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Retraction

The Editor-in-Chief of the International Journal of Contemporary Pediatrics has retracted the article titled "Association of serum ferritin with disease activity in juvenile idiopathic arthritis patients" following an authorship dispute that violates the journal's editorial policies.[1]

REFERENCES

1. Talukder MK, Ali MA, Haque M, Islam MM, Islam MI. Association of serum ferritin with disease activity in juvenile idiopathic arthritis patients. Int J Contemp Pediatr 2025;12:703-8. DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20251087.

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Original Research Article

Association of serum ferritin with disease activity in juvenile idiopathic arthritis patients

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ABSTRACT

Background: Juvenile idiopathic arthritis (JIA) is the most prevalent rheumatic condition in childhood and adolescence. This study aimed to observe the association of serum ferritin level with the disease activity among all sub-types of JIA by using Juvenile Arthritis Disease Activity Score (JADAS 27).
Methods: In this cross-sectional study, 94 newly diagnosed patients of JIA who attended Pediatric Rheumatology clinic and Inpatient Rheumatology Division, Department of Pediatrics of Bangabandhu Sheikh Mujib Medical University (BSMMU) from June 2022 to July 2023 were selected as cases. Serum ferritin was done and JADAS 27 score was calculated in all the cases.
Results: Mean age of patients was 9.10±3.68 years with a male: female ratio of 1.4:1. Enthesitis-related arthritis (ERA) (33%) was the most common subtypes of JIA followed by sytemic JIA and others. At presentation all subtypes of JIA had high disease activity and systemic JIA had the highest frequency (81.8%) of high disease activity. Serum ferritin and ESR level was highest among the systemic JIA followed by ERA. Also, serum ferritin was significantly increased in systemic JIA as compared to non-systemic JIA patients. Here, positive correlation of serum ferritin level and JADAS 27 among all sub-types of JIA was observed, but only the positive correlation of ERA was statistically significant.
Conclusions: Serum ferritin showed a significant moderately positive correlation with JADAS 27 in ERA. Here, serum ferritin level in JIA patients was highest in high disease activity. Serum ferritin was significantly increased in systemic JIA as compared to non-systemic JIA patients.

Keywords: Juvenile idiopathic arthritis, Serum ferritin, Juvenile Arthritis Disease Activity Score 27

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the most common rheumatic illness of childhood characterized by chronic inflammation of one or more joints in children and adolescents resulting short and long-term morbidity and disability. According to the International League of Associations for Rheumatology (ILAR), JIA is defined as definite arthritis of unknown etiology that begins before the 16th year of age and persists for at least 6 weeks.[1] The incidence of JIA varies widely worldwide. In developed countries prevalence of JIA varies between 16 and 150 per 100,000.[2] A study conducted in a semi-urban area of Bangladesh showed the estimated point prevalence of JIA was 60.5 per 100,000 children.[3]

JIA is a complex inflammatory disease with a multifactorial immune pathogenesis namely a certain genetic predisposition, also environmental factors play a role leading to a chronic inflammatory response, which involves uncontrolled activation of both innate and adaptive immunities. The resulting autoimmune damage

targets primarily, though not exclusively, synovial membrane of joint, leading to chronic joint inflammation.[4] Both immunogenic susceptibility and external triggers play role in the pathogenesis of the disease.

ILAR 2001 classification criteria provided 7 sub types of JIA consisting of systemic arthritis, oligoarthritis persistent and oligoarthritis extended, polyarthritis (rheumatoid factor negative), polyarthritis (rheumatoid factor positive), enthesitis-related arthritis (ERA), psoriatic arthritis and undifferentiated/unclassified arthritis.[5]

Serum ferritin is an acute phase reactant and is increased in variety of inflammatory diseases and is also seen in JIA and is an important biomarker in systemic JIA. In a study it was found that serum ferritin was strongly associated with systemic JIA even with low disease activity but in non-systemic JIA it was significantly increased but only with high disease activity.[6] The Juvenile Arthritis Disease Activity Score (JADAS) is the most widely accepted disease scoring system for patients with JIA identifying levels of disease activity. JADAS is calculated by the sum of four components: physician's global assessment of disease activity by visual analogue scale (VAS); parents/patients global assessment of well-being by visual analogue scale (VAS), counts of joints with active disease and ESR.[7] This study also assessed their association with the disease activity by using JADAS 27.

METHODS

This cross-sectional study was performed at Pediatric Rheumatology Clinic and Inpatient Rheumatology Division, Department of Pediatrics and Department of Biochemistry, Bangabandhu Sheikh Mujib Medical University (BSMMU) from June 2022 to July 2023. A total of 94 newly diagnosed cases of JIA who attended Pediatric Rheumatology clinic and Inpatient Rheumatology Division, Department of Pediatrics of BSMMU, during the study period were selected as cases in this study.

The study was performed by ethical standards stated in the 1964 declaration of Helsinki and its later amendments. Informed written consent was obtained from parents and institutional review board clearance certificate [No. BSMMU/2022/5314(22), Date: 8/7/2021] was taken before enrolment of the study. All newly diagnosed cases of juvenile idiopathic arthritis (JIA) who attended Pediatric Rheumatology clinic and inpatient Division, Department of Pediatrics, BSMMU and fulfill the selection criteria during the study period were enrolled in the study. After explaining the aims and objectives of the study, informed consent from all patients was obtained for this study. History and clinical examination findings related to the study was recorded in the predesigned data collection sheet. Those JIA patients with evidence of infections, chronic liver disease, renal failure, metabolic syndrome (obesity, hypertension, DM), malignancy and history of blood transfusion within past 3 months was excluded from the study. With the aseptic precaution, 3ml of venous blood will be withdrawn from ante-cubital vein and collected in an EDTA test tube and then the sample was sent for estimation of ESR by Starrsed RS in Clinical Pathology lab of BSMMU. Juvenile idiopathic arthritis (JIA) disease activity was assessed by Juvenile arthritis disease activity score (JADAS).

Three ml blood was drawn from each patient from the antecubital vein aseptically by a disposable syringe. The blood was collected in a dry test tube with a gentle push to avoid hemolysis and the test tube with the sample of blood was sent to the Lab section of the Biochemistry department, where it was allowed to remain at room temperature for approximately 30 mins to 1 hr. Samples will then be centrifused and serum was collected in a labelled test tube. Serum will then be refrigerated at -200 C until analysis. Serum ferritin level was assessed using Liaison XL (Dia Sorin) in the Laboratory section of the Biochemistry department of BSMMU. Normal range of ferritin in children 1-9 years 10-60 ng/ml and 10-18 years (Male) 10-300 ng/ml (Female) 10-70 ng/ml.[8]

The relationship of the disease activity with the Serum ferritin was evaluated. All relevant data was collected from each respondent by interview schedule and recorded in pre-designed data collection sheet. Appropriate statistical tests were used to analyze the demographic, clinical and laboratory data. Non-normally distributed quantitative variables were expressed by median with interquartile range and frequency distribution were calculated by percentages. Statistical analysis to compare between multiple categorical variables were done by using Kruskal Walis test and between two quantitative variables were done by using independent samples t-test. P values less than 0.05 were considered statistically significant.

RESULTS

A total of 94 newly diagnosed cases of Juvenile Idiopathic Arthritis (JIA) who attended Pediatric Rheumatology clinic and Inpatient Rheumatology Division, Department of Pediatrics of BSMMU, during the study period were selected as cases in this cross sectional study. Table 1 demonstrated that the mean age of JIA patients was 9.10±3.68 years. Male were predominant with Male:Female ratio of 1.4:1. Maximum no. of cases (43.6%) were of age group 11-16 yrs. Our study revealed that that the ERA (33%) was the most common subtypes of JIA followed by systemic JIA (23.4%), poly JIA RF(-) 19.1%, Oligoarticular JIA (16%) and poly JIA RF(+) 8.5% respectively (Figure 1).

Table 2 showed that at presentation of all subtypes of JIA had high disease activity and systemic JIA had the highest frequency (81.8%) of high disease activity in comparison to the other subtypes. In this study, we observed that the serum ferritin level was highest among the systemic JIA (mean 609.2±589.9 ng/ml) followed by ERA (mean 363.1±976.7 ng/ml) [p value<0.001] and ESR was also raised in systemic JIA followed by ERA (Table 3).

Table 1: Demographic data of JIA patients (n=94).

Demographic characteristics	Number of patients	Percentage (%)
Age group (years)		
0-5	21	22.3
6-10	32	34.0
11-16	41	43.6
Mean±SD; Range	9.10±3.68; (2-16) years	
Gender		
Male	54	57.4
Female	40	42.6
Male: female ratio	1.4:1	

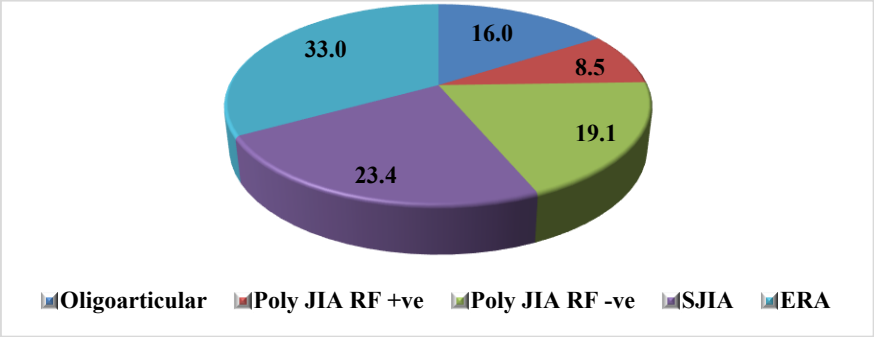

Figure 1: Types of JIA among the study group (n=94)

Table 2: Disease activity status of the study cases by JADAS 27 (n=94).

Parameters	Low disease activity N (%)	Moderate disease activity N (%)	High disease activity N (%)	P value
Oligoarthritis (n=15)	4 (26.7)	5 (33.3)	6 (40.0)	
Poly JIA RF+ve (n=8)	1 (12.5)	2 (25.0)	5 (62.5)	
Poly JIA RF-ve (n=18)	0 (0.0)	5 (27.8)	13 (72.2)	0.04
SJIA (n=22)	0 (0.0)	4 (18.2)	18 (81.8)	
ERA (n=32)	2 (6.5)	4 (12.9)	25 (80.6)	
Total (n=94)	7 (7.4)	20 (21.3)	67 (71.3)	

P value obtained by Chi-square test, p<0.05 considered as a level of significant.

Table 3: Serum ferritin and ESR in different subgroups of JIA and disease activity (n=94).

Parameters	Oligo JIA (n=15)	Poly JIA RF+ve (n=8)	Poly JIA RF-ve (n=18)	SJIA (n=22)	ERA (n=31)	P value
S. Ferritin						
Mean±SD	56.4±72.2	249.8±510.9	251.9±469.9	609.2±589.9	363.1±976.7	
Median	36.7	47.8	95.3	410.1	120.5	<0.001
Range (min-max)	15.2-299.3	17.8-1500.0	12.2-1999.0	31.5-2207.0	14.8-5477.0	
ESR						
Mean±SD	37.9±31.2	47.8±30.7	67.3±41.2	75.9±36.7	70.6±42.3	
Median	28.0	41.5	60.0	84.0	73.0	0.025
Range (min-max)	8.0-113.0	10.0-105.0	9.0-120.0	10.0-120.0	10.0-137.0	
JADAS27						
Mean±SD	6.5±5.6	15.7±8.6	17.6±8.5	16.4±7.5	15.0±8.7	
Median	3.0	17.5	15.9	14.5	13.3	0.006
Range (min-max)	2.0-22.0	3.0-25.5	7.2-31.0	5.0-30.0	3.0-36.0	

P value obtained by Kruskal Walis test, p<0.05 considered as a level of significant.

Table 4: Serum ferritin in different disease activity level in JIA patients (n=94).

Serum ferritin	Low disease activity (n=7)	Moderate disease activity (n=20)	High disease activity (n=67)	P value
Mean±SD	26.3±12.4	128.9±135.6	436.9±798.1	0.003
Median	20.3	44.2	152.9	
Range (min-max)	15.4-47.4	17.8-450.4	12.2-5477.0	

P value obtained by Kruskal Walis test, p<0.05 considered as a level of significant.

Table 4 demonstrated that serum ferritin level was the highest in High disease activity group which was statistically significant (p=0.003). Our study revealed that serum ferritin level was high in systemic JIA in comparison to other types of JIA (Table 3). In this study, we analyzed the correlation between serum ferritin level and JADAS 27 in all the sub-types of JIA which was strongly positive in Poly JIA RF(+) (r=+0.60), moderately positive in ERA (r=+.528), weakly positive in Poly JIA RF(-) (r=+.392) and systemic JIA (r=+.289) and very weakly positive in oligo JIA (r=+.009) but among these, only the positive correlation in case of ERA (p value 0.002) was statistically significant (Figures 2-6).

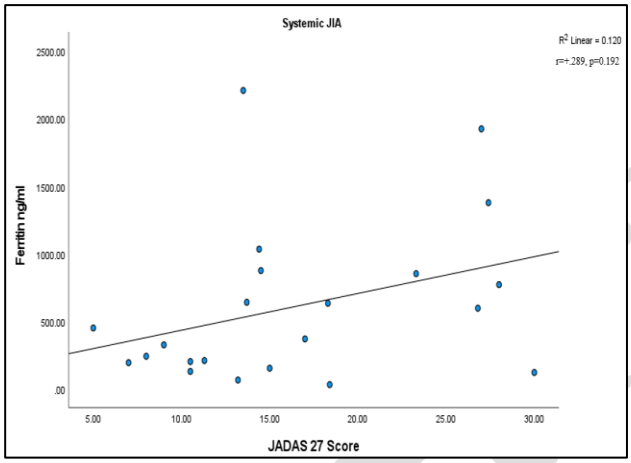

Figure 2: Correlation of serum ferritin with JADAS 27 (Juvenile Arthritis Disease Activity Score) in systemic JIA.

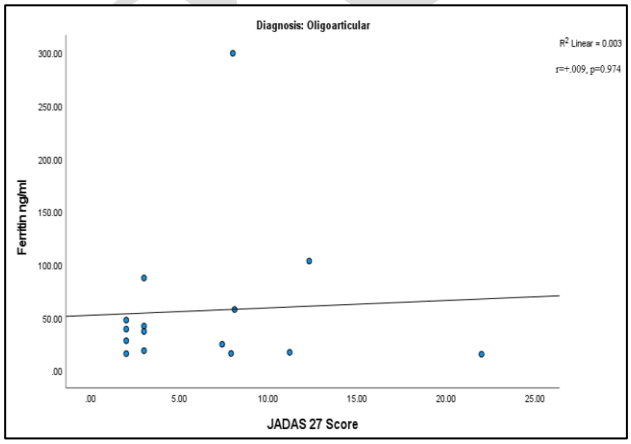

Figure 3: Correlation of serum feritin with JADAS 27 in oligoathritis.

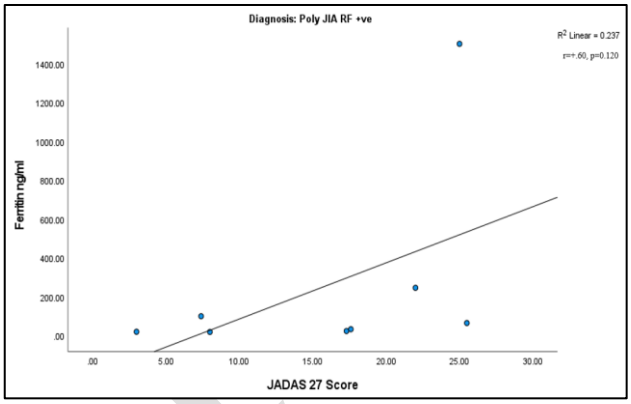

Figure 4: Correlation of serum ferritin with JADAS 27 in polyathritis (RF positive).

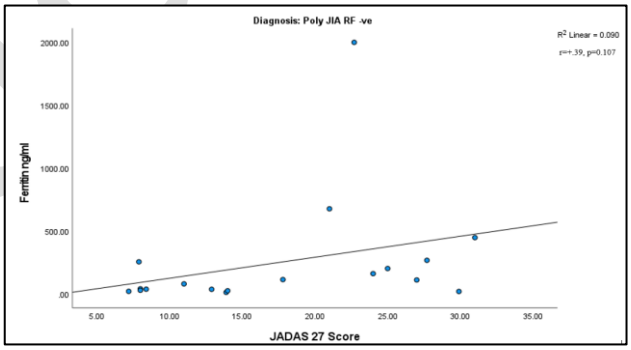

Figure 5: Correlation of serum ferritin with JADAS 27 in polyathritis (RF negative).

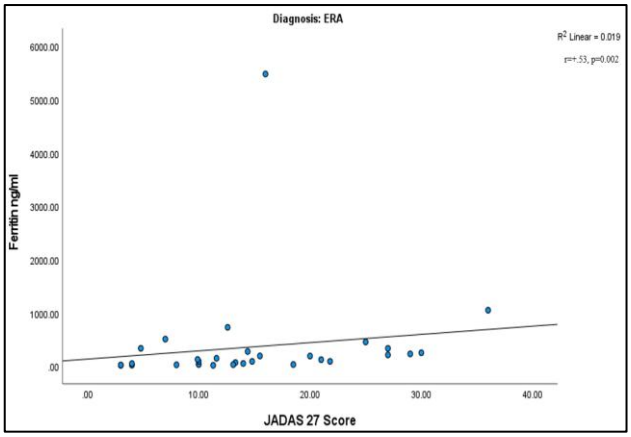

Figure 6: Correlation of serum ferritin with JADAS 27 iSSn ERA.

DISCUSSION

Juvenile Idiopathic arthritis is the most common chronic pediatric disease and characterized by joint inflammation, which leads to joint damage, pain and disability.[2] The pathogenesis is still unclear but it is often referred to as autoimmune inflammatory arthritis in which various cytokines are involved viz IL-1, IL-6, TNF-alpha which leads to synovial and multisystem inflammation.[9]

Serum ferritin is an iron storage protein. Although it is not synthesized in the serum, it is present in high titre during the acute phase of inflammation and is a marker of cellular damage and a leakage from the damaged cell could be responsible for the high ferritin level.[10] In adult patients, with arthritis and other inflammatory diseases such as SLE, serum ferritin is a well-established marker of inflammation.[11,12] It also has been established that in patients with systemic JIA and macrophage activation syndrome (MAS), ferritin level has a valuable role to aid in the diagnosis and also has a prognostic value.[13,14] Though the role of ferritin level has been established in systemic JIA but its role in other subtypes of JIA has been underexplored so this study was aimed to study the effect of ferritin in other subtypes of JIA and whether there was any correlation with the disease activity.

In this cross sectional study, 94 patients of newly diagnosed JIA patients who attended the Rheumatology clinic and Inpatient department were enrolled. The mean age of patients were 9.10±3.68 years and male were predominant with male:female ratio of 1.4:1. In an Indian study male predominance (58.3%) was observed and ERA was the single largest category (36%).[15] Although females are more commonly affected4 our data showed slight male predominance, as in our study we found that ERA (33%) was the most common subtypes, similar to the study done by Kunjir et al, where there was male predominance.[15]

Serum ferritin level and ESR are acute phase reactants which was highest among the systemic JIA patients in our study. Serum ferritin level was significantly raised in systemic JIA (mean 609.2±589.9 ng/ml) in comparison to non-systemic JIA (mean 258.8±704.3 ng/ml). We also observed that serum ferritin and ESR were high in ERA and Poly JIA RF negative patients apart from systemic JIA. Other previous studies have also shown that serum ferritin was highest among systemic JIA patients in comparison to other sub-types of JIA.[13,16] In this study among all subtypes of JIA patients, the majority that presented in our clinic and inpatient department, had high disease activity with systemic JIA patients (81.8%) being the majority who had high disease activity. In an another study conducted by Das, Sarkar and Datta on 2021 observed that serum ferritin and ESR was high in those patients who had high disease activity score.[6]

Overall we observed that serum ferritin level was highest in case of JIA with high disease activity and was statistically significant. While using Spearmans correlation in different subtypes of JIA between Ferritin level and JADAS 27 score we observed that the correlation was strongly positive in Poly JIA RF positive (r=+0.60), moderately positive in ERA (r=+.528), weakly positive in Poly JIA RF negative (r=+.392) and systemic JIA (r=+.289) and very weakly positive in oligo JIA (r=+.009) but among these, only the positive correlation in case of ERA (p value 0.002) was significant. In a previous study done by Das et al, they found a similar strongly positive correlation between ferritin level and JADAS 27 in both Poly JIA RF positive and Poly JIA RF negative, although in their study there were no ERA patients.[6] There were a few limitations in this study such as it was a single centered study and the sample size was small.

CONCLUSION

In this study, serum ferritin showed a significant strongly positive correlation with JADAS 27 in ERA. Although positive correlation was also observed in polyarticular and systemic JIA but it was not statistically significant. Overall we found that serum ferritin level in JIA patients was highest in high disease activity. It was also observed that serum ferritin was significantly increased in systemic JIA as compared to non-systemic JIA patients.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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