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Study of clinical spectrum of juvenile idiopathic arthritis in children in a tertiary referral hospital.

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Abstract

Juvenile idiopathic arthritis (JIA) also called juvenile rheumatoid arthritis (JRA) is characterized by chronic synovitis of peripheral joints manifesting as soft tissue swelling and effusion. The incidence and prevalence vary among ethnic and geographically different population. The overall prevalence of JIA is estimated to be from 0.07 to 4.1 per 1000 children, with an incidence of 0.008 to 0.226 cases of JIA per 1000 children. It differs from adult rheumatoid arthritis because RF-factor usually absent and antinuclear antibody sero-positivity is common. In children there is a 2:1 female predominance. The present study was carried out over a period of 4 years. All consecutive patients who fulfilled the American College of Rheumatology (ACR) criteria of JRA were enrolled in the study. Out of 112 children 46 (41%) were male and 66 (59%) were female children. Out of these children 10 (8.93%) had systemic onset, 62 children (55.36%) had poly-articular on set and 40 children (35.71%) had pauci-articular onset JIA. Predominant clinical features of systemic onset JIA was fever (100%), joint pain and swelling (100%), lymhadenopathy (70%), hepatomegaly (60%), spleenomegaly (40%), cardiac involvement (40%) and skin rashes was found in one case (10%). Polyarticular JIA sub-type is the commonest type in this hospital based study, followed by pauciarticular JIA. Recognition of these different subtypes is useful in the diagnosis and long-term management of these patients. Treatment according to the sub-types and induction of newer therapeutic agents in the management of JIA will prevent morbidity.

Keywords: Juvenile idiopathic arthritis, Polyarticular, Pauciarticular, systemic onset

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Introduction

Juvenile idiopathic arthritis (JIA) also called juvenile rheumatoid arthritis (JRA) 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, each of which has distinct modes of presentation and may have same or different causes [1]. Juvenile idiopathic arthritis is the most common rheumatic disease in children, with active disease that can persist into adulthood and may result in short or long term morbidity [1, 2]. The incidence and prevalence vary among ethnic and geographically different population. The overall prevalence of JIA is estimated to be from 0.07 to 4.1 per 1000 children, with an incidence of 0.008 to 0.226 cases of JIA per 1000 children [3]. While oligoarticular being 40% of newly diagnosed among Caucasian population, polyarticular is predominant in African, East Indian and Indian population. It differs from adult rheumatoid arthritis because RF-factor usually absent and antinuclear antibody sero-positivity is common. In children there is a 2:1 female predominance [4].

The diagnosis will be based upon the pattern of symptoms i.e; morning stiffness (>1 hour), distribution of the inflammed joints and blood & x-ray findings. Primary symptoms of rheumatoid arthritis are the inflammation of synovial membrane. There is no known cure for rheumatoid arthritis; the goal of treatment in rheumatoid arthritis is to reduce joint inflammation, pain and stiffness, maximize joint function and prevent articular damage, joint destruction and deformity [5-8]. The present study was conducted to evaluate the spectrum of clinical presentation, laboratory parameters and drug therapy required in patients with JIA seen at a tertiary care dedicated children's hospital.

Material and Methods

The present study was carried out in the department of Pediatrics, Sri Siddhartha Medical College, Tumkur, Karnataka, India, over a period of 4 years, from November 2009 to November 2013. All consecutive patients who fulfilled the American College of Rheumatology (ACR) criteria of JRA were enrolled in the study. ACR criteria include age less than 16 years, signs of arthritis in one or more joints, disease duration 6 weeks or longer, onset type defined in first 6 months (i) polyarthritis: when 5 or more inflamed joints; (ii) oligoarthritis: when less than 4 joints and (iii) systemic onset disease: arthritis with characteristic fever and exclusion of other forms of juvenile arthritis [9].

Data collected at first clinical visit included age, gender, number of joint involvement, associated systemic features like morning stiffness, fever, rash, lymphadenopathy and hepatosplenomegaly. Type of arthritis was assigned according to ACR criteria. Clinical uveitis was diagnosed by slit lamp examination by ophthalmologist. Relevant laboratory data was noted including, haemoglobin (Hb), total leukocyte count (TLC), platelet count (PLT), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and presence of rheumatoid factor (RF) and antinuclear antibodies (ANA). Patients were treated with non-steroidal anti-inflammatory drugs (NSAIDs), steroids and methotrexate as per protocol and course of their disease was followed in outpatient clinic.

Results

A total of 112 children were included in the study. Out of 112 children 46 (41%) were male and 66 (59%) were female children. Out of these children 10 (8.93%) had systemic onset, 62 children (55.36%) had poly-articular on set and 40 children (35.71%) had pauci-articular onset JIA. There was male preponderance of 1.5:1 in systemic onset, female preponderance 2.1:1 in poly-articular on set and in pauci-articular JIA, there was no much difference in the sex ratio (M: F= 1:1). The mean age of onset in systemic type was 5.8 years, in pauci-articular was 7.2 years and in poly-articular was 9.5 years. Predominant clinical features of systemic onset JIA was fever (100%), joint pain and swelling (100%), lymhadenopathy (70%), hepatomegaly (60%), spleenomegaly (40%), cardiac involvement (40%) and skin rashes was found in one (10%) case (Table 1). Smaller joints of the hands both proximal interphalangeal joints and meta-carpo phalangeal joints were more involved in the systemic and poly-articular JIA. Most commonly involved joints in the order of decreasing frequency were knee, ankle, wrist, and elbow in all the subtypes. Hip was involved in 6.45% of cases in polyarticular JIA and only one case in systemic JIA. Cervical spine was involved in 20% of cases in polyarticular and systemic type of JIA.

Rheumatic factor was positive in 16.13% cases of polyarticular JIA and only one case in systemic onset type (10%). Antinuclear antibodies was positive in over all in 6 cases (5.3%) of all subtypes in which pauciarticular 3 (7.5%), polyarticular 2 (3.2%) and only one case in systemic onset. C- reactive protein was positive above 0.6mg/dl in 100% of systemic onset, 64.52% in polyarticular and 25% of pauciarticular JIA. Anti-StreptoLysin-O (ASLO) was positive in 80% of systemic, 30% of polyarticular and 15% of pauciarticular JIA. ESR was raised above 20mm/1st hr commonly in systemic and polyarticular type but in pauciarticular only 50% cases ESR was raised. Anemia was commonly found in systemic onset (80%) and polyarticular (48.4%) JIA.

Table 1. *Clinical features of JIA*

Clinical features	Systemic on set		Poly-articular		Pauci-articular	
	n=10	%	N=62	%	n=40	%
Joint pain	10	100	62	100	40	100
Joint swelling	10	100	62	100	25	62.50
Fever	10	100	16	25.81	10	25
Morning stiffness	04	40	40	64.52	22	55
Skin rashes	01	10	-	-	-	-
Lymphadenopathy	07	70	06	09.67	01	02.50
Hepatomegaly	06	60	06	09.67	01	02.50
Spleenomegaly	04	40	01	01.61	01	02.50
Cardiomegaly	02	20	03	04.84	-	-
Pericardial effusion	01	10	-	-	-	-
Mitral regurgitation	01	10	03	04.84	-	-
Pallor	08	80	30	48.39	12	30

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Table 2. *Mean age of onset in years of JIA in various studies*

JIA Subtypes	Seth et al	Porkodi et al	Chandrashekaran et al	Present study
Systemic on set	5.2	7.2	6.4	6.1
Polyarticular	6.8	8.1	10.7	9.5
Pauciarticular	7.2	8.6	11.0	7.2

Table 3. *Comparison of extra articular manifestations of JIA*

Extra articular manifestations	A N Chandrashekar et al						Present study					
	Systemic		Polyarticular		Pauciartcular		Systemic		Polyarticular		Pauciarticular	
	n-44	%	n-171	%	n-116	%	n-10	%	n-62	%	n-40	%
Fever	44	100	42	24.56	17	14.66	10	100	16	25.81	10	25
Rash	19	43.18	-	-	-	-	01	10	-	-	-	-
Lymphadenopathy	40	90.90	13	07.60	06	05.17	07	70	06	09.67	01	02.50
Hepatomegaly	24	54.55	10	05.85	01	0.86	06	60	06	09.67	01	02.50
Spleenomegaly	18	40.90	05	02.92	01	0.86	04	40	01	01.61	01	02.50
Eye changes	-	-	05	02.92	05	04.31	-	-	-	-	-	-
Sub cutaneous nodules	-	-	08	04.68	-	-	-	-	-	-	-	-
Cardiac involvement	03	06.92	08	04.68	-	-	02	20	03	04.84	-	-

Table 4. *Comparison of immunological parameters in JIA*

Author	Type of JIA	Immunological parameters			
		Rhumatoid Factor	Anti nuclear Antibodies	Anti Streptolysin-O Titers	C-Reactive Protein
Seth et al %	Systemic	09.50	-	-	-
	Polyarticular	14.80	06.50	-	-
	Pauciarticular	03.00	04.50	-	-
Chandrashekaran et al %	Systemic	02.27	11.36	25.00	100.00
	Polyarticular	13.45	38.59	29.00	85.96
	Pauciarticular	-	05.17	31.00	81.89
Present study %	Systemic	10.00	10.00	20.00	100.00
	Polyarticular	16.13	03.24	30.00	64.52
	Pauciarticular	-	07.50	15.00	25.00

Table 5. *Comparison of hematological parameters in JIA.*

Author	Type of JIA	Hematological parameters		
		Hb <10gm%	ESR > 20mm/1st Hr	WBC >10,000cells/mm^3
Seth et al %	Systemic	52.30	100.00	67.80
	Polyarticular	36.80	95.90	57.60
	Pauciarticular	35.80	91.10	67.90
Chandrashekaran et al %	Systemic	54.50	100.00	100.00
	Polyarticular	27.48	87.13	11.60
	Pauciarticular	20.60	88.79	25.80
Present study %	Systemic	80.00	100.00	70.00
	Polyarticular	48.39	96.77	09.68
	Pauciarticular	30.00	50.00	07.50

Discussion

Although, juvenile rheumatoid arthritis is not a rare disease, its true frequency is not known in our country. JIA has been divided into various subgroups. This categorization helps in diagnosis, follow-up and subsequent care of these children [10]. The commonest type of JIA in our experience is polyarticular type JRA, a finding which is in consonance with other studies [11, 12]. However other worker from India had found pauciarticular type JIA to be more common [13]. Although, it is difficult to provide an explanation for these differences, it may be related to the

different genetic backgrounds of the populations under study. It is known that some HLA haplotypes are closely associated with certain subtypes of JIA [1].

Rheumatoid Arthritis is strongly associated with the inherited tissue type major histocompatibilty complex (MHC) antigen HLA-DR4, hence family history is an important risk factor. The causes of rheumatoid arthritis are still incompletely known. Even though infectious agents such as viruses, bacteria (mycoplasma, parvovirus B19, rubella etc.) and fungi have been suspected not has been proven as the causes. Environmental factors e.g. smoking tobacco also seems to play some role in causing rheumatoid arthritis [14]. The nature of the autoimmune reaction (CD4+T-helper cell activation), the mediators of tissue injury (cytokines TNF and IL-1), genetic susceptibility (HLA-DR4 allele) and the arthritic antigen are key consideration in pathogenesis of disease [15].

In this study female children (59%) are affected more than the male children (41%) who are in concordance with other studies [1, 13, 14, 15 & 16]. The age of onset of JRA is usually 1-3 years and the disease is unusual below 6 months of age. In our study the mean age of onset in systemic type was 5.8 years, in pauci-articular was 7.2 years and in poly-articular was 9.5 years, as compared with other studies (Table 2). In the present study fever was the most common extra articular manifestation in the systemic onset type JIA, which was comparable with the study conducted by Chandrashekaran et al (Table 3). Immunological and hematological parameters in the present study were not in concordance with other studies (Tables 4, 5).

Unlike studies from western countries, we had no case of uveitis. Uveitis could be detected only with slit lamp examination of patients by an ophthalmologist. Low frequency of uveitis has been a uniform finding in all Indian series reported so far. Occurrence of uveitis is closely related to ANA positivity [11], which again is reported to be very low in Indian children with JIA. Thus low rates of ANA positivity and infrequent occurrence of uveitis are certain unique features of the disease as seen in India. Rheumatoid nodules were not present in our study. Other Indian workers have reported rheumatoid nodules in 3-8% patients [14, 15] but a series [13] found these in only 0.8%. In the western literature, rheumatoid nodules have been reported in up to 10% of such patients [1].

Rheumatoid factor positivity is seen in 15-20% children with JIA [1]. Two Indian series [13, 14] have also reported similar figures. However, we found rheumatoid factor positivity in only one (10%) patient of systemic type and ten (16.13%) patients of polyarticular type. Rheumatoid factor positivity is seen more often in polyarticular JIA [l]. Rheumatoid factor positivity is said to be closely associated with occurrence of rheumatoid nodules [1]. However, in our series none of the children who had rheumatoid factor positive had rheumatoid nodules.

Heart disease is a rare complication of JIA. In our study cardiomegaly was seen in 2 (20%) cases of systemic onset type and 3 (3.84%) cases of polyarticular type. Pericardial effusion was seen in 1 (10%) case of systemic onset type. Mitral regurgitation was seen in 1 (10%) case in systemic onset type and 3 (3.84%) cases in polyarticular type, which was comparable with chandrashekaran A N et al.
Non steroidal anti-inflammatory drugs (NSAIDs) are the mainstay of treatment of IRA. Aspirin is the most useful NSAID in the treatment of JIA as it is safe, effective and economical. Naproxen is another useful alternative therapy because of its prolonged half life allowing twice a day dosing [17]. Second line agents in the management of JIA are disease modifying antirheumatic drugs which are used when NSAIDs alone are not effective in controlling the disease [18]. Methotrexate is the most frequently used drug of this category [19] Chloroquine can be used only in older children, because it is difficult to monitor visual fields in young subjects. Even in such patients chloroquine was never found to be very useful in inducing remission. Glucocorticoids have been used for acute and severe life threatening disease, for rapidly progressive disease and uveitis. We have frequently used short courses of steroids in severely symptomatic patients and have found them to be quite effective. Intra-articular steroids are useful for monoarticular arthritis or in a child with polyarticular disease where a single joint is resistant to systemic therapy [1].

Conclusion

Polyarticular JIA sub-type is the commonest type in this hospital based study, followed by pauciarticular JIA. Recognition of these different subtypes is useful in the diagnosis and long-term management of these patients. Treatment according to the sub-types and induction of newer therapeutic agents in the management of JIA will prevent morbidity.

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