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Relationship between red cell distribution width and serum ferritin level among pre-school childrenattending in a tertiary care hospital.

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Abstract
Background: *Pre-school children are vulnerable to iron deficiency anemia (IDA). As most of the testing tools to detectIDA rely on markers involving high costs, hence cheaper and easier potential screening tools are warranted. The objective of the study was to identify the discriminative ability ofred cell distribution width (RDW)fordetecting ID among children aged up to 5 years in our settings.*
Methods: *A cross-sectional approach was adopted to conduct the study based on the data collected from the Barind Medical College, Rajshahi. The study duration was for six months. Children aged up to 60 months were included in this study. A total of 200 children were enrolled after getting informed written consent from their parents. A case record form was used for data collection. Both sociodemographic characteristics and investigation details were recorded. A serum ferritin level of less than 12 µg/l was considered as confirmatory for iron-deficiency. The collected data were analyzed by SPSS V-21. Ethical measures were taken in accordance with the current Declaration of Helsinki.*
Result: *The mean age of the studied children was 27.28±15.29 (SD) months. Male children accounted for three-fourths of the studied children. Of all, 9.5% of the children were malnourished according to World Health Organization (WHO) criteria.The frequency of anemia and iron deficiency was 55.5% and 23.5% accordingly.The mean red cell distribution width (RDW) was 32.71±4.78(SD)%, and the mean serum ferritin level was 55.07±91.07µg/l.RDW was significantly higher in children with low serum ferritin levels(19.21 µg/l Vs 15.10 µg/l, p<.05).Receiver operating characteristic (ROC) curve acceptable diagnostic property of RDW with 72.3% sensitivity and 73.2% specificity at a cut-off value of 16.96%. A strong negative linear relationship was also observed between RDW and serum ferritin levels among children with iron deficiency (r=-616, p<.001).*
Conclusion: *RDW was higher among children with low serum ferritin levels. However, further study is warranted before using it in a clinical or community setting.*

Keywords: ***Red Cell Distribution Width, RDW, Serum Ferritin, IronDeficiency Anemia, Pre-schoolChildren***

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I. Introduction

Globally, childhood anemia is a significant public health concern affecting almost half of the under-five children (47.4%) worldwide[1]and Iron Deficiency Anemia (IDA) is the commonest form.[2–4]IDA mostly results from insufficient iron-containing food in a regular diet, low or malabsorption of iron, or increased nutritional requirements[5,6]and causes delayed cognitive development, poor physical &behavioral growth,

incompetent immune status, impaired motor & sensory system functioning which severelyhamper the quality of later life.[7]In Bangladesh, the prevalence of childhood anemia is 52.10%.[8]Iron deficiency anemia is a significant cause of childhood mortality and morbidity, especially among developing countries.[10]

Prevention of iron deficiency among pediatric populationis a simple but life-changing strategy. Conversely, evidence suggests routine iron supplement without differentiating the presence of iron deficiency results to morbidity and infections.[11,12] So, it is very crucial to determine the presence of IDA among pre-school children in order to replenish the iron shortage and to prevent the further consequences.

Usually, iron deficiency is confirmed by the serum iron profileincluding total iron concentration, serum ferritin level, serum transferrin level which are not routinely available. Additionally, these markers might get altered by presence of inflammation or other conditions except IDA.Recently, Red Cell Distribution Width (RDW), a hematological parameter has been shown to reflect the early changes of red blood cell which occur due to iron deficiency in . [11,13,17–19]Moreover, red cell distribution width tends to start increasing due to iron deficiency even before the hemoglobin concentration falls to an anemic level.[17]It is a routine hematological parameter included in complete blood count, which is widely available, even in less facilitated centers. This parameter can express even slight variation and changes in the size of red blood cells.[18,19]The efficiency of this tool to distinguish iron deficiency is yet to evaluate among children up to five years old.

In the human body, the majority of iron is stored in the form of serum ferritin; thus, evaluating serum ferritin levels indicates any changes in iron stores.[20,21] During iron deficiency, red blood cells undergo morphologic changes that affect the overall RDW. RDW tends to increase due to appearance of microcytic population.Serum ferritin indicates iron storage in the human body, and RDW also indicates morphologic changes due to iron deficiency. Therefore, the present study aimed to determine the relationship between serum ferritin level and red cell distribution width among childrenup to five years of age attending a tertiary care hospital.

II. Methods And Materials

Study design, locale & period: The study was a cross-sectional study conducted in the Barind Medical College Hospital. This hospital is a private facilitated hospital situated in northern Bangladesh. The study period was six months, extending from June 2022 to December 2022.

Study participants, sampling method and sample size: Children aged ≤ 60 months attending the Outpatient Department (OPD) of the studied hospital were considered the study population. Children with acute infections, chronic comorbid conditions, received iron therapy or blood transfusion in last 3 months, and children required hospital admission were excluded from the study.Informed assent was obtained from the mother/father of the children before enrollment in this study. Finally, a total of 200 children were included in this study according to the inclusion and exclusion criteria. Purposive sampling method was adopted in this study.

Data collection procedure:

A semi-structured questionnaire was developed for data collection that included sociodemographic parameters of children and investigation findings (hematological parameters and serum ferritin level). Pretesting was performed among twenty children and updated according to the findings of the pretesting.

Face-to-face interviews of the mothers/fathers of the studied children were conducted. Information regarding age, sex, monthly family income, and residence was collected. Anthropometric measurements of the children were taken. A bathroom scale was used for measurement of weight for the children who could stand properly. For childrenaged less than 24 months who could not stand properly, a portable salter hanging scale was used. For measurement of height, a height measuring stick was used in children aged 24 months to 60 months. A length measuring board was used for children less than 24 months of age. For assessment of nutritional status, the Gomez classification was used. The Z score was calculated according to WHO criteria in terms of stunting (height for age) and wasting (weight for height) and weight for age. Children with a z score from -2.00 to +2.00 were classified as children with normal nutritional status, and others were considered malnourished.

Complete blood count (CBC) and serum ferritin level were estimated for all children. For investigation purposes, 5 ml of venous blood was drawn from each child and divided into two halves- 2.5 ml in each portion- one for CBC and one for serum ferritin level.

Complete blood count was analyzed by the ABX PENTRA 60. The blood was mixed well and then placed in the analyzer. Serum ferritin was assayed by sandwich enzyme link immunosorbent assay.

Red cell distribution width (RDW) was calculated by the following formula:

RDW: {Standard deviation of mean corpuscular volume (MCV) ÷ MCV} × 100

A serum ferritin level of <12 µg/l was considered as low level of serum ferritin. Children with a serum ferritin level of <12 µg/l was considered to have iron deficiency in this study.[22]

Data were recorded in separate case record forms. Following data collection, data were checked for errors and prepared for data analysis.

Ethical issue:
Prior to conducting the study, ethical approval was obtained from the appropriate authority. The study was conducted in accordance with the guidance and principles of the Declaration of Helsinki.

Statistical analysis
Characteristics of children and investigation findings were reported as the mean ± standard deviation, median (minimum-maximum) in case of continuous variables and as frequency (percentage) in case of categorical variables. Data were analysed by the software 'Statistical Package for the Social Sciences (SPSS) V-21'. The normality of the continuous variable was determined by the Shapiro–Wilk test. The difference in RDW among children with and without iron deficiency was determined by a nonparametric test(Mann–Whitney U). A receiver operating characteristic curve was constructed to determine the diagnostic property of RDW in the detection of iron deficiency. A p value of <.05 was considered significant. Charts and tables were used to present the final results.

III. Result

The mean age of the studied children was 27.28±15.29 (SD) months, with a majority aged 13-24 months. Male predominance was observed, with 61.5% male and 38.5% female. The majority of the respondents hailed from urban areas, and their mean monthly family income was 28925.14±6564.81 (SD) Bangladesh Taka. The mean weight and height of the studied children were12.12±2.86 (SD) kg and 85.42±12.34 (SD) cm. The nutritional status of the children was assessed according to World Health Organization (WHO) criteria, and 90.5% had normal nutritional status. Among the rest, 5% were underweight and 4.5% were overweight.

Table 1: Sociodemographic characteristics and anthropometric measurements of the studied children (n=200)

Variables	n	%
Age group (months)		
≤6	6	3
6-12	37	18.5
13-24	72	36
25-36	40	20
37-48	25	12.5
49-60	20	10
Mean±SD*	27.28±15.29	
Sex		
Male	123	61.5
Female	77	38.5
Residence		
Rural	81	40.5
Urban	119	59.5
Monthly family income (BDT)		
10,000-25,000	57	28.5
26,000-40,000	140	70
>40,000	3	1.5
Mean±SD*	28925.14±6564.81	
Anthropometric measurements		
Height (cm)*	85.42±12.34	
Weight (kg)*	12.12±2.86	
Nutritional status		
Normal	181	90.5
Malnourished	19	9.5
Underweight	10	5
Overweight	9	4.5

Variables are expressed as the mean±SD*

The hematological parameters of the studied children are tabulated below. The mean values of red cell distribution width and serum ferritin were 32.52±4.90 (SD) % and 249.66±908.06 µg/l, respectively.

Table 2: Hematological parameters and serum ferritin levels of the studied children (n=200)

	Mean±SD
Serum hemoglobin (g/dl)	10.28±1.86
Erythrocyte Sedimentation Rate (ESR) (mmHg in 1st hour)	17.11±14.60
Total count of white blood cell (WBC) (/cmm)	13.36±6.04
Total count of red blood cell (RBC) (/cmm)	6.49±26.33
Total count of platelets (/cmm)	331230±102911.52
Mean corpuscular hemoglobin (MCH) (pg)	23.59±13.98
Mean corpuscular volume (MCV) (fl)	70.84±8.56
Hematocrit (HCT) (g/dl) (%)	31.25±2.09
Red cell distribution width (RDW) (%)	32.71±4.78
Serum ferritin (µg/l)	55.07±91.07

Approximately55.50% of the studied children had anemia, and 23.5% of them had iron deficiency.

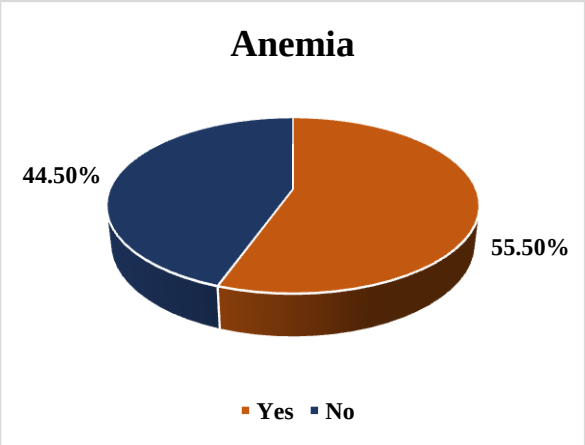

Figure 1a: Frequency of anemia (n=200)

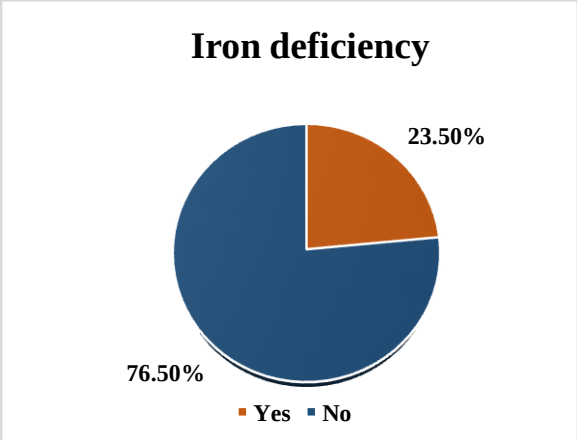

Figure 1b: Frequency of iron deficiency (n=200)

RDW was significantly higher in patients with low serum ferritin levels (iron deficiency).

Table 3: Relationship between RDW and serum ferritin level (n=200)

	Serum Ferritin level		p value*
	Low (<12 µg/l) n=47 median (min-max)	Normal (≥12 µg/l) n=153 median (min-max)	
RDW (%)	19.21 (12.80-26.44)	15.10 (11.80-35.90)	**<.001**

***p value was determined by the Mann–Whitney U test.**

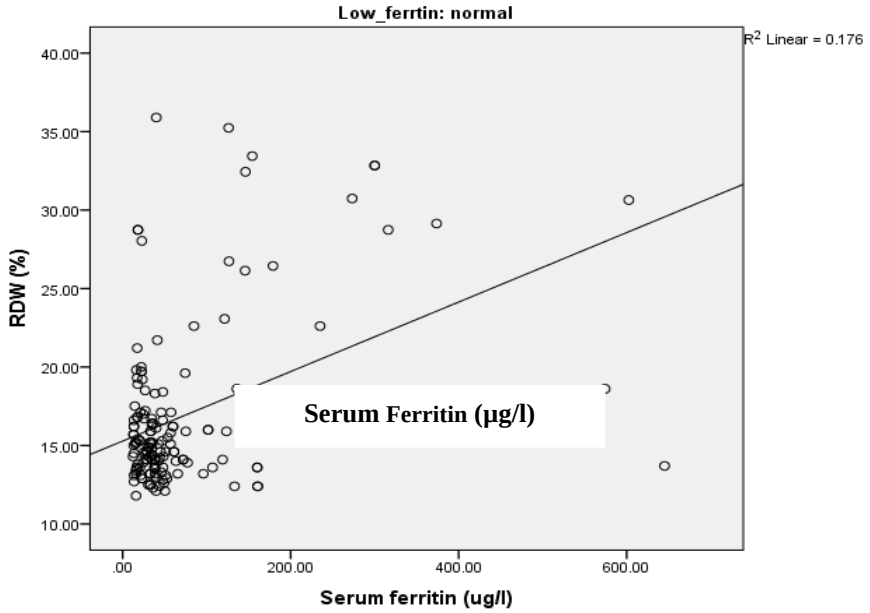

Figure 2: Scatter plot diagram showing the correlation between RDW and serum ferritin levelamong the studied pre-school children with low serum ferritin level (iron deficiency) (n=153)

According to the Scatter plot diagram showing linear relationship between RDW and serum ferritin level- RDW increases significantly with the decrease of serum ferritin level which indicates a negative correlation (r=-616, p<.001).

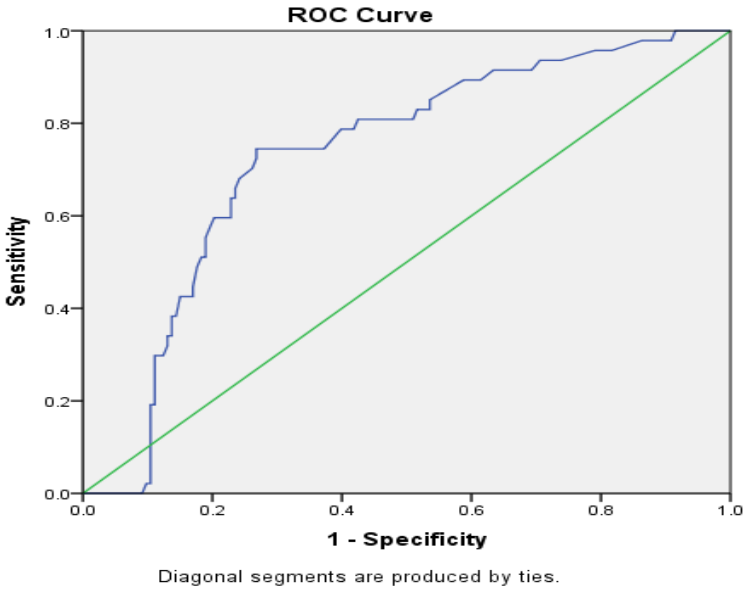

Figure 3: Receiver operating characteristic (ROC) curve of RDW to detect iron deficiency among studied children (n=200)

Receiver operating characteristic (ROC)curve analysis showed an area under the curve of.730 with 72.3% sensitivity and 73.2% specificity at a cut-off value of 16.96. The calculated positive predictive value, negative predictive value and accuracy were 45.33%, 89.6% and 73%, respectively.

IV. Discussion

In this study, RDW had a negative relationship with serum ferritin level with statistical significance. Iron deficiency was detected in one-fifth of the studied children underfive years of age who had a statistically higher red cell distribution width (RDW) than children with normal iron levels. In the present setting, RDW showed a fair area under the receiver operating characteristic curve to detect iron deficiency among the studied children. The sensitivity and specificity were 72.2% and73.3%, respectively, with an accuracy of 73%. The positive predictive value was 45.3%, and the negative predictive value was 89.6%. Role of RDW to differentiate the presence of iron deficiency has been evaluated among varieties of population group and some of them observed acceptable diagnostic properties.[17,14,11]Unlike these studies, poor diagnostic properties of RDW was also observed.[24] But RDW was observed statistically higher among population group with iron deficiency in various previous studies.[23,14,24,11]In the present study, a strong negative linear correlation was observed between serum ferritin and RDW levels among the children with iron deficiency, where RDW tended to increase with decreasing ferritin levels.

The average age of the studied children was 27 months, and three-fifths were male children. The majority of the children hailed from urban areas and belonged to a socioeconomic group with a monthly income of 26000-40000 Bangladesh Tk. As the study was conducted in a corporate hospital situated in a division of Bangladesh, people belonging to very low- and low-facilitated areas, such as slums or remote villages, rarely visit this hospital. Among the studied children, more than half of the children were anemic, which could be much more if this study could include more centers and a generalized sample population. Yousuf et al. performed a study among preschool children in Bangladesh and observed a 52.10% prevalence of anemia.[8]The prevalence of childhood anemia in Bangladesh is higher thanthe global prevalence.[1] Anemia and malnourishment are interrelated with each other.[25] In this study, 9.5% of the children were malnourished.

The present study indicates a negative relationship between serum ferritin and RDW, where RDW is higher among children with low serum ferritin levels. Therefore, RDW could be used as a potential marker to detect iron deficiency among children up to 60 months of age. Markersdedicated to estimating iron storage are not widely available and are also expensive, especially in low-resource settings. If RDW could function as an effective screening tool for the detection of iron deficiency, screening services could be conducted even in school or community settings. Early detection of iron deficiency and iron deficiency anemia could prevent the associated gracious consequences.

Although this study rendered a diagnostic property of RDW, there were some limitations. The studied children were selected from a single center dedicated to a specific population. The relationship between RDW and serum ferritin was evaluated in this study, andother investigations indicatingthe iron status of the human body could not be performed in this study. Moreover, detailed iron staining from bone marrow could not be performed because it was invasive and costly.

V. Conclusion

RDW was significantly higher among childrenup to five years of age with low serum ferritin levels, along with a recommendable diagnostic property to detect iron deficiency. However, a larger multicentered study should be performed before practicing RDW as a screening tool for iron deficiency among preschool children.

Declarations

Ethics approval:

The study was approved by the Ethical Review Committee, Barind Medical College Hospital, Rajshahi. Informed written consent was obtained from all participants following their agreement on participation in this study. The authors declare that the procedures followed the regulations established by the Helsinki Declaration of the World Medical Association.

Consent for publication: Not applicable.

Availability of data and materials: Patient-level data will be available on request from the corresponding author.

Conflict of interest: The authors declare that they have no competing interests.

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