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Subtype Patterns of Juvenile Idiopathic Arthritis Among Libyan Children

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Abstract:-

➢ ***Background***

Although JIA is the most common childhood rheumatic disease in the western world; its prevalence differs according to genetic factors and ethnicity. The current prevalence among Arab children as well as in Libya still needs further research. The purpose of the present paper was to identify the pattern and laboratory features of JIA in Libyan children.

➢ ***Methods***

All children diagnosed with JIA between January 2009 and January 2020 were included in the study.

➢ ***Results***

There were 66 girls and 24 boys with a mean duration of disease of 4.1 years. With a mean age of 11.9 (SD=4.3) years old. The mean age at disease onset was 5.9 (SD=3.4) years old, and that for diagnosis was 7.0 (SD=3.8) years old. Polyarticular JIA was the most frequent type (38.9%) other subtypes included oligoarthritis (31.1%), systemic arthritis (21.1%), psoriatic arthritis (6.7%), enthesitis-related arthritis (2.2%) respectively. The majority of polyarthritis were RF negative (94.0%), and the persistent type constituted 61.7% of all oligoarthritis cases. Out of 87 valid cases, 78 (89.7%) were ANA negative, and of 83 cases, 78 (94.0%) were RF negative.

➢ ***Conclusion***

The most common type of JIA was polyarticular JIA, higher prevalence among girls. Further studies are required to defining the characteristics of JIA.

Keywords:- *Children, Juvenile Idiopathic Arthritis, Subtypes, Libya.*

I. INTRODUCTION

Juvenile Idiopathic Arthritis (JIA) is the most common chronic rheumatic disease and chronic arthritis in children worldwide. Which cause short and long term disability. It is a heterogeneous inflammatory disease and defined as arthritis persisting 6 weeks or longer with onset before the age of 16 years with no identifiable aetiology. (1)

The term Juvenile Idiopathic Arthritis has replaced the older terms Juvenile Rheumatoid Arthritis (JRA) and Juvenile Chronic Arthritis (JCA) proposed by the International League of Associations for Rheumatology (ILAR) in the late 1990s.

The ILAR classified JIA according to the pattern of the arthritis in the first 6 months after onset of the disease into 8 subtypes known as persistent oligoarticular, extended oligoarticular, polyarticular Rheumatoid Factor- (RF-) negative, polyarticular RF-positive, enthesitis-related arthritis (ERA), psoriatic arthritis, systemic, and undifferentiated arthritis. Each JIA subtype has its own diagnostic criteria (Table 1) [1].

ISSN No:-2456-2165

Table 1 The ILAR classification of JIA.[1]

Systemic arthritis	Arthritis with or preceded by daily fever of at least 2-weeks duration That is documented for at least 3 days and accompanied by one or More of the following: (i) Evanescent, nonfixed, erythematous rash; (ii) Generalized lymph node enlargement; (iii) Hepatomegaly and/or splenomegaly; (iv) Serositis *Exclusion criteria: A, B,C and D*
Oligoarthritis	Arthritis in 1_4 joints during the first 6 months of disease. Two Subtypes: (i)Persistent oligoarthritis affects not more than four joints throughout The disease course; (ii) Extended oligoarthritis affects a total of more than four joints after The first 6 months of the disease *Exclusion criteria: A, B,C and D*
Polyarthritis (RF-negative)	Arthritis affecting 5 or more joints during the first 6 months of disease Tests for RF are negative *Exclusion criteria: A, B,C and D*
Polyarthritis (RF-positive)	Arthritis affecting 5 or more joints during the first 6 months of disease Tests for RF are positive *Exclusion criteria: A, B,C and D*
Psoriatic arthritis	Arthritis plus psoriasis at least two of the following: Dacylitis, nail pitting or onycholysis, psoriasis in a first-degree relative *Exclusion criteria: A, B,C and D*
Enthesitis-related Arthritis	Arthritis plus enthesitis or arthritis, plus at least two of the following: presence of HLA-B27 antigene, onset of arthritis in a male over 6 years of age, acute (symptomatic) anterior uveitis, history of AS, ERA, sacroilitis with IBD, reactive arthritis or acute anterior uveitis In a first-degree relative. *Exclusion criteria: A, B, C and D*
Undifferentiated arthritis	Arthritis that do not fulfill criteria in any way in any of the above Criteria in any of the above categories or fulfills criteria in two or More of the above categories

Exclusion criteria: A: Psoriasis in the patient or a first-degree relative, B: Arthritis in an HLA-B27-positive male with arthritis onset after 6 years of age, C: Ankylosing spondylitis, enthesitis-related arthritis, sacroiliitis with inflammatory bowel disease, Reiter's syndrome, or acute anterior uveitis in a first-degree relative, D: Presence of IgM rheumatoid factor on at least two occasions for at least 3 months apart, E: Presence of systemic arthritis.

Adapted from © The Journal of Rheumatology Publishing, 2001. All rights reserved. Petty et al. [1].

The major manifestation of JIA is joint inflammation and the presence of synovitis, which causes synovial tissue thickening, and accumulation of synovial fluid. This is manifested clinically as joint swelling, morning stiffness, joint pain, tenderness, and functional disability. Arthritis can occur in any joint but large joints are more commonly affected. Joint involvement can be mild and self-limiting and it can be more severe causing joint destruction, severe disability, and loss of joint function.

Extra-articular manifestations in JIA may cause significant morbidity. These include uveitis, fever, skin rash hepatomegaly, splenomegaly, lymphadenopathy, and serositis. Apart from uveitis, most of these extra-articular features occur in SoJIA.

There are no diagnostic laboratory investigations for JIA but some laboratory findings can help to exclude other causes of arthritis and help in JIA classification.

Aim of JIA management is to control active symptoms and to prevent chronic complications in order to improve quality of life, which requires comprehensive multidisciplinary team care including rheumatologists, rehabilitation specialists, occupational therapists, physical therapists, social workers, nurses, podiatrists, dieticians, psychologists or psychiatrists, and orthopaedic surgeons.

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There is no curative treatment for JIA but early and aggressive management has led to prolonged remission and improved outcome.[1,2,3]

Various studies from different parts of the world showed differences in JIA characteristics including incidence, prevalence, age of onset, gender, and frequency of JIA subtypes [2,3].

Most data about JIA disease come from studies carried out in Europe and North America. [1–4] Very little is known about JIA in other parts of the world. [5,6] These areas have a lower incidence of oligoarticular disease, ANA positivity, and eye involvement. [7,8] Similar findings have also been reported in African–Americans living in the USA. [3]

JIA is the most common rheumatic illness in children in the Western world [9]. According to the literature, oligoarticular JIA is the most common accounts (50–60 %) , polyarticular JIA (30–35 %), systemic JIA (10–20 %) and ERA (1–7 %) are the most common JIA subtypes [10]. However, there is a worldwide discrepancy in the prevalence and subtypes or phenotypes distribution of JIA, which may be affected by ethnicity and genetic factors [9].

There is paucity or lack of data on epidemiology of JIA and defining the characteristics of JIA in children in Arabs.

Therefore, the Purpose of this study to describe subtype distribution of JIA among Libyan children and to compare our results with other ethnic population worldwide. To the best of our knowledge, this was the first single centre comprehensive study describing JIA in Tripoli-Libya.

➢ *Objective*

- To describe the demographic, clinical and laboratory characteristics profile of children diagnosed with JIA, and examined the differences in JIA clinical presentation across males and females in the Libyan clinical setting
- To describe subtype of JIA pattern and examined the differences in JIA clinical presentation across males and females in children in the Libyan
- To compare JIA subtypes among in children in Libya with those from international data

II. METHODOLOGY

➢ *Patients and Methods*

Medical records of all 90 patients who diagnosed JIA between January 2009 and January 2020 were retrospectively reviewed in Paediatric Rheumatology clinic at Tripoli Children's Hospital.

All the medical records of the children who were diagnosed to have 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) from January 2009 to January 2020 were included.

The diagnosis of JIA that was done by a paediatric rheumatologist and JIA classification was according to ILAR classification criteria (Table 1).

Medical files of all identified JIA cases were reviewed, and data relevant to their sociodemographic (age, sex, nationality), clinical (samples: age of onset of JIA, JIA type), and laboratory (samples: ANA status) characteristics were extracted. Data on their medical profile were also collected. JIA-associated uveitis status is the outcome variables in this study, and was defined as a dichotomous variable (uveitis and no uveitis)

➢ *Data Analysis*

Data analysis was performed using the Statistical package for social sciences (SPSS), version 26. Data cleaning was done before the main analysis, whereby missing values and outliers were identified and appropriately managed. The normality of the distribution of the numerical variables was also explored.

Frequency and percentage were used to present the categorical variables, while mean and standard deviation, or median and interquartile range were used to summarize the numerical variables as appropriate to their distribution. Bivariate analysis was performed to test for differences in the socio-demographic, clinical and laboratory characteristics between males and females. In testing the bivariate association between gender and the categorical independent variables, as the Chi-square test assumptions were violated, Fisher's exact test, or the maximum likelihood ratio Chi-square test were used as appropriate to size of the contingency table. The difference in each numerical variable between males and females was tested using the independent t test or Mann Whitney test as appropriate to the distribution of that numerical variable. The statistical significance of the findings was based on a p value of less than 0.05

III. RESULTS

Among 90 patients with JIA, females constituted 73.3% of the patients, and the majority of them were Libyan, with a mean age of 11.9 (SD=4.3) years old. The mean age at disease onset was 5.9 (SD=3.4) years old, and that for diagnosis was 7.0 (SD=3.8) years old and boys 24 (26.7%; female/male ratio: 2.8:1) with a mean duration of disease of 6.2 years. All JIA patients were followed for a mean period of 4.4 years. The age at onset of disease ranged from 8 months to 15 years (mean, 11.9 years).

Subtypes of JIA at disease onset included polyarthritis (38.9%),oligoarthritis (31.1%), systemic arthritis (21.1%), psoriatic arthritis (6.7%), and enthesitis-related arthritis (2.2%). The distribution of onset types, gender, mean age at onset, and ANA positivity in each subgroup are summarized in **Table2**. Polyarticular JIA was the largest of all onset types (35 patients; 38.9%). RF-positive and RF-negative polyarticular JIA was observed in 3 patients (3.3%) and 32 patients (35.5%), respectively. Twenty-eight patients (31.1%) were allocated to oligoarticular JIA, which was

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observed to be the second most frequent sub-type in 28 patients (31.1%). Seventeen of the oligoarticular JIA patients (18.9%) were persistent oligoarticular JIA, eleven patient (12.2%) were extended oligoarticular JIA. ANA, 19 patients had systemic onset JIA (SoJIA) Six patients had psoriatic arthritis. Two patients had enthesitis-related arthritis. Antinuclear antibody and RF were positive in 9 patients (10.3%) and 5 patients (6%), respectively. Out of 87 valid cases, 78 (89.7%) were ANA negative, and of 83 cases, 78 (94.0%) were RF negative.

Table 2 Socio-Demographic, Clinical and Laboratory Characteristics of Children Diagnosed with JIA (N=90)

Variable	f	(%)	Range
Socio-demographic characteristics			
Current age (years) †	11.9	±4.3	3-20
Sex			
Females	66	(73.3)	
Males	24	(26.7)	
Nationality			
Libyan	**87**	**(96.7)**	
Non-Libyan	3	(3.3)	
Clinical profile			
Age of onset of JIA (years) †	5.9	±3.4	(0.6-15)
Age at JIA diagnosis (years) †	6.9	±3.7	(0.60-15)
Duration of JIA (years) †	6.2	±3.5	(0.40-17)
Duration of JIA follow-up (years) ‡	4.4	(3-7)	(0.20-17)
JIA Type*			
Polyarthritis	**35**	**(38.9)**	
Polyarthritis (RF -ve)	**32**	**(35.5)**	
Polyarthritis (RF +ve)	**3**	**(3.3)**	
Oligo-arthritis	28	(31.1)	
Persistent	17	(18.9)	
Extended	11	(12.2)	
Systemic arthritis	19	(21.1)	
Psoriatic arthritis	6	(6.7)	
Enthesitis related arthritis	2	(2.2)	
Laboratory profile			
ANA (n=87)*			
+ve	9	(10.3)	
-ve	78	(89.7)	
RF (n=83)*			
+ve	5	(6.0)	
-ve	78	(94.0)	
Anti-CCP (n=10)*			
+ve	2	(20.0)	
-ve	8	(80.0)	
HLA -27 positive (n=3)*			
+ve	0	(00.0)	
-ve	3	(100.0)	

† (Mean± SD), ‡Median (IQR), * valid cases (all presented percentages were for the valid cases)

IV. DISCUSSION

This retrospective study was carried out in Paediatric Rheumatology department at Tripoli Children's Hospital, which is a tertiary care hospital in Tripoli Libya, western area of Libya.

We aimed at this study to describe subtype patterns of JIA in children followed up in our center as knowing the characteristics of this disease in our community is essential to provide a better planning for medical care. There is a lack of hospital-based studies about JIA patterns among Libyan children and this is the first report on JIA in Libya, describing the pattern of JIA in Libya according to the currently used ILAR classification system for JIA. In the current study, medical records of ninety children at the.

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Table 3 Pattern of JIA in Different Countries

Country Subtype	Current study Libya N=90	Saudi Arabia[14] N=82	Oman[15] N=107	Egypt[16] N=196	Tunisia[17] N=54	Turkey[4] N=634	Spain[18] N= 145	India [19] N= 244
Polyarthritis	38.9%	29.26%	46.70%	34.70%	66%	23.50%	12.40%	29%
Oligoarthritis	31.1%	28.04%	31.80%	41.30%	15.10%	41%	51%	21%
Systemic arthritis	21.1%	36.50%	17.8%	24%	7.60%	14.50%	6.90%	8%
Enthesitis related Arthritis	2.2%	12.1%	2.80%	0%	9.40%	18.90%	12.40%	36%
Psoriatic arthritis	6.7%	4.87%	0.90%	0%	1.90%	2.10%	6.20%	1%
Undifferentiated Arthritis	0%	0%	0%	0%	0%	0%	11.10%	5%

- Paediatric rheumatology clinic were retrospectively analyzed. The prevalence of JIA is variable among different parts of world and different ethnic groups [2, 11]. This variability appears to include the frequency of JIA subtypes.
- According to published international reports, oligoarticular JIA is the most common JIA subtype, as reported in Spain (51%), and Turkey (41%). [4,18]
- Unlike most of previous similar studies where oligoarticular JIA was found to be the most common, mainly in Egypt, Europe, USA, Canada, South America, and Turkey [4, 12,13]
- The frequency of JIA subtypes in our study showed that polyarticular- JIA was the most common subtype: 35/90(38.9%).
- Polyarticular JIA was also the predominant JIA subtype in some other cohorts in Oman (46.7%) [15] and Tunisia (66%)[17]
- SOJIA occurs in our study only in 21.1%, while in a large population-based study in Japan, which included 540 children, SoJIA constituted 54% of JIA cases [3,14].
- Our study was similar also from two studies from Arabic countries (Oman, and our neighbour Tunisia) in which the most predominant JIA subtype was polyarticular JIA [15,17].
- On contrary to Saudi Arabia study[14] systemic onset was the most common type. Moreover, our results matched previous studies conducted in Oman and Tunisia but with different frequencies from ours (46.7%, 66%, 38.9% respectively) because of variability of environmental and genetic factors.[15, 17]
- We compared our data in this study with those from countries in Middle East, North Africa, Europe and other regions, as shown in Table 3.
- Our present data shows female predominance as 66/24 patients (73.3%) were male (female/male ratio: 2.8:1). Contrary to Indian[21] and Turkish[20] studies. This is similar to the studies from Western countries, Spain, and Middle East, [14,15,1822,23] with female predominance.
- A major limitation of our study is being a retrospective record-based in nature and a single centre-based with a relatively small sample size. However our study can be a starting point for further future nationwide multicenter- based study.

V. CONCLUSION

We conclude that The most common type of JIA was polyarthritis.which lead the patterns of Libyan children with JIA are different from those of European and North American children and some Arabic countries Saudi Arabia Egypt and similar to other Arabic countries (Oman and Tunisia). Taken together, we suggest that the difference in immunogenetic background of ethnic groups may account for the differences in expression of disease. There is a need for further studies from different ethnic groups and geographic location in order to improve our knowledge about how genetic and environmental differences influence JIA expressions.

RECOMMENDATIONS

More research is needed to study JIA in Libya to find the prevalence and outcome of the disease.

REFERENCES

[1]. R. E. Petty, T. R. Southwood, P. Manners et al., “International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001,” The Journal of Rheumatology, vol. 31, no. 2, pp. 390–392, 2004.

[2]. V. C. Kok, J.-T. Horng, J.-L. Huang et al., “Population-based cohort study on the risk of malignancy in East Asian children with Juvenile idiopathic arthritis,” BMC Cancer, vol. 14, no. 1, pp. 634–644, 2014.

[3]. S. Fujikawa and M. Okuni, “Clinical analysis of 570 cases with juvenile rheumatoid arthritis: results of a nationwide retrospective survey in Japan,” Pediatrics International, vol. 39, no. 2, pp. 245–249, 1997.

[4]. E. Demirkaya, S. O ̈zen, Y. Bilginer et al., “The distribution of juvenile idiopathic arthritis in the eastern Mediterranean: results from the registry of the Turkish paediatric rheumatology association,” Clinical and Experimental Rheumatology, vol. 29, no. 1, pp. 111–116, 2011.

[5]. V. Kunjir, A. Venugopalan, and A. Chopra, "Profile of Indian patients with juvenile onset chronic inflammatory joint disease using the ILAR classification criteria for JIA: a community- based cohort study," The Journal of Rheumatology, vol. 37, no. 8, pp. 1756–1762, 2010.
[6]. M. M. Moued, H. M. Al-Saggaf, H. S. Habib, and M. A. Muzaffer, "Oligoarticular juvenile idiopathic arthritis among Saudi children," Annals of Saudi Medicine, vol. 33, no. 6, pp. 529– 532, 2013.
[7]. W. A. Garout and M. A. Muzaffer, "A single-center experience of systemic onset juvenile idiopathic arthritis at a tertiary hospital in Jeddah, Saudi Arabia," Open Journal of Rheumatology and Autoimmune Diseases, vol. 4, no. 4, pp. 212–218, 2014.
[8]. F. A. Khuffash, H. A. Majeed, M. M. Lubani, K. N. Najdi, S. S. Gunawardana, and R. Bushnaq, "Epidemiology of juvenile chronic arthritis and other connective tissue diseases among children in Kuwait," Annals of Tropical Paediatrics, vol. 10, no. 3, pp. 255–259, 1990.
[9]. Thierry S, Fautrel B, Lemelle I, Guillemin F. Prevalence and incidence of juvenile idiopathic arthritis: A systematic review. Joint Bone Spine. 2014;81:112–7.
[10]. Weiss J, Ilowite N. Juvenile idiopathic arthritis. Pediatr Clin North Am. 2005;52:413–42.
[11]. R. K. Saurenmann, J. B. Rose, P. Tyrrell et al., "Epidemiology of juvenile idiopathic arthritis in a multiethnic cohort: ethnicity as a risk factor," Arthritis & Rheumatism, vol. 56, no. 6, pp. 1974–1984, 2007.
[12]. C. Modesto, J. Anto´n, B. Rodriguez et al., "Incidence and prevalence of juvenile idiopathic arthritis in Catalonia (Spain)," Scandinavian Journal of Rheumatology, vol. 39, no. 6, pp. 472– 479, 2010.
[13]. N. Adib, K. Hyrich, J. Thornton et al., "Association between duration of symptoms and severity of disease at first presen- tation to paediatric rheumatology: results from the Childhood Arthritis Prospective Study," Rheumatology, vol. 47, no. 7, pp. 991–995, 2008.
[14]. Al-Hemairi MH, Albokhari SM, Muzaffer MA. The pattern of juvenile idiopathic arthritis in a single tertiary center in Saudi Arabia. Int J Inflamm. 2016; 2016:7802957.
[15]. Abdwani R, Abdalla E, Al Abrawi S, Al-Zakwani I. Epidemiology of juvenile idiopathic arthritis in Oman. Pediatr Rheumatol Online J. 2015;13(1):33. https://doi.org/10.1186/s12969-015-0030-z.
[16]. Salah S, Hamshary A, Lotfy H, Rahman H. Juvenile idiopathic arthritis, the Egyptian experience. J Med Sci. 2009;9(2):98–102.https://doi.org/10.3923/ jms.2009.98.102.
[17]. Alaya Z, El Amri N, Zaghouani H, Baccouche K, Amri D, Belghali S, et al. AB1030 juvenile idiopathic arthritis in Central Tunisia: clinical and therapeutic features (about 54 cases). Ann Rheum Dis. 2015;74(Suppl 2): 1243.1–1243. https://doi.org/10.1136/annrheumdis-2015-eular.4550.
[18]. Moe N, Rygg M: Epidemiology of juvenile chronic arthritis in northern Norway: A ten-year retrospective study. Clin Exp Rheumatol 1998, 16:99–101.
[19]. Aggarwal A, Misra R: Juvenile chronic arthritis in India: Is it different from that seen in Western countries? Rheumatol Int 1994, 14:53–56.
[20]. Yilmaz M, Kendirli SG, Altintas DU, Karakoc GB, Inal A, Kilic M. Juvenile idiopathic arthritis profile in Turkish children. Pediatr Int. 2008 Apr;50(2):154-8.
[21]. Kunjir V, Venugopalan A, Chopra A. Profile of Indian patients with juvenile onset chronic inflammatory joint disease using the ILAR classification criteria for JIA: a community- based cohort study. J Rheumatol. 2010;37(8):1756-62.
[22]. Gutierrez-Suarez R, Pistorio A, Cespedes Cruz A, Norambuena X, Flato B, Rumba I, et al. Health-related quality of life of patients with juvenile idiopathic arthritis coming from 3 different geographic areas. The PRINTO multinational quality of life cohort study. Rheumatology. 2007;46(2):314-20.
[23]. Hyrich K, Lal S, Foster HE, Thornton J, Adib N, Baildam E, et al. Disease activity and disability in children with juvenile idiopathic arthritis one year following presentation to paediatric rheumatology. Results from childhood arthritis prospective study. Rheumatology. 2010;49:116-22.