presentation was shorter[8-9,11-14] . Possible reasons for this could be that of late presentations at the clinic due to late referrals after the onset of the initial symptoms, cultural stigma surrounding JIA and socioeconomic reasons. This is an area for future studies.

The predominant subtype of JIA was the polyarticular arthritis rheumatoid factor negative arthritis was most common at 38.2%. This differs with most studies where oligoarticular arthritis is the most common[4 - 8]. This is likely due partially at least to the low prevalence of oligoarticular arthritis observed in studies from Africa and India as compared to Western cohorts. Young preschool females predominate in this particular subset in European and UK studies[7]. It has been described in the literature that non-European populations have a decreased relative risk of suffering from oligoarthritis[15]. Since our study was undertaken in a tertiary center, we believe that selection bias may have contributed to the lower numbers of oligoarticular arthritis. Milder forms of JIA especially oligoarticular may be treated by general paediatricians or orthopaedic doctors and end up not being referred to a secondary care facility[10,13,16]. It is possible therefore that some children classified as polyarticular may in reality be "oligoarthritis extended". In this context it is of interest that in true community based studies in the developing world the prevalence of oligo articular disease matches or exceeds that of polyarticular disease[16].

The relatively high prevalence of the rheumatoid factor positive group in our study and three other Africa studies to date [9,10,17], seems to support the notion that Africans are at an increased risk for this particular type of JIA[15.] We must mention there is a limitation in getting two positive RF assays at least 3 months apart in the first 6 months of the disease in order to diagnose RF positive polyarthritis as required in the ILAR diagnostic criteria due to financial constraints[1]. As standard practice in our clinics one positive or negative assay is considered to be sufficient to classify a patient with polyarthritis. This is one of the drawbacks of using ILAR diagnostic criteria in low income resource set ups. This difficulty is mentioned in South Africa, India and a study of Nordic children[9,13,18]. Thus it is possible RF positive polyarthritis patients may be overrepresented in our polyarticular subtype thus reducing the RF negative numbers as the patients were classified using one positive assay.

Table 3: Comparative JIA epidemiology: developing and developed countries

JIA subtypes	Kenya	Zambia[8]	South Africa[7]	Morocco[9]	Egypt[12]	Oman[11]	India[13]	Turkey[10]	Saudi Arabia[14]	Latin America[6]	United Kingdom[20]
Number in the studied series	68	78	78	80	196	107	235	196	82	397	507
Female: Male Ratio	2.4:1	1.2:1	1:1	1.4:1	1.09:1	2.5:1	1:1.4	1:1.1	1.64:1	2.125:1	1.8:1
Mean age of onset	8.45	9.4	8(7.3)		6.257	6.85	12	7	7.11	6.6	6.8
Systemic JIA (%)	14.7	14.1	7.7	26	24	17.8	8	5.3	36.5	28.5	5.3
Polyarticular (%)				31.5	34.7					40.6	
Polyarticular RF (−) JIA (%)	38.2	34.6	14			39.2	17	30.6	24.39		13
Polyarticular RF (+) JIA (%)	17.6	11.5	26.9			7.5	12	6.6	4.87		2.3
Oligoarticular arthritis (%)	23.5	32.1	26	42.5	41.3	31.8	21	34.1	28.04	30.9	46
Psoriatic arthritis JIA (%)		1.3	1.3				1	1	4.87		7
Enthesitis related arthritis (%)	5.9	6.4	23			3	36	10.3	1.21		6.3

The main symptoms were large joints (85.2%) and fever (73.5%). The number of affected patients' small joints were lower at 44%. Literature shows that large joints apart from the hips are most affected as compared to small joints[4]. A higher percentage of patients with fever was reported in our cohort. The numbers with systemic JIA were low but comparable with other studies, of which 80% of these patients reported fever[9,10,14]. Picking up other extra-articular features is a challenge in our low resource set-up and Africa as a whole that is burdened by infectious disease. We found one patient with uveitis. As rheumatology knowledge increases amongst doctors and other care providers in low resource settings like Africa, leading to the application of standard diagnostic and classification criteria, prevalent cases are likely to continue to resemble those reported elsewhere. The subgroup of ERA is uncommon though follow up studies on prevalence of HLA B27 will also be required. This is similar to data from Zambia but differs from South Africa where they found large numbers with ERA[9]. However, it's important to note the South African study wasn't a pure African population.

Majority of our patients had anaemia (61.37%) with a mean haemoglobin of 10.82mg/dl. This was comparable to other studies on JIA populations[14]. Anaemia in JIA is commonly caused by iron deficiency or due to chronic inflammation[14,19]. This is higher than what is quoted in local data at 28.8%[18]. Rheumatic fever is still common in our set-up, ASOT titers were done on 14 samples, of which one turned out positive. ANA was positive in 5 out of the 46 (10.9%) samples tested (oligoarticular arthritis 3, polyarticular arthritis RF positive at 2). This is similar to other studies that found low numbers of ANA positivity [9,20]. As expected most ANA positivity cases were in oligoarticular JIA.

The goals of management of JIA are control active symptoms, achieve remission, prevent joint damage, and preserve joints function to prevent disability as well as maintaining normal growth. Pharmacologic therapy of JIA has major advances over the last two decades especially with the introduction of biologics. In low resource setups like ours, patients have difficulties accessing these rheumatic drugs let alone biologics mainly due to costs and their availability. Another stumbling block is the lack of local clear guidelines on diagnosis and management of common rheumatic conditions including JIA. Our practice is to start with NSAIDs for 4 to 6 weeks followed by DMARDs, most commonly methotrexate in case of no adequate response to NSAIDs. IAC are used to relieve joint inflammation and systemic steroids are usually used for a short time with the lowest effective dose and are tapered once we get the desired response. In case of failure of methotrexate, the options include trial of another DMARD or biologic therapy is introduced. NSAIDs were used in all the patients. NSAIDS were combined with corticosteroids in 55.9% patients while NSAIDs, corticosteroids and methotrexate were used in 23.5% patients and biologics were received by 6 patients at different and varying length of time. Biologics used included etanercept (Enbrel), rituximab (Mabthera), and tocilizumab (Actemra). It's important to note a number of patients met the criteria for biologics but due to costs were not started on them.

A major limitation of our study is being a retrospective record-based in nature and a single center-based with a relatively small sample size. Another limitation is that the patients attending this rheumatology clinic may have more severe disease than those in the community. Milder forms of JIA have a higher chance of going into remission and may not need to be referred to a rheumatology clinic. However, our study can be a starting point to raise the awareness about JIA and possible more studies on prevalence, disease activity and its impact on the school going children nationwide. We recommend that more needs to be done to improve on diagnosis through education and diagnostic equipment and management of these patients by availing appropriate medicines. This study also suggests that there should be a modification of the ILAR diagnostic criteria to suite low income resource areas.

Conclusion

This is the first JIA study done in Kenya. JIA in this study population has similarities and differences with profiles compared to other international JIA studies. It shares characteristics with other studies that it is predominantly female, affects large joints with polyarticular arthritis subtype being the most common form in our population. There are difficulties with the ILAR classification in our setting, specifically regarding the requirement of 2 rheumatoid factor tests. The subgroup of ERA is uncommon though follow up studies on prevalence of HLA B27 will also be required. The most common presentation of a JIA patient in our set-up is fever, affects large joints and anaemia. The most common form of pharmacological interventions is NSAIDS and corticosteroids. The use of biologics in this set up is still very low. Late presentation coupled with the absence of specialized health services are issues that will need to be addressed.

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Conflict of interest

The authors declare no conflict of interest.

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