Journal of Medical Sciences

ISSN 1682-4474

science alert

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Research Paper

J. Med. Sci., 9 (2): 98-102
15th February, 2009

JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued eight times per year on paper and in electronic format.

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Juvenile Idiopathic Arthritis, the Egyptian Experience

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To study the characteristics of Juvenile Rheumatoid Arthritis (JRA) in the Egyptian population, comparing it to other populations. We retrospectively studied the charts of 196 Egyptian children with Juvenile Rheumatoid Arthritis (JRA), who fulfilled the ILAR (International League Association for Rheumatology) classification of JIA and were followed up between 1990 and 2006 in the Children's Hospital, Cairo University. Their clinical features and laboratory data were collected and statistically analyzed. The male to female ratio was 1:1.09 and the mean age of disease onset was 6.257±3.41 years. The mode of onset was oligoarticular in 41.3%, polyarticular in 34.7% and systemic in 24%. Chronic uveitis was found in 5.6% of the children. Antinuclear antibody (ANA) status was determined in all patients and was positive in 21.7%. Amyloidosis was present in 1.76% of patients. The spectrum of clinical presentation of the disease in Egyptian children shows both some similarities and some differences from other populations, with oligo and polyarticular onset subtypes being commonest. The cause of these differences may be due, in part, to ethnic and environmental factors. Referral bias may be another cause.

Key words: Childhood arthritis, rheumatoid epidemiology

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INTRODUCTION

Juvenile Idiopathic Arthritis (JIA) is a term referring to a group of disorders characterized by chronic arthritis manifesting by synovitis with or without systemic features (Sircar *et al*., 2006). It is the most common chronic rheumatic illness in children and is a significant cause of short and long term disability (Weiss and IIowite, 2005) According to the International League of Associations for Rheumatology (ILAR) classification, JIR includes several subgroups, including systemic arthritis, oligoarthritis, polyarthritis, enthesitis-related arthritis, psoriatic arthritis and others, all of which are distinguished by clinical and laboratory features (Weiss *et al*., 2005). However, in spite of being a common disease, it is still one of the most enigmatic problems in rheumatology (Borchers *et al*., 2006). The clinical presentation of the disease differs in different populations, reflecting the effect of genetic and environmental factors (Bahabri *et al*., 1997). The disease has been studied extensively in Western countries. Studies have shown the following characteristics: a predominance of the pauciarticular onset type, lower incidence of systemic onset disease and a higher risk of secondary amyloidosis (Bahabri *et al*., 1997). Reports from Arab countries are insufficient (Bahabri *et al*., 1997). The management of JIA combines anti inflammatory and immuno-modulatory medications with physical and occupational therapy, psychosocial and educational partnership with patients and their parents in addition to the occasional need for surgery and nutritional support for these children (Hashkes *et al*., 2005).

During the past few years, remarkable advances in the treatment of JIA have been made with the advent of new disease-modifying antirheumatic agents (DMARDS) and biologic therapy (Martini *et al*., 2006).

The objective of this retrospective study was to describe the demographic, clinical and laboratory features of JIA among Egyptian children, comparing them to those of other populations.

MATERIALS AND METHODS

We retrospectively analyzed the medical records of 196 Egyptian children with JIA followed up from January 1990 until December 2006 at the Pediatric Rheumatology Clinic of the Children's Hospital, Cairo University, Egypt. One hundred and two female and 94 male patients who fulfilled the ILAR (International league association for Rheumatology) criteria for classification of JIA (Weiss *et al*., 2005) were enrolled in the study. All patients had been followed up for at least 18 months. We recorded the age of disease onset, main presenting features and also clinical and laboratory manifestations of the disease. We performed a urine examination for these children every 3 months in order to search for proteinuria. A chest x ray was carried out for all patients, in addition to an echocardiography when cardiac affection was suspected. Antinuclear antibody (ANA) screening was carried out by indirect immunoflourescence (IF) using Hep-2 cells. Slit lamp examination was used for screening of uveitis. The disease course was considered remittent if the disease activity lasted less than 2 years from the onset and terminated in remission without recurrence. Progressive or unremitting disease course was characterized by active disease for more than two years (Bahabri *et al*., 1997). We summarized our results using simple descriptive statistics, such as the mean, median and range. The t-test was used to compare numerical data. The Chi-square test was used to compare nominal data. Overall, $p<0.05$ were considered significant.

RESULTS

We included in present study 196 Egyptian JRA patients (94 males and 102 females, male- to-female ratio of 1:1.09) with a mean age of 11.93± 4.423 years (range 3-25 years). Their ages at disease diagnosis ranged from 6 months-12 years with a mean of 6.257± 3.41 years. Six (3.06%) patients were below 5 years of age while the highest percentage of patients (43.88%) was in the age range of 10-15 years. Patients were almost evenly distributed between urban (50.51%) and rural areas (49.48%). Eleven patients (5.6%) had a positive family history for rheumatoid arthritis. While 27 cases (13.8%) showed a positive family history of other autoimmune rheumatologic diseases (e.g., SLE).

The mode of onset was oligoarticular in 81 (41.3%), polyarticular in 68 (34.7%) and systemic in 47 patients (24%).

Table 1 shows the frequency of the clinical characteristics according to the type of onset.

In oligoarticular onset JRA, 2 subtypes were detected, persistent oligoarticular arthritis, which was present in 77.8% (n = 63) and extended oligoarticular arthritis which was present in 22.2% (n = 18).

The distribution of joint affection in different onset types is shown in Table 2.

The laboratory parameters of different types are shown in Table 3.

Albuminuria was detected in 6 (1.75%) of the patients, one in the oligoarticular onset subtype, two in the polyarticular onset subtype and three in the systemic onset subtype.

Table 1: Clinical characteristics of children with juvenile arthritis, according to the onset type

JIA subtypes	SO-JRA	OligO-JRA	PoO-JRA
No. of patients (%)	47(24%)	81 (41.3%)	68(34.7%)
Male to female ratio	1.04:1	1:1.1	1:1.19
Mean age (years)	11.6±5.3	11.13±6.1	13.15±6.9
Mean duration of illness (years)	5.5±2.9	4.99±3.25	6.53±3.9
Age at disease onset (years)	6±3	6.28±3.8	6.42±3.7
Morning stiffness	30(63.8%)	53 (65.4%)	45(66.2%)
Intermittent fever (%)	80.9	3	15
Skin rash (%)	51.1	0	0
Lymphadenopathy (%)	27.2	0	2
Hepatosplenomegaly (%)	27	0	2
Uveitis (%)	0	7.4	7.35
Pleuritis (%)	7	0	0
Cardiac involvement (%) (pericarditis/myocarditis)	21.3	0	0
Renal disease (%)	1	0	0

The percent sign represents the percentage of patients in that particular subtype of JRA manifesting the clinical characteristic

Table 2: Distribution of joint affection in different modes of onset in the study group

	The onset		
Joints	Polyarticular	Oligoarticular	Systemic onset
Knee	67(98.5%)	75(92.6%)	44(93.6%),
Ankle	56(82.4%)	55(67.9%)	37(78.7%)
Wrist	60(88.2%)	37(45.7%)	35(74.5%)
Hip	29(42.6%)	14(17.3%)	21(44.7%)
PIPs	47(69%)	9(11.1%)	17(36%)
MCPs	42(61.7%)		
Shoulder		8(9.9%)	
Elbow	39(57%)		21(44.7%)
Cervical joints	22(32.4%)		
MTPs	21(30.9%)		
Sacroiliac and shoulder	20(29%)		

PIPs: Proximal interphalangeal; MCPs: Metacarpophalangeal; MTPs: Metatarsophalyngeal. The percent sign represents the percentage of patients in that particular subtype of JRA manifesting the clinical characteristic

Table 3: Laboratory parameters in different JIA subtypes

JIA subtypes	SO-JRA	OligO-JRA	PoO-JRA	Total
Thrombocytosis platelets>450×10^9	24(51.06%)	21(25.9%)	20(29.41%)	65(33.1%)
Leukocytosis WBC>13×10^3	13(27.65%)	10(12.34%)	10(14.7%)	33(16.3%)
Anemia Hb<10 (g L^{-1})	21(44.7%)	27(33.3%)	35(51.4%)	83(42.3%)
ESR>15 (mm h^{-1})	40(85.1%)	45(55.5%)	50(73.5%)	135(68.8%)

The percent sign represents the percentage of patients in that particular subtype of JRA manifesting the clinical characteristic

Table 4: Results of ANA in the present study group

JIA subtypes	Positive cases
Oligoarticular	30 (37%)
Polyarticular	7 (10.3%)
Systemic	0

Table 5: The prognosis and fate of present study group

Fate	Remitting	Unremitting	Amyloidosis	Amyloidosis and death
Oligoarticular	54.3% (n = 44)	45.7% (n = 37)	0	0
Polyarticular	45.6% (n =31)	54.4% (n =37)	2.9% (n = 2)	0
Systemic	36.2% (n =17)	63.8% (n =30)	2.1% (n = 1)	2.1% (n = 1)

ANA was positive (1:80-1:60), in 37 (18.9%) of the patients and the distribution in different subtypes is shown in Table 4.

Slit lamp examination showed positive findings suggesting chronic uveitis in 5.6% of patients (n = 11).

The prognosis and fate of present study group were also studied and shown in Table 5.

DISCUSSION

Juvenile Idiopathic Arthritis (JIA) is one of the most common rheumatic diseases in childhood (Niehues and Lankisch, 2006). We studied by retrospective analysis 196 Egyptian children with juvenile rheumatoid arthritis who were following up in the Children's Hospital of Cairo University which is a tertiary referral center. The results of this retrospective analysis showed some differences and some similarities in the clinical profiles of our patients with JRA, when compared to other populations. The mean age of disease onset was 6.257±3.41 years, which was close to that seen in Saudi Arabia (6 years) and Spain (5.6 years) (Bahabri *et al*., 1997; Mengual *et al*., 2007). Disease prevalence was almost equal in patients form both urban and rural areas. This was contrary to other studies (Kurahara *et al*., 2007) where rural areas showed a higher prevalence. Perhaps this was due to the fact that present study was conducted in a public hospital, where most of the patients come from the low or middle socioeconomic classes.

In contrast to some countries such as Saudi Arabia were systemic onset is the commonest type (Khuffash and Majeed, 1988), the oligoarticular onset disease was the most frequently observed type found in the patients followed by the polyarticular JRA. Other countries, such as France and Spain, described similar presentations to ours, whereby the oligoarticular onset was the commonest (41.7%) (Quartier and Prieor, 2007; Mengual *et al*., 2007).

This variability in the relative frequency of the subtypes of arthritis may be due to differences in environmental and genetic factors, with possible exposure to different types of infections (Chantler *et al*., 1985). All throughout the course of the disease morning stiffness was the commonest manifestation in 65.3% (similar to studies by Grassi *et al*., 1998), while spiky fever was the next commonest (19.4% of all patients and 80.9% of patients of the systemic onset type. Work done in Lithuania revealed the presence of spiky fever in 73% of patients with systemic onset type (Baksiene *et al*., 2003), but other studies (Chandrasekaran *et al*., 1996) described spiky fever in all patients with systemic onset type.

Table 6: Comparative epidemiological data of JRA in 5 countries

Variables	Egypt (present study)	Saudi Arabia (Bahabri *et al*., 1997)	Kuwait (Khuffash and Majeed, 1988)	Turkey (Ozdogan *et al*., 1991)	Europe (Gäre and Fasth, 1995)
Total No. of cases	196	115	41	144	112
M:F	94:102	52:63	18:23	82:62	36:76
Age at onset					
Mean (years)	6.257	6	5.9	8.4	10.9
Range (years)	0.6 -12	0.75-16	0.70-12	0.5-3.9	1-15.8
Systemic onset	47 (24%)	50 (44%)	16 (39%)	37 (26%)	4 (4%)
Polyarticular onset	68 (34.7%)	35 (30%)	16 (39%)	26 (18%)	36 (32%)
Oligoarticular onset	81 (41.3%)	30 (26%)	9 (22%)	81 (56%)	72 (64%)
ANA+ve (%)	18.9	30	12	5	29
Uveitis (%)	5.6	1.7	7	7	8
Amyloidosis (%)	1.7	0	NA	7	8
Remission rate (%)	46.9	29.5	54	24	30.6
Mortality (%)	0.5	0	0	25	1

NA: Not applicable

Families of 5.6% of our patients had a history of JRA, while 13.8% of the families had a history of some other rheumatological disease, which is higher than the 4% incidence in the Saudi study (Niehues and Lankisch, 2006), but close to that in other studies (Zeft *et al*., 2008). ANA was positive in 18.9% of cases, which is close to the results of Gare and Fasth (1995). This might reflect a higher incidence of infections inducing the illness, or more likely the use of more sensitive techniques (Grassi *et al*., 1998) in detecting ANA (Schaller, 1977). In different studies, the reported incidence of uveitis in JIA patients in Western countries ranged between 10 and 20% (Khuffash and Majeed, 1988; Steinbrocker *et al*., 1949) and can reach up to 50% in younger patients with PaO-JRA and positive ANA (Ozdogan *et al*., 1991) which is higher than the prevalence of uveitis (5.6%) observed in this study, but the results of this study are close to that in other studies (Schaller *et al*., 1976) and even higher than the 1.7% reported by in the Saudi study (Niehues *et al*., 2006) which my be attributed to genetic susceptibility influencing the disease expression and the larger number of cases in this study that decreases the referral bias.

Secondary amyloidosis is a known complication of JRA, especially of SO-JRA. The highest frequency (up to 10%) of this complication was reported by various European series (Svantesson *et al*., 1983). Amyloidosis was diagnosed in only 3 c ases (1.76%) in present study group, but the lower incidence in this series may be due to the younger age of the patients, as amyloidosis is more common in adults with JRA. Another influencing factor might be the effect of ethnicity on disease expression.

Table 6 show comparative epidemiological data between several studies including the present study.

In conclusion, this is one of the largest series of patients with JRA recorded in an Arab country. Epidemiological data is comparable to earlier reports. Onset types show increased frequency of Oligoarticular-JRA and PaO-JRA compared to SO-JRA and a lower incidence of amyloidosis. Whether this represents referral bias to tertiary care centers or due to the effect of genetic and environmental factors, has to be proved by further studies in other centers.

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