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Serum level of Interleukin 23 in Patients with Juvenile Idiopathic Arthritis

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ABSTRACT

Background: Juvenile idiopathic arthritis is considered to be the commonest rheumatic disease in children, IL-23 has a major role in promoting inflammation in target organs.

Aim of the work: To assess the serum interleukin-23 level in Juvenile Idiopathic Arthritis and its correlation to the disease activity.

Patients and Methods: Fifty JIA patients fulfilling the ILAR classification criteria were included in a case-control study and classified into three groups: Polyarticular Rheumatoid factor positive JIA (n = 15), Polyarticular Rheumatoid factor Negative JIA (n = 17), Oligoarticular JIA (n = 18), and eighteen healthy children as a control group. The juvenile arthritis disease activity score (JADAS 71), CHAQ (Childhood Health Assessment Questionnaire), serum IL 23 level, ESR, CRP, ANA and RF were measured for all cases.

Result: Mean age for Polyarticular Rheumatoid factor positive JIA (10.47±4.12), Polyarticular Rheumatoid factor negative JIA (9.19±3.33), Oligoarticular JIA(9.61±3.5) and for healthy children (8.67±3.47). Highest serum IL-23 levels were in Polyarticular Rheumatoid factor negative (median 34.31 ng/ml) followed Polyarticular Rheumatoid factor positive JIA and Oligoarticular JIA (median 22.03 ng/ml) and (median 11.87 ng/ml) respectively. The least values were found in the sera of normal children (median 2.75ng/ml). A significant positive correlation between IL-23 levels and JADAS 71 & CHAQ score most pronounced in the Polyarticular Rheumatoid positive JIA patients.

Conclusion: JIA patients had significantly more serum IL-23 than healthy individuals, and positively correlated with disease activity indices.

Keywords: *Juvenile idiopathic arthritis;Activity;IL-23; JADAS-7; CHAQ.*

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INTRODUCTION

Juvenile Idiopathic Arthritis (JIA) is the commonest rheumatic disease that affects children. [1]

JIA is diagnosed in children younger than 16 years with arthritis which presist for more than 6 weeks with no other underlying cause. [2]

JIA is accounted as a significant cause of acquired impairment and disabilities in children.[3]

The prevalence of JIA in Egypt is estimated to be 3.43 - 20 cases in every 100,000 occupant and worldwide is 1-3 per 1,000 children. [4]

Interleukin-23 as one of the IL-12 cytokine family with pro-inflammatory properties. it is responsible for various autoimmune responses in JIA as it promotes the expansion of the T helper type 17.[5]

IL-23 has a crucial role in the progression and severity of JIA. [6]

This work aimed to evaluate serum IL 23 as a novel biomarker for JIA diseases activity.

PATIENTS AND METHODS

A case-control study included Fifty JIA patients fulfilling the ILAR classification criteria were classified into three groups: Group A: Polyarticular Rheumatoid factor positive JIA (n = 15), Group B: Polyarticular Rheumatoid factor Negative JIA (n = 17), Group C: Oligoarticular JIA (n = 18), and eighteen healthy children as a control group. They were selected from AL Al-Azhar university hospitals Rheumatology Departments, between March 2017 and June 2020. Other reasons of childhood arthritis were excluded, such as Infection, malignancy,

rheumatic fever with obtained informed consent from all participants.

All participants were subjected to Disease activity assessment by Juvenile arthritis disease activity score (JADAS 71) [7], CHAQ (Childhood Health Assessment Questionnaire) [8]. As well as , laboratory assessment including C - reactive protein (CRP), Erythrocyte sedimentation rate (ESR), complete blood count (CBC), RF, ANA and Serum IL-23 by ELISA.

Statistical analysis was done as follows; the statistical package for the social sciences, version 23.0, has been employed to collect, code, revise, and enter data (SPSS Inc., Chicago, Illinois, USA). The quantitative data has been presented as mean, standard deviations when the parametric distribution is normal. In contrast, non-normally distributed variables (non-parametric data) have been shown to have a median with an inter-quartile range (IQR). Numbers and percentages have also been employed to represent qualitative variables. Data was examined for normalcy employing the Kolmogorov-Smirnov and Shapiro-Wilk tests, as well as the relationship between qualitative variables employing the Chi-square test (X2). ANOVA or Kruskal-Wallis, Spearman's correlation to compare differences between quantitatively independent multiple groups. The margin of error acceptable was 5%, with a confidence interval of 95%. As a result, the significance of the p-value was determined as follows: p-values > 0.05 indicate non-significant (NS), p-values < 0.05 indicate significance (S), and p-values < 0.01 indicate highly significant (HS).

RESULTS

The mean age of JIA patients included were (9.40±10.1) and for healthy children (8.6±3.4).

The serum IL-23 receiver operating curve (ROC) has been discovered at levels greater than ≥15.00 pg/ml for JIA subgroups with 80 % sensitivity, 91.7% specificity, 92.3% positive predictive value (PPV), and 78.6 % negative predictive value (NPV) (Table 1).

Groups	Cut-off	Sen.	Spe.	PPV	NPV	AUC [95% C.I.]	p-value
JIA PATIENTS	**≥15.00** pg/ml	80%	91.7%	92.3%	78.6%	0.944 [0.782-0.993]	<0.001

Table 1: The IL 23 cutoff value, sensitivity, and specificity.

There was a highly statistically significant difference between JIA subgroups according to serum IL-23 with p-value (p<0.001). The highest value was found in the group A and group B (29.77±13.41 & 34.31±9.14), followed by Group C (11.87±5.80), while the lowest value was found in control group (2.75±2.16) (Table 2) (Figure 1).

Serum IL-23	Group A *(n=15)*	Group B *(n=17)*	Group C *(n=18)*	Control group *(n=18)*	Test value	p-value
Mean±SD	29.77±13.41#	34.31±9.14#	11.87±5.80≠	2.75±2.16¥	38.997	<0.001**
Range	2-40	8.9-42	1-19	0-16		

Table 2: Comparison between study groups according to serum IL-23 in pg/ml.

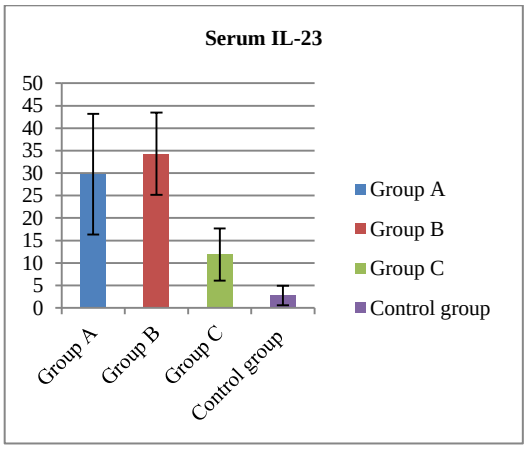

Fig. 1: Bar chart between groups according to serum IL-23.

A highly statistically significant positive correlation between serum IL-23 with JADAS 71(figure 2) & CHAQ in group A and significant positive correlation in group B Polyarticular JIA.

In group C Oligoarticular JIA we discovered a positive correlation only with the JADAS71(table 3).

JIA Subgroups		Serum IL-23 R	Serum IL-23 p-value
Group A	**CHAQ**	0.825	<0.001**
	JADAS 71	0.881	<0.001**
Group B	**CHAQ**	0.519	0.033*
	JADAS71	0.567	0.018*
Group C	**CHAQ**	0.356	0.147
	JADAS71	0.480	0.044

Table 3: correlation between IL-23 and JADAS 71 and CHAQ in JIA subgroups.

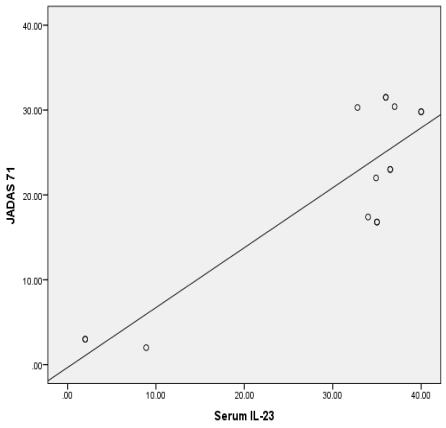

Fig. 2: Statistically significant positive correlation between serum IL-23 and JADAS 71 in group A.

DISCUSSION

JIA is a group of inflammatory arthritis affecting children aged less then 16 years .[9]

Commencement of the JIA pathological process incorporates dysregulated activation of T-cells, B-cells, dendritic cells, natural killer cells, neutrophils and macrophages which produce cytokines leading joints affection and other systemic manifestations. The studied cytokines which lead to progression of JIA and various autoimmune disease have recently included IL-23.[10]

The current study goal was evaluation of the level of IL-23 in JIA patients so that it may be used as a novel marker for activity as well as reinforcing the trial of IL23 antagonists as a potential therapeutic option in controlling the refractory JIA disease activity.

Our study showed significant increased levels of serum IL23 in JIA subgroups compared to healthy controls. There was a highly statistically significant difference between groups according to serum IL-23 level with p-value ($p<0.001$). The highest value was found in the group A and group B (29.77±13.41 & 34.31±9.14 pg/ml) respectively, followed by Group C (11.87±5.80 pg/ml), while the lowest value was found in control group (2.75±2.16 pg/ml).

This is in agreement with Prahalad et al.,10 who discovered the presence of significant difference in the IL-23 levels between JIA patients and controls, in which the highest level was in the Polyarticular JIA with average level (25.7 pg/ml).

This is in line with Tzimouli et al.,6 who measured IL -17, IL23 in synovial fluid and serum of 69 JIA patients and found that serum and synovial fluid IL-23 was significantly higher in JIA patients compared to control.

Yet Szymańska-Kałuża et al.,11 reported the presence of higher IL-23 level in patients with persistent oligoarthritis when comparing them to normal individuals.

We discovered a highly statistically significant positive correlation between the IL-23 in the serum of JIA subgroups and JADAS 71.

So far, no studies have looked into the association between IL-23 levels with JADAS71 & CHAQ in JIA.

So, the IL-23 is predicted to have a potential role as a biomarker to the JIA disease activity.

CONCLUSION

Serum interleukin 23 is elevated in JIA patients with higher prevalence in polyarticular JIA followed by Oligoarticular JIA. In addition, it was found to be correlated with the disease activity. IL 23 may be considered as a potential biomarker for JIA disease activity. As well as, children with refractory JIA might get benefit of trial IL-23 inhibitors.

Conflict of interest : none

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