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Patterns Variety of Rheumatic Diseases in Pediatrics

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ABSTRACT

Background: Rheumatoid arthritis in children and their families can be a significant health burden. They're linked to the risk of physical impairment, a lower quality of life, and a lot of direct and indirect expenditures. The goal of this study is to characterise the clinical spectrum of Juvenile Idiopathic Arthritis (JIA) in children at Zagazig University hospitals, as well as the frequencies and various patterns of JIA. Patients and methods: A cross-sectional research comprised 120 patients with an average age of 16 years. From December 2017 to December 2019, data on juvenile idiopathic arthritis was gathered during a two-year period. Complete blood count, reactive protein, ANA, RF, C3&C4, creatine phosphokinase, and EMG were all performed. Management and treatment strategies were implemented, and data on the outcomes was gathered. Results:Females account for the majority of our rheumatological illness patients.In our analysis, JIA was the most frequent rheumatological illness, followed by SLE and lastly HSP.In our study, oligoarticular JIA was the most prevalent subtype of JIA, followed by polyarticular and then systemic onset type.SLE is the second most prevalent illness in our research, with the majority of patients being women.The majority of individuals had cutaneous symptoms and a fever.The most commonly utilised drugs were corticosteroids, cyclophosphamide, and mycophenolate mofetil.HSP was the most prevalent kind of vasculitis found in our research.The majority of patients are females, and those with severe GI symptoms and nephritis got corticosteroids. Conclusion: The prevalence of rheumatological disorders in children is underestimated, and there is a lot of overlap in diagnosis. Because paediatric onset is less apparent than adult start, some patients have a significant diagnostic lag. Early identification and proper care of these children is critical for them to have a normal or near-normal life, particularly in patients with rheumatological illnesses that cause chronic morbidity, such as JIA.

Keywords: Rheumatic Diseases; Systemic Lupus Erythematosus; Dermatomyositis

INTRODUCTION

Pediatric rheumatic diseases (PRDs) are any of a variety of disorders marked by inflammation, degeneration, or metabolic derangement of the connective tissue structures, especially the joints and related structures in children. Approximately 1 in 1000 children suffers from childhood rheumatic diseases **(1).** Although they share

many common symptoms, like pain, joint swelling, redness and warmth, they are distinct and each has its own special concerns and symptoms. Some pediatric rheumatic diseases affect the musculoskeletal system, but joint symptoms may be minor or nonexistent component. Pediatric rheumatic diseases can involve the eyes, skin, muscles and gastrointestinal tract as well **(2).** Pediatric rheumatic diseases can cause considerable disease burden to children and their families. They are associated with the potential for physical disability, diminished quality of life and significant direct and indirect costs**.** This underscores the importance of early diagnosis and treatment **(3)**. Rheumatic diseases include many types such as, juvenile idiopathic arthritis, juvenile systemic lupus erythematosus, juvenile dermatomyositis, mixed connective tissue disease, Kawasaki disease, juvenile scleroderma and fibromyalgia **(4).** We aim to describe the clinical spectrum and the frequencies and different patterns of pediatric rheumatic diseases (PRDs) in children in Zagazig University hospitals.

PATIENTS AND METHOD:

A cross sectional study was carried out in Pediatrics and Rheumatology Departments of Zagazig University Hospitals included 120 cases less than 16 years with rheumatic disorders either inpatient or outpatient collected over two years from December 2017 to December 2019.

Inclusion criteria:

Patients diagnosed to have rheumatic diseases<16 years.

Exclusion criteria:

Age above 16 years and Lack of consent.

Full history taking and duration of symptoms were collected from all patients. Clinical examination including systematic examination including the skin, mucous membrane, cardiopulmonary auscultation and assessment of enlarged organs and glands. After performing the complete general examination, examining the joints was done. The examination of the joints, crucial in rheumatology, is what finally confirms both the diagnostic impression suggested by the medical history (presence of arthritis or other finding and the type, oligoarthritis or polyarthritis) (5).

Laboratory investigations:

Complete blood count. for all samples using sysmex KX-21N (Sysmex Corporation, New York, USA) for red blood cell (RBC) count, hemoglobin level, hematocrit value, WBC count (total and differential), and platelet count **(6).**

C- reactive protein. Estimation was carried out using the test kit (Cromatest) at 0h of clinical presentation. The AVITEX- CRP latex particles are coated with antibodies to human CRP. When the latex suspension is mixed with serum containing elevated CRP levels on a slide, clear agglutination was seen within 2 minutes. Specimen collection and storage: Fresh sample of venous blood was allowed to clot

form and retract centrifuge clotted blood sample and collect serum, store at 2-8^{o}C AVITEX-CRP had a detection limit of 6 mg/L of CRP in the patient's serum **(7).** Erythrocyte sedimentation rate by using Westergren method recorded mm/hour **(8).**

Tests needed to confirm rheumatic diseases like antinuclear antibody (ANA), antidsDNA antibody, antibodies to Extractable Nuclear Antigens (ENA) as(ENAs include anti-Ro, anti-La, anti-Smith, anti-RNP). A test for antibodies to ENAs (anti-ENA) should be ordered only if there is a suspected or known connective tissue disease and the ANA test is positive at a significant titre, Antineutrophil cytoplasmic antibodies (ANCAs), rheumatoid factor (RF), anti-cyclic citrullinated peptide antibodies, complement C3&C4, creatine phosphokinase, EMG.

Treatments:

Disease-Modifying Antirheumatic Drugs (DMARDS) included Hydroxychloroquine, Penicillamine, Sulfasalazine, Methotrexate. Immuno-suppressant Drugs like Cyclophosphamide. Also, corticosteroids, nonsteroidal anti-inflammatory drugs were used.

Statistical analysis:

Data was performed using the software SPSS version 20. Quantitative variables were described using their means and standard deviations. Categorical variables were described using their absolute frequencies and were compared using Chi square test, Fisher exact test, Kolmogorov-Smirnov and Levene tests were used to verify assumptions for use in parametric tests. One way ANOVA test (used with normally distributed data) and Kruskal Wallis test, (for normally distributed data) were used to compare more than two groups two groups. The level statistical significance was set at 5% ($P<0.05$). Highly significant difference was present if $p\leq0.001$.

RESULTS:

The obtained results showed females patients are more liable to have rheumatic disease even in childhood and teenage. Their age ranged from 2 to 16 years with mean 10.37 years **(Table 1)**. Distribution of the studied patients according to provisional diagnosis was shown in **(Figure 1)**.

Most of our patients (77.5 %) presented by arthritis and 44% presented by skin manifestations, 42% by fever , 11% had GI symptoms, only 10% had serositis , 3.3% had organomegaly , 5.8% had ocular manifestations and 10% had lymph node enlargement **(Figure 2).**

About 77.5% of patients had leukocytosis. 77.5% of patients had normal platelet count. About 98%, 99%, 88%, 98% and 84% had normal reticulocytic count, comb test, liver, kidney function test, and normal urine analysis. About half of patients had elevated ESR level, 72% had abnormal CRP **(Table 2).**

There is statistically non-significant difference between JIA patients regarding organomegally, arthritis, or enlarged lymph node. There is statistically significant

difference between JIA patients regarding fever (only in systemic JIA) and skin manifestations (higher in systemic JIA) **(Figure 3).**

There is statistically non-significant difference between JIA patients regarding presence of positive ANA or rheumatoid factor. There is significant difference between them regarding presence of leukocytosis, anemia, thrombocytosis, elevated ESR (higher in patients with systemic JIA), and abnormal CRP (lower percentage of it in patients with systemic JIA) **(Figure 4).**

About 96.3% of patients with SLE and 92.6% had positive ANA anti dsDNA respectively. All patients had consumed C3,88.9% had consumed C4 ,one patient had positive antiphospholipid antibodies.Renal biopsy was done in 14 patients **(Table 3)**.

Table (1): Distribution of the studied patients regarding demographic characteristics.

	N=120	%
Gender:		
Female	84	70
Male	36	30
Age (years):		
Mean ± SD	10.37 ± 4.03	
Range	2 – 16	

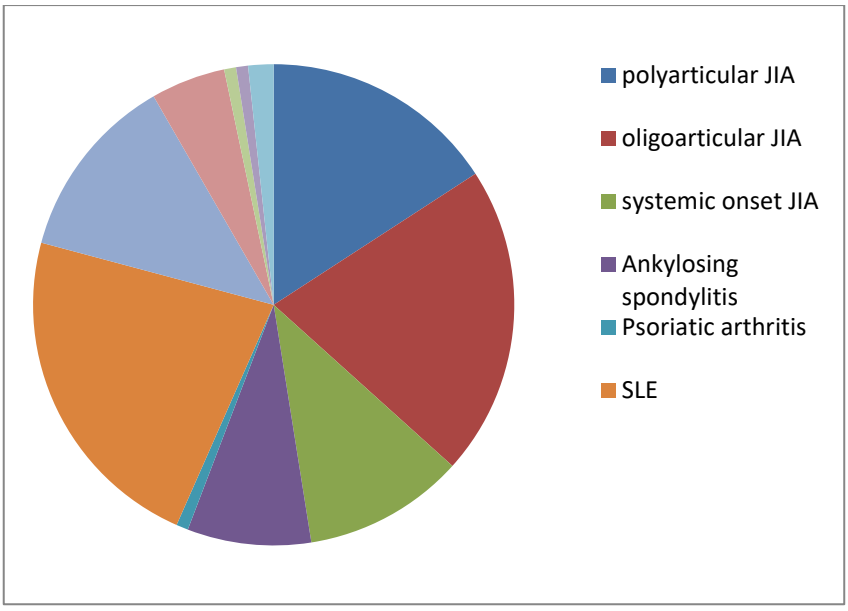

Figure (1): Pie chart showing distribution of the studied patients regarding diagnosis.

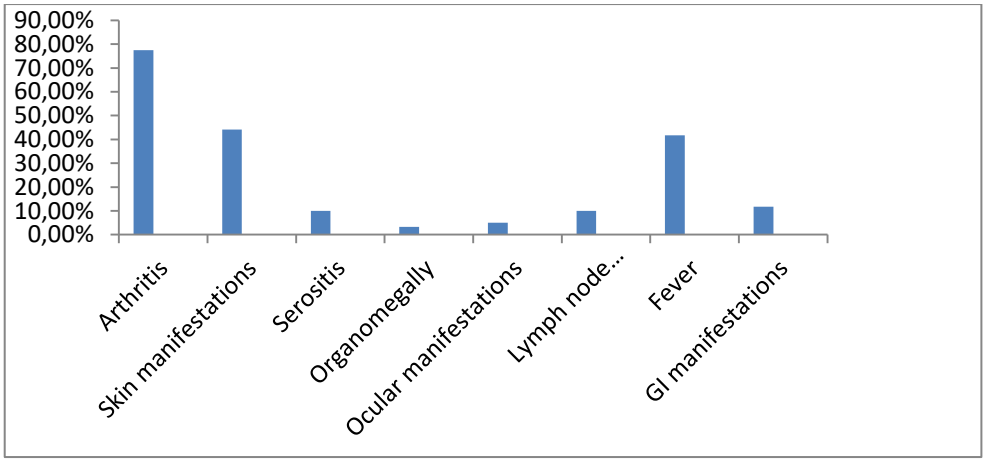

Figure (2): Simple bar chart showing distribution of the studied patients according to clinical presentation.

Table (2): Distribution of the studied patients regarding routine laboratory data.

	N=120	%
TLC:		
Normal	9	7.5
Leukocytosis	93	77.5
leucopenia	18	15
Hemoglobin:		
Normal	83	69.2
Anemic	37	30.8
Platelet count:		
Normal	93	77.5
Thrombocytosis	11	9.2
Thrombocytopenia	16	13.3
Reticulocytic count:		
Normal	117	97.5
Reticulocytosis	2	1.7
Reticulopenia	1	0.8
Coomb test:		
Normal	119	99.2
Abnormal	1	0.8
Liver function test:		
Normal	106	88.3
Abnormal	14	11.7
Kidney function test:		
Normal	117	97.5
Abnormal	3	2.5
Urine analysis:		
Normal	101	84.2
Abnormal	19	15.8
ESR:		
Elevated	60	50
Normal	60	50
CRP:		
Normal	34	28.3
Abnormal	86	71.7

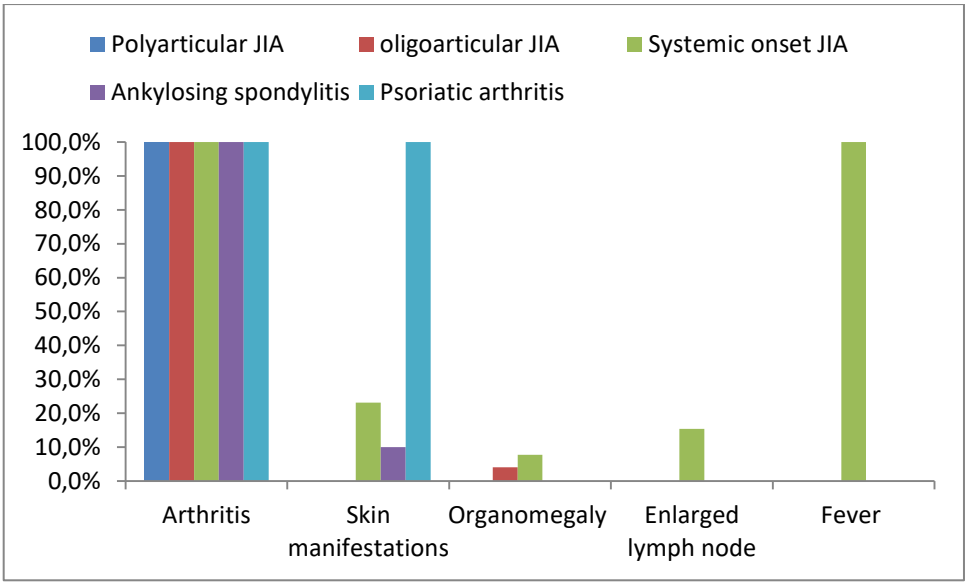

Figure (3): Combined bar chart showing comparison between groups of patients with JIA regarding clinical presentation.

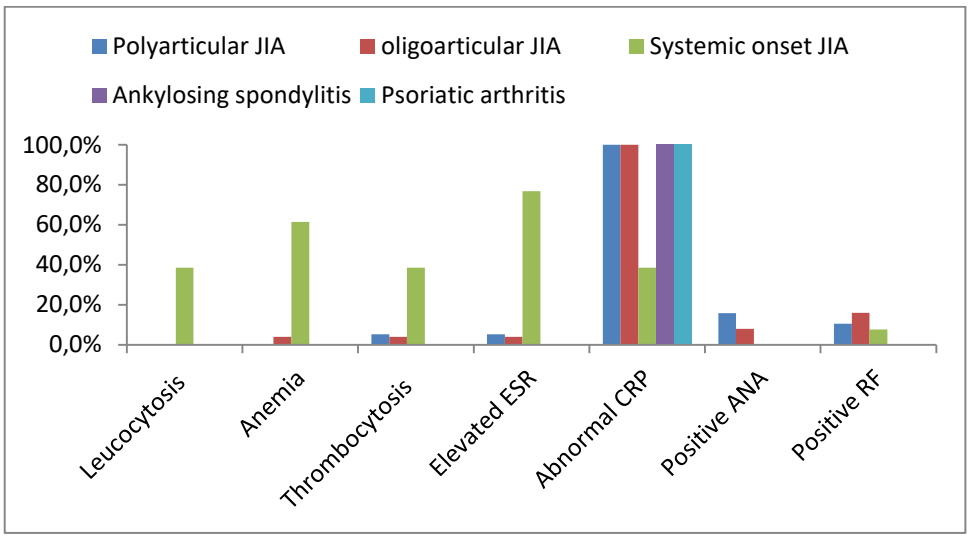

Figure (4): Combined bar chart showing comparison between JIA patients regarding laboratory data.

Table (3):Distribution of SLE patients regarding serological markers.

	N=27	%
ANA:		
Positive	26	96.3
Negative	1	3.7
Anti ds DNA:		
Positive	25	92.6
Negative	2	7.4
C3:		
Consumed	27	100
C4:		

Consumed	24	88.9
Antiphospholipid antibody:		
Positive	1	3.7
Renal biopsy class:	N=14	
II	4	28
III	5	35
IV	5	35

DISCUSSION

Rheumatological diseases are commonly seen in children and include juvenile idiopathic arthritis(JIA), Kawasaki disease(KD), Henoch-Schonlein purpura (HSP), systemic lupus erythematosus (SLE), chronic uveitis, Takayasu arteritis (TA) and juvenile dermatomyositis (JDM). The initial presentation may overlap with each other, and even with non-rheumatological disorders such as infections (**9).** The diagnosis of these conditions is primarily clinical. Laboratory tests can facilitate screening, confirmation of diagnosis, and monitoring the disease activity and response to treatment **(10).**

In our study, we detected these rheumatological conditions: juvenile idiopathic arthritis(JIA), Systemic lupus erythematosus (SLE), ,Kawasaki disease (KD), Henoch-Schonlein purpura (HSP),Mixed connective tissue disease , Systemic sclerosis and Hypermobility syndrome.The most common rheumatological disease detected is juvenile idiopathic arthritis (JIA) about 57% in all its types followed by systemic lupus 22.5% and about 12.5 % had HSP, 5% had Kawasaki disease, 1.7 % had mixed connective tissue disease, 0.8% had hypermobility syndrome and 0.8 % had systemic sclerosis. This matches the results of **Huang et al. (11) and Okong'o and Scott (12)** found that Juvenile idiopathic arthritis (JIA) is the most common pediatric rheumatologic disease. SLE was the second diagnosis in frequency (22.5%) in our study after JIA and this result was higher than those reported by **Dahman (13)** in Yemen(13.5%)and in Singapore by **Tan et al.(14)** (6.2%).

In our study about 93% of patients were females with age ranged from 7 to 15 years with diagnosis lag ranged from 10 months to 5 years. This matches **Hiraki et al. (15)** and **Pluchinotta et al. (16)** found that the disease is rare in children younger than 5 years. As in adult-onset SLE, approximately 80% of patients with SLE were females.

According to clinical presentation about 56% of the studied patients had arthritis, 93% of had skin manifestations, 40.7% had serositis, one patient had organomegaly, three patients had lymph node enlargement, 81.5% had fever, 74.1% had hematological manifestations, 29.6% had neurological manifestations, two thirds had nephritis, 7.4% has AVN and osteoporosis, this mismatch **Spinosa et al. (17)** found that arthritis is present only in 26% of patients and cutaneous manifestation in 54%of them,fever in 34.0%, renal involvement in 38.3% and hematological disorder in 51.1% and nearly matches **Bader-Meunier et al. (18)** reported malar rash in 39-55%, arthritis in 61-65%, fever in 41-58%, renal involvement in 20-67% and hematological disorder in 24-72%.

Lab results showed 63% had leucopenia, 77.8% had anemia, 51.9% had thrombocytopenia, 3.7% had positive Coomb's test, 44.4% had abnormal LFT, 11.1% had abnormal KFT and 55.6% had abnormal urine analysis. This mismatch **Bakr (19)** found that hemolytic anemia was demonstrated in 51%, thrombocytopenia in 29.2%, and leucopenia in 27.5%. We found that all patients had elevated ESR, 51.9% had abnormal CRP, 96.3% and 92.6% had positive ANA, anti dsDNA respectively .All patients had consumed C3, 89% had consumed C4 and this matches **Bakr (19)** results in Antinuclear antibodies were positive in 92.7%, while positive anti-double-stranded DNA 95.6% and but mismatch the results of hypocomplementemia were demonstrated in 67.4%.

Renal biopsy was done in half of the patients 28% of them was class II, 35% class III and 35% class IV nephritis this matches **Bakr (19)** who found that the histopathological findings of the initial renal biopsies were classI (4.9%), classII (22%), classIII (36.3%), and class IV (36.3%) in which class III, IV are the most common .

Finally, we advised that the value of various serological tests be increased and that they be used properly in the diagnosis and follow-up of rheumatological disorders. Expand the use of genetic diagnosis in various rheumatological diseases; slit lamp examination should be performed for patients with oligoarticular JIA, particularly those who are ANA positive, for early detection of iridocyclitis; and regular follow-up is essential to ensure proper drug use and early detection of disease complications and drug side effects.

CONCLUSION:

The prevalence of rheumatological disorders in children is underestimated, and there is a lot of overlap in diagnosis. Because paediatric onset is less apparent than adult start, some patients have a significant diagnostic lag. Early identification and proper care of these children is critical for them to have a normal or near-normal life, particularly in patients with rheumatological illnesses that cause chronic morbidity, such as JIA.

Conflict of Interest: No conflict of interest.

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