



## ASSESSMENT OF ANAEMIA IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS AND ITS RELATIONSHIP WITH DISEASE ACTIVITY AND DISEASE DURATION

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### ABSTRACT

**Background:** Anaemia is a common complication of JIA and it usually correlates with disease activity and duration. **Objective:** To assess anaemia in JIA patients including its severity, morphological types and determine its relationship with disease activity and duration. **Methodology:** This cross sectional study was done in the department of paediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU) from January 2017 to June 2018. Eighty new cases of JIA fulfilling ILAR classification criteria were included in this study. A detailed questionnaire was completed for each participant which included clinical and laboratory characteristics, severity of anaemia and disease activity. **Results:** Mean age of JIA patients was 9.36 years with male: female ratio 1.57:1. Most of the JIA patients (91.25%) were suffering from anaemia. Ninety six percent of polyJIA patients were anaemic followed by SJIA (95%), ERA (88%) and Oligoarticular cases (71%). All the patients with severe disease activity were anaemic of which majority were moderately anaemic (47.7%) followed by severely anaemic (29.5%). Significant relationship of anaemia with disease activity and disease duration were observed in this study. **Conclusion:** Most of the JIA patients were suffering from anaemia. Disease duration and disease activity of JIA patients were significantly related with anaemia in this study.

**KEYWORDS:** JIA, Anaemia, Disease Activity.

### INTRODUCTION

Juvenile idiopathic arthritis (JIA) is defined by the International League of Associations for Rheumatology (ILAR) as arthritis of unknown etiology beginning before the sixteenth birthday and persisting for at least six weeks with other known conditions excluded.<sup>[1]</sup>

Anaemia is a common feature of JIA and has been found to correlate with disease activity and types of JIA as well. It has been reported that anaemia is more severe in polyarticular and systemic JIA patients with a more severe disease course compared to others.<sup>[2]</sup>

Elevated levels of cytokines such as interleukin -1 may increase the macrophage's ability to ingest and destroy erythrocytes. Defective erythropoiesis due to cytokine driven inhibition of erythropoietin and hyperproduction of hepcidine are the causes of anaemia.<sup>[3]</sup> Hepcidine influences IL-6 which trigger transport of iron from circulation to reticuloendothelial system.<sup>[4]</sup>

Patients of JIA have anaemia may be due to chronic

disease, iron deficiency or both. It is difficult to find out iron deficiency in the presence of chronic disease because some of the laboratory characteristics of iron deficiency may be changed by chronic disease and active disease states. In both conditions serum iron concentration may be decreased.<sup>[5]</sup>

Serum iron and total iron binding capacity (TIBC) are both low in anaemia of chronic disorder in comparison to simple iron deficiency anaemia where the TIBC is always elevated.<sup>[6]</sup>

Serum ferritin is expected to decrease in iron deficiency but may not be found in active disease states of JIA patients with iron deficient anaemia. As ferritin is an acute phase reactant; the ferritin levels may increase in these patients during active disease state<sup>[7]</sup>. Serum ferritin has been reported to correlate with disease severity in JIA and return to normal with remission of the disease particularly in systemic JIA.<sup>[8]</sup>

Objectives of the present study were to assess the

severity and pattern of anaemia in different subtypes of JIA patients and to determine its relationship with disease activity and duration in a tertiary care hospital of Bangladesh.

## METHODOLOGY

This cross sectional study was carried out in the paediatric rheumatology follow up clinic and inpatient department of paediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU) from January 2017 to June 2018. Eighty newly diagnosed cases of different subtypes of JIA fulfilling ILAR criteria were included in this study. Children who had received iron preparations or DMARDs, had any associated acute infection or history of recent blood transfusion, chronic renal failure, hematological abnormalities and malignancies were not included in this study. History, clinical examination and relevant investigations were recorded in the predesigned questionnaire. Level of disease activity was assessed by parameters according to 2011 American College of Rheumatology recommendations.<sup>[9]</sup> These included: (i) number of joint involvement, (ii) ESR, (iii) physician global assessment of disease activity and (iv) patient global assessment of overall wellbeing.

Global assessment of disease activity by physician and patient/parent were measured by using visual analog scale. A 0- 10cm horizontal line was taken to represent

the status of global assessment of disease activity. The line starts from zero which indicates absent disease activity and the extreme ends of the line is 10 cm which indicates the disease activity as maximum (100%). After taking informed written consent blood samples were collected for complete blood count, serum iron, serum ferritin and serum total iron binding capacity. This study was conducted with prior approval of the Institutional Review Board of BSMMU, Dhaka, Bangladesh.

Data were checked, verified and analyzed by SPSS (statistical program for social science) software 22. Mean and standard deviation (SD) were used for analysis and reporting. Chi-square test was used to see association between categorical data. Pearson's coefficient was used to investigate the correlation between the two variables. A p-value less than 0.05 was considered as significant.

## Working definition

### Anaemia

Anaemia is a condition in which the number of red blood cells (consequently their oxygen carrying capacity) is insufficient to meet the body's physiologic needs.

In this study, WHO guideline 2011 was used to define anaemia (mild, moderate and severe) and non anaemia.<sup>[10]</sup>

Population	NonAnaemia	Anaemia			mg/dl
		Mild	Moderate	Severe	
<b>Children 6-59 months of age</b>	110 or higher	100-109	70-99	lower than 70	
<b>Children 5-11 years of age</b>	115 or higher	110-114	80-109	lower than 80	
<b>Children 12-14 years of age</b>	120 or higher	110-119	80-109	lower than 80	
<b>Girl 15 years of age and above</b>	120 or higher	110-119	80-109	lower than 80	
<b>Boy 15 years of age and above</b>	130 or higher	110-129	80-109	lower than 80	

WHO guideline of Anaemia diagnosis, 2011.<sup>[10]</sup>

## RESULTS

Mean age of children was  $9.36 \pm 3.51$  years and majority(51%) of cases were older than 10 years. 61.3% of our study cases were male and 38.8% were female. Enthesitis related arthritis and polyarticular JIA were the most common type and equally distributed (32.5%), followed by 26.3% cases of systemic JIA and 8.8% cases of oligoarticular JIA patients.

Diagnosis was done within 6 months of onset in 38.8% cases and in 36% cases disease duration at diagnosis was more than 1 year. Most of the JIA patients (91.25%) had anaemia in this study. Majority of polyarticular cases (96.15%) had anaemia followed by SJIA (95.3%), ERA (88.46%) and oligoarticular cases (71.43%) (Table I).

Mean haemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC), serum iron and total iron binding capacity (TIBC) were significantly reduced in anaemic group in comparison to non anaemic group. Total leucocyte count, platelet count, ESR and serum ferritin were significantly

higher in anaemic group in comparison to nonanaemic group of patients (Table II). Forty one percent of JIA patients had moderate anaemia followed by mild anaemia (31.5%) and severe anaemia (27.4%). Oligoarticular patients (100%) had mild anaemia, 48% of polyarticular patients were moderately anaemic but 50% of systemic JIA patients were moderately anaemic and 50% of them were severely anaemic. Forty eight percent and 17.4% of ERA patients were mildly and severely anaemic respectively. This result was statistically significant (Table III).

Majority (67.1%) of JIA patients had microcytic hypochromic anaemia in this study. Most of the patients with mild disease activity (83.3%) were mildly anaemic. Patients with moderate disease activity had moderate anaemia in 34.8% and severe anaemia in 30.4% cases. All the patients with severe disease activity were anaemic and among them 47.7% had moderate anaemia and 29.5% were severely anaemic. The distribution of these variables were significant (Table IV).

Significant negative correlation ( $r = -0.290$ ,  $p = 0.009$ ) was found between Hb concentration and disease duration which indicates that Hb level decreases as disease duration increases (Fig I).

**Table I: Distribution of Anemia in different types of JIA patients (n=80).**

	Anaemic	Nonanaemic	*p-value
Oligoarticular (n=7)	05(71.43%)	02(28.57%)	0.179
Polyarticular(n=26)	25(96.23%)	01(3.84%)	
SJIA (n=21)	20(95.23%)	01(4.76%)	
ERA (n=26)	23(88.46%)	03(11.53%)	
Total	73(91.25%)	07 (8.75%)	

\*Chi-square test

**Table-II: Comparison of haematological parameters of JIA patients with and without anaemia (n=80).**

	Anaemia (+) (Mean ± SD) (n = 73)	Anaemia (-) (Mean ± SD) (n = 7)	* p- value
Hb (gm/dl)	8.71 ± 1.82	12.33 ± 0.63	0.000
MCV (fl)	71.75 ± 7.19	80.50 ± 4.59	0.001
MCHC (g/dl)	29.32 ± 4.71	32.78 ± 1.08	0.000
Total WBC (mm3)	12130 ± 5840	8930 ± 1540	0.001
Platelet (lac/mm3)	5.37 ± 1.84	3.33 ± 0.53	0.005
ESR (mm in 1 hr)	76.55 ± 32.45	29.63 ± 14.85	0.000
Serum Iron (μg/dl)	27.79 ± 31.04	68.71 ± 37.02	0.026
TIBC (μg/dl)	262.92 ± 68.76	330.75 ± 45.28	0.006
Serum Ferritin(μg/L)	1737.98 ± 4876.77	69.37 ± 38.91	0.005

\*Unpaired Student's 't' test

**Table III: Degree of anaemia in different subtypes of JIA patients (n=73).**

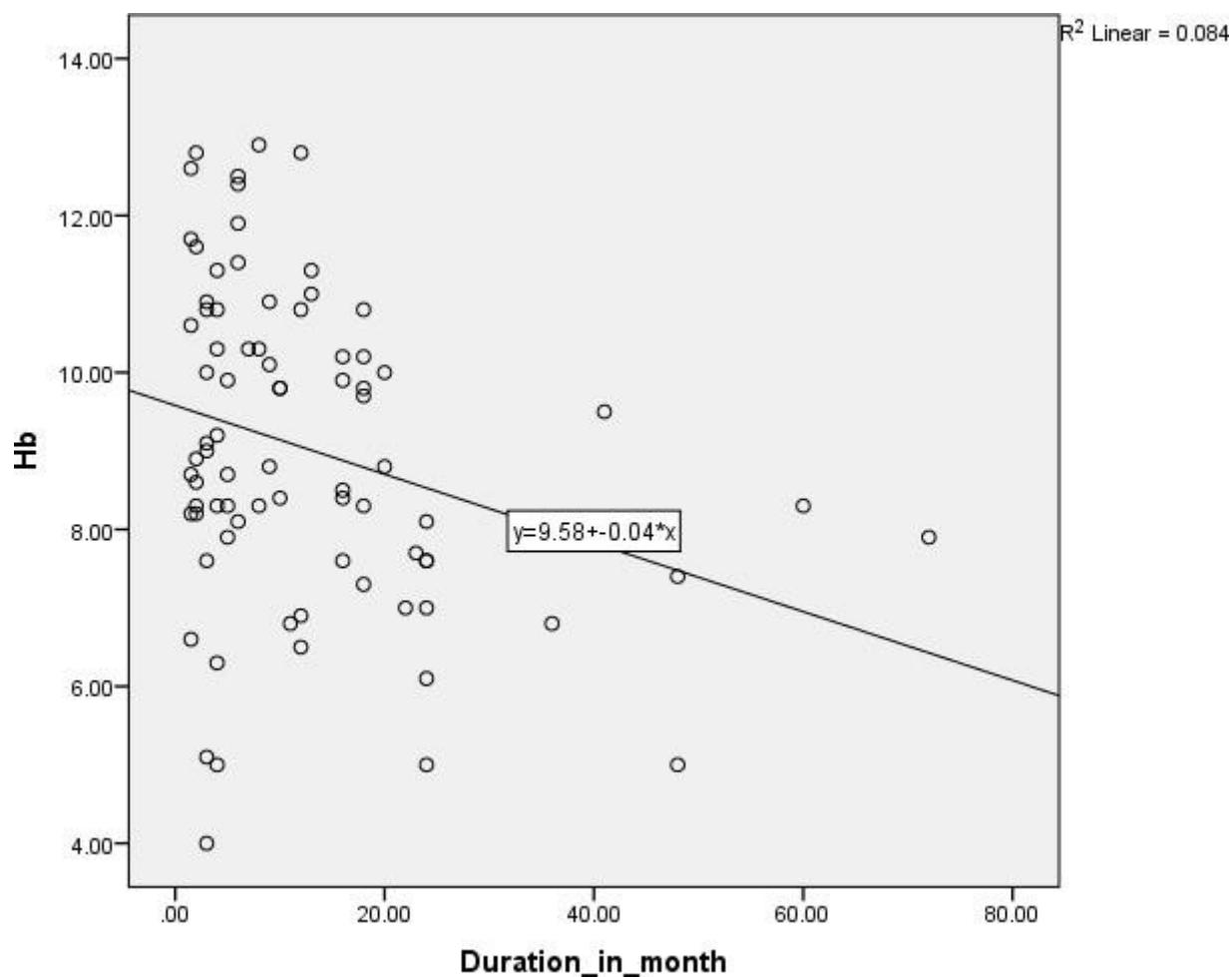
Subtypes of JIA	Mild n (%)	Moderate n (%)	Severe n (%)	*p-value
Oligoarticular (n=5)	05(100%)	00	00	.000
Polyarticular (n=25)	07 (28%)	12 (48%)	06 (24%)	
Systemic JIA (n=20)	00	10 (50%)	10 (50%)	
ERA (n=23)	11 (47.8%)	08 (34.8%)	04 (17.4%)	
Total n (%)	23 (31.5%)	30 (41.1%)	20 (27.4%)	

\*Chi-square test

**Table-IV: Relationship of anaemia with disease activity (n=73).**

Disease activity	Mild n(%)	Moderate n(%)	Severe n(%)	*p-value
Mild (n=6)	05(83.3%)	01 (16.7%)	00	.047
Moderate (n=23)	08(34.8%)	08(34.8%)	07(30.4%)	
Severe (n=44)	10(22.7%)	21(47.7%)	13(29.5%)	

\*Chi-square test



**Figure-I:** Scatter diagram showing the correlation between hemoglobin and disease duration.

## DISCUSSION

Anaemia is a common manifestation of juvenile idiopathic arthritis. This anaemia may be anaemia of chronic disease, which is often indistinguishable from anaemia due to iron deficiency.

In this study mean age of the patients was 9.3 years which was similar to the study done by Kirel et al.<sup>[11]</sup> Another Bangladeshi study done by Laila et al. found the mean age of JIA patients as 10.8 years which was almost similar to the present study.<sup>[12]</sup> Though it is well known that females are generally more commonly affected than males in JIA, but our data shows male predominance. Similarly male predominance was also found in a Bangladeshi study done by Rahman et al., where male: female ratio was found as 2:1.<sup>[13]</sup>

In this study polyarticular RF negative and enthesitis related arthritis were the most common type (32.5% each) followed by systemic JIA (26.3%). The reasons behind polyarticular preponderance in our study may be multifactorial. Some of the oligoarticular extended cases may be classified as polyarticular due to longer duration between disease onset and diagnosis. Another possibility is that polyarticular patients having more severe disease likely to visit hospital early. The reason behind higher ERA cases may be due to higher discriminative

attitudinal preference for boys. Our study differs from a study of a tertiary care hospital of Saudi Arabia, where it was found that systemic JIA was the most common subtype of JIA.<sup>[14]</sup> Demirkaya et al. described oligoarticular persistent cases as the most common subtype of JIA in a cohort of 634 JIA patients.<sup>[15]</sup>

Majority (38.8%) of the patients presented within six months of disease onset. A previous Bangladeshi study done by Rahman et al. found that duration of disease at presentation was more than 12 months in the majority (48.6%).<sup>[13]</sup> The duration of illness at presentation is decreasing, may be due to increased awareness of the people regarding rheumatological illness.

In our study mean Hb, MCV, MCHC, serum iron and TIBC were significantly reduced in anaemic group in comparison to non anaemic group. TIBC usually increases in iron deficiency anaemia but low in chronic disease like JIA as there is no iron deficiency rather iron may be sequestered in reticuloendothelial system.<sup>[3]</sup> Although serum ferritin is expected to decrease in iron deficiency anaemia but may not be apparent in active states of JIA as liver increases synthesis of apoferritin which leads to increase ferritin level.<sup>[11]</sup> Total WBC count, platelet count, ESR and serum ferritin were significantly higher in anaemic group in comparison to

nonanaemic group of patients. ESR was inversely related to Hb concentration. These findings are almost consistent with a study done previously by Kirel et al where they found significant differences of Hb, WBC and ESR in between anaemic and nonanaemic group.<sup>[11]</sup>

In this study most of the patients had anaemia (91.25%). More than 95% of polyarticular and systemic JIA patients had anaemia in this study. Longer duration of disease, nutritional deficiency and change in iron kinetics due to disease process were the reason for anaemia. Al-Hemairi et al. also found anaemia as the most common abnormal laboratory investigation (59.75%) and it was recorded in 80% of systemic JIA patients.<sup>[14]</sup> S. M. Kivivuori et al, at his study found that 50% of patients with JIA had anaemia.<sup>[15]</sup>

We found a significant relationship of disease activity with anaemia in JIA patients. All the patients with severe disease activity were anaemic. Buaboonnam and Charuvanij found that Hb level was negatively correlated with JIA disease activity parameters like ESR and CRP.<sup>[16]</sup>

In this study we also found a significant negative correlation between Hb concentration and disease duration. Smyrnova found that duration and activity of Rheumatoid Arthritis were significantly higher in patients with anaemia compared to patients with normal hemoglobin.<sup>[17]</sup>

## CONCLUSION

Most of the JIA patients (91.25%) were suffering from anaemia and it was more pronounced in systemic and polyarticular JIA patients. Relation between disease activity of JIA patients and anaemia was significant. There was a significant negative correlation between hemoglobin level and disease duration in patients with JIA.

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