The Professional Medical Journal
www.theprofesional.com

DOI: 10.29309/TPMJ/18.4348

ORIGINAL PROF-4348

1. MBBS, MCPS, FCPS
Assistant Professor
Department of Paediatrics
Shaheed Muhtrama Benazir Bhutto
Medical College, Layari
2. MBBS, MCPS, FCPS
Assistant Professor
Department of Paediatrics
Shaheed Muhtrama Benazir Bhutto
Medical College, Layari
3. MBBS, FCPS
Assistant Professor
Department of Pediatrics
Dow University of Health Sciences
4. MBBS, MCPS, FCPS (Paediatrics),
FCPS (Neonatology)
Assistant Professor
Department of Paediatrics
Shaheed Muhtrama Benazir Bhutto
Medical College Layari
5. MBBS, MCPS, FCPS
Assistant Professor
Department of Paediatrics
Hamdard Medical College
6. MBBS, MCPS, FCPS
Principal
Head of Department
Gynecology and Obstetrics
Shaheed Muhtrama Benazir Bhutto
Medical College Layari Sindh, Pakistan.

Correspondence Address:
Dr. Nathumal Maheshwari
Assistant Professor
Department of Paediatrics
Shaheed Muhtrama Benazir Bhutto
Medical College Layari
General Hospital Karachi, Sindh, Pakistan.
drnathumal@gmail.com

Article received on:
25/09/2017
Accepted for publication:
15/02/2018
Received after proof reading:
04/05/2018

IRON DEFICIENCY ANEMIA;

EVALUATING DIAGNOSTIC UTILITY OF RED BLOOD CELL WIDTH DISTRIBUTION FOR PREDICTING IRON DEFICIENCY ANEMIA IN CHILDREN

Nathumal Maheshwari[1], Omperkash Khemani[2], Bilawal Hingorjo[3], Mehmood Shaikh[4], Sirichand[5], Anjum Rehman[6]

ABSTRACT… Objectives: To evaluate the predictive value of Red blood cell distribution width (RDW) for the iron deficiency anemia in children. **Study Design:** Cross sectional study. **Place and Duration:** Department of Paediatrics, Layari General Hospital Shaheed Muhtrama Benazir Bhutto Medical College from December 2015 to March 2016. **Methodology:** A sample of 100 children (53 male and 47 female) was selected through non- probability (purposive sampling). 5 ml venous blood was collected, 3 ml was shifted to EDTA containing vacutainers and remaining was processed and centrifuged to separate sera. Complete blood counts and iron profile were performed. Data of cases and controls was analyzed on *Statistix 10.0 software* (USA) ($P \leq 0.05$). **Results:** Severe iron deficiency and iron deficiency anemia were noted. Serum Iron, TIBC and Ferritin were noted as 63.49±32.94 and 76.06±40.38 µg/dl, 468.7±142.2 and 445.5±135.2 µg/dl, & 36.2±14.12 and 43.2±13.5 ng/dl respectively. RDW proved a sensitivity and specificity of 78% and 56% respectively (0.001). **Conclusion:** We observed severe iron deficiency anemia in children and Red blood cell distribution width showed high sensivity in predicting iron deficiency anemia.

Key words: Iron Deficiency Anemia, Red Blood Cell Index, RDW, Children.

Article Citation: Maheshwari N, Khemani O, Hingorjo B, Shaikh M, Sirichand, Rehman A. Red blood cell width distribution; evaluating diagnostic utility of red blood cell distribution width for predicting iron deficiency anemia in children. Professional Med J 2018; 25(5):659-663. **DOI:**10.29309/TPMJ/18.4348

INTRODUCTION

Iron deficiency anemia (IDA) is most common type of anemia among children in the developing countries like Pakistan. IDA increases the health problems in the children as growth may be retarded but this depends upon its severity. Chances of morbidity and mortality are increased. Most negative consequence of iron deficiency is the iron deficiency anemia (IDA).[1] IDA has various casues, but most common cause is the dietary iron deficiency and malnutrition in the developing countries. Poor iron in diet, impaired intestinal iron absorption, severe malaria, and chronic blood loss from gut for example due to the worm infestations are a few common causes.[2,3] IDA impairs neurological development with poor cognitive performance. Delayed motor and sensory development are other consequences. Timely iron supplementation in early childhood life may prevent these consequences[4], on the contrary iron therapy in non iron deficient children may exert adverse effects.[5,6] Hence, before commencing iron supplements, the iron deficiency must be established. This shows the importance of analyzing the serum iron profile in the anemic children for evidence based iron supplements. Eliminating iron deficiency and IDA may prevent the adverse developmental and behavioral effects.[6,7] Estimation of iron profile is a costly laboratory investigation, therefore new alternative cost effective testing should be searched. Hence, a gap remains there to invent and validate a new clinical test which should be easy and simple to perform and inexpensive in particular for the developing countries like Pakistan. Currently, one such red blood cell parameter called red blood cell distribution width (RDW) is under rigorous research in medical literature.[7-9] RDW represents the coefficient of RBC volume distribution curve. It is an index of RBC cell volume heterogeneity

called the anisocytosis. A low hemoglobin (Hb) concentration with a high degree of anisocytosis as detected by RDW may be a valuable diagnostic tool in detecting the iron deficiency anemia.[8] One of the earliest blood manifestations of IDA is the rise in the RDW value,[9] and it is highly cost effective tool to exploit it for the early diagnosis of IDA.[9-11] RDW is generated by auto-hematology analyzer as part of routine complete blood count.[12] The present prospective study evaluated the discriminative and predictive value of RDW as a alternative test for detecting iron deficiency anemia among children.

MATERIAL AND METHODS

The materials for the present cross sectional study were collected from the Department of Paediatrics, Layari General Hospital Shaheed Mohtrama Benazir Bhutto Medical College from December 2015 to March 2016. Prior Institutional ethical approval was taken for this study as per "declaration of Helsinki" for conducting the human research.

A sample of 100 cases was selected through non-probability (purposive) technique. Inclusion criteria were age 3-10 years, diagnosis of iron deficiency anemia, volunteers and both genders. Age <3 years, malabsorption syndrome and other major systemic diseases were excluded. 5 ml of blood was collected by Venepuncture using disposable syringe (BD, USA). Attendants of children were communicated in friendly environment for a detailed general interview regarding the purpose of research. Legal heirs of children were informed about the benefit and loss to the participants. They were informed that the research does not cause any type of harm to the children. The study needs consent of participants, clinical history and blood samples. They were informed that the information obtained will benefit the community in the future. Consent proforma was signed by volunteers. Clinical history of patients was taken in elaborated way. After this, 5 ml venous blood was collected, 3 ml was shifted to EDTA containing vacutainers and remaining was processed and centrifuged (3000 rpm for 15 minutes) to separate sera. Complete blood counts (Sysmex hematoanalyzer) and iron profile were estimated (Elisa method). Sera transferred into sterilized Eppendorf plastic tubes and stored at −20°C. Serum ferritin was estimated by Fortress Elisa assay kit. Anemia was defined as hemoglobin ≤10 g/dL.[13] Patient data and laboratory investigations were noted in pre-structured proforma. Confidentiality of data was maintained by keeping the proforma and laboratory investigations in lockers. Only the concerned researchers were authorized to access and observe the patients data.

Raw was typed on Microsoft Excel sheet, and copied to the SPSS (v 22.0 IBM, Incorporation, USA) sheet for statistical analysis. Student`s t-test and Pearson`s chi square tests were used for the analysis of continuous and categorical research variables of the study. Logistic regression analysis was run to analyze the RDW by Enter method for predicting iron deficiency. ROC curve and area under curve (AUC) were obtained by plotting sensitivity vs. 1-specificity. Sensitivity and specificity were calculated at an optimal cut-off value in our population. Data was analyzed at 95% α- level of significance ($P \leq 0.05$).

RESULT

Means± SD age of male and female children was noted as 8.45±1.75 and 7.97±1.90 years respectively (P=0.19) (Table-I). Gender distribution is shown in Table-II. Hemoglobin, hematocrit, RBC counts, MCV, and MCHC were reduced in both groups. Hemoglobin showed significant difference (P=0.02). Serum Iron, TIBC and Ferritin were noted as 63.49±32.94 and 76.06±40.38 µg/dl (P=0.21), 468.7±142.2 and 445.5±135.2 µg/dl (P=0.40), & 36.2±14.12 and 43.2±13.5 ng/dl (P=0.43) respectively. Receiver operating characteristic curve (ROC) showed AUC of 0.786 (78.6%) (Figure-1). Sensitivity and specificity was noted as 78% and 56% respectively (0.0011) (Table-III).

DISCUSSION

The present is the first report on the predictive value of RDW in IDA in the children reporting at our tertiary care hospital. Clinically, the iron profile is costly laboratory investigation.[14]

	Male	Female	P-value
Age	8.45±1.75	7.97±1.90	0.19
Hemoglobin (g/dl)	7.80±2.06	8.68±1.80	0.02
Hct (%)	32.17±4.43	33.9±3.68	0.03
RBC (/μL)	3.10±0.59	3.18±0.57	0.51
MCV (fl)	64.83±15.26	68.80±17.97	0.23
MCH (pg/dl)	24.20±4.67	24.27±4.85	0.93
RDW (%)	17.15±4.03	16.27±2.87	0.33
Fe (μg/dl)	63.49±32.94	76.06±40.38	0.21
TIBC(μg/dl)	468.7±142.2	445.5±135.2	0.40
Ferritin (ng/dl)	36.2±14.12	43.2±13.5	0.43

Table-I. Age distribution of study subjects (n=100)

Gender	No.	%	P-value
Male	53	53	0.056
Female	47	47	

Table-II. Gender distribution of study subjects

Test result variable(s): Predicted probability				
Area	Std. Error[a]	P-value[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.786	0.001	0.0011	0.812	0.754
a. Under the non-parametric assumption				
b. Null hypothesis: true area = 0.5				

Table-III. ROC area under the curve (AUC) showing the RDW predictive value for the iron deficiency anemia

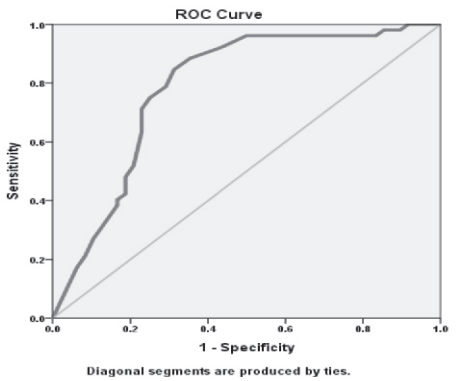


Figure-1. Receiver operative characteristic curve showing predictive value of RDW for the Iron deficiency anemia

It needs instruments and trained expert laboratory persons. Some of these tests have also confounding variables which adversely affect their estimation, for example serum ferritin is altered by inflammatory phenomena making its clinical interpretation unreliable.[15] Another drawback of iron profile studies is their poor sensitivity and specificity, because of various ongoing inflammatory disease processes. The present research has a step ahead to validate the diagnostic utility and predictive value of RDW for the iron deficiency anemia.[14-16] The present study analyzed 100 diagnosed cases of IDA for analyzing the diagnostic utility of RDW. The means± SD age of male and female children was noted as 8.45±1.75 and 7.97±1.90 years respectively. The findings are in agreement with previous studies.[17,18] A recent study[19] reported similar age findings in male population. Of 100 study subjects, 53% were male and 47% were female, this is in accordance to recent study.[19] Sharma et al[19] has reported more female compared to male i.e. 62% versus 38%. The gender distribution of present study shows equal distribution of both male and female (P=0.056) and this excludes gender bias. Hemoglobin, hematocrit, RBC counts, MCV, and MCHC were reduced in both groups. Hemoglobin showed significant difference (P=0.02). The findings are in agreement with previous studies.[20,21] Serum Iron, TIBC and Ferritin were noted as 63.49±32.94 and 76.06±40.38 μg/dl (P=0.21), 468.7±142.2 and 445.5±135.2 μg/dl (P=0.40), & 36.2±14.12 and 43.2±13.5 ng/dl (P=0.43) respectively. The findings suggest the severity of nutritional iron deficiency anemia and are in keeping with studies

from developing countries.[19-21] With the advent of automated analyzers, red blood cell (RBC) indices have emerged as low cost parameters for early detection of anemias.[22] RDW has emerged as a better RBC index to differentiate iron deficiency anemia from other causes of microcytosis especially thalassemia trait. RDW is the first RBC index to become abnormal during the development of IDA.[23] Logistic regression analysis of RDW for prediction of IDA showed ROC- AUC of 0.786 (78.6%). Sensitivity and specificity was noted as 78% and 56% respectively (0.0011). Sharma 2016 et al[19] and Aulakh et al[24] reported the RDW specificity of 57.14% and 53.40% respectively. Specificity of 56% of present study is in keeping with above studies. Similarly, the RDW sensitivity of 78% is also in keeping with previous studies.[19,24,25] A previous study by Nesa et al[26] reported RDW specificity of 17.50% that is contrary to present and previous studies.[1,24,25] Raised RDW in iron deficiency anemia is also reported by Suri et a[27] and Choudhary et al[28] who reported a sensitivity and specificity of 90% and 51%, 94% and 59% and 91.30%and 43.47% respectively. Our study is in accord with a number of studies which suggest that increase in RDW is sensitive for iron deficiency. However, frequent occurrence of increased RDW in thalassemia and other conditions limits it specificity in the diagnosis of microcytic anemias.

CONCULSION

The present study reports severe iron deficiency anemia in children. Red blood cell distribution width showed high sensivity in predicting iron deficiency anemia, hence it may be used a simple, easy and inexpensive parameter. RDW may be used as a sensitive screening test for iron deficiency anemia. However, further large scale studies are recommended to establish the cut off values and interpretation for our population.

REFERENCES

1. Saeed T, Zahoor ul Haq M, Kanwal A, Zulfiqar R, Raja TM. **Association of iron deficiency anaemia and febrile seizures in children.** J Rawalpindi Med Coll; 2013; 17(2):175-177.

2. Malik SA, Malik MAS, Malik SA. **Iron deficiency anemia in Bahawalpur Region of Pakistan: A descriptive study.** Pak J Med Health Sci 2016; 10 (1):89-91.

3. Lal V, Kumar H, Hanif S, Parkash O, Arwani S. **Association of iron deficiency anemia in children with febrile convulsions.** Pak J Neurol Sci 2016; 11(3):1-8.

4. Kashif I, Javeid I. **Effect of Iron deficiency anemia on intellectual performance in school children.** Trop J Pharmaceut Res 2015; 10.4314/tjpr.v14i2.14.

5. de Carvalho FS, de Medeiros IA, Antunes H. **Prevalence of iron deficiency anemia and iron deficiency in a pediatric population with inflammatory bowel disease.** Scandinavian J Gastroenterol 2016; 52 (10): 1099-1103.

6. Krishnaswamy S, Bhattarai D, Bharti B, Bhatia P, Das R, Bansal D. **Iron deficiency and iron deficiency anemia in 3–5 months-old, Breastfed Healthy Infants.** Indian J Pediatr July 2017; 84(7):505–508.

7. Finkelstein JL, O'Brien KO, Abrams SA, Zavaleta N. **Infant iron status affects iron absorption in Peruvian breastfed infants at 2 and 5 mo of age.** Am J Clin Nutr 2013; 98:1475-84.

8. Jadhav MN, Agarwal SA, Kadgi NV, Khedkar SS. **Utility of automated RBC parameters in evaluation of anemia.** Int J Healthcare Biomed Res 2015; 3(3):170-181.

9. Gupta SK, Bansal D, Malhi P, Das R. **Developmental profile in children with iron deficiency anemia and its changes after therapeutic iron supplementation.** Indian J Pediatr 2010; 77:375–9.

10. Agarwal R, Virmani D, Jaipal M. **Investigators of LBW micronutrient study group. Iron stores in low and normal birth weight infants at birth and in early infancy.** Indian J Pediatr 2014; 81:279–82.
11. Saroja CN, Alapaty S, Jeyan M. **Efficacy of red cell distribution width (RDW) as a screening test for diagnosing children with iron deficiency anaemia.** Sch J App Med Sci 2014; 2(6):3412-5.

12. Chaudhary M, Sharma D, Shekhawat DS, Dabi D. **Significance of red cell distribution width in the diagnosis of iron deficiency anemia: an observational study from India.** J Pediatr Neonatal Care 2015; 2(6):00102.

13. Guyatt GH, Oxman AD, Ali M, Willan A, McIlroy W, Patterson C. **Laboratory diagnosis of iron deficiency anemia.** J Gen Inter Med 192; 7 (2): 145-153.

14. Koplan KE, Senese MD, Orav EJ, Sequist TD. **The impact of cost displays on primary care physician laboratory test ordering.** J Gen Int Med 2014; 29 (5):

708-714.

15. Vanarsa K, Ye Y, Han J, Xie C, Mohan C, Wu T. **Inflammation associated anemia and ferritin as disease markers in SLE.** Arthritis Research & Therapy 2012 14:R182.

16. Sazawal S, Dhingra U, Dhingra P, Dutta A, Shabir H, Menon VP, Black RE. **Efficiency of red cell distribution width in identification of children aged 1-3 years with iron deficiency anemia against traditional hematological markers.** BMC Pediatrics 2014 14:8.

17. Agarwal R, Virmani D, Jaipal M, et al; **Investigators of LBW micronutrient study group. Iron stores in low and normal birth weight infants at birth and in early infancy.** Indian J Pediatr 2014; 81:279–82.

18. Zhang Y, Zhang W, Wang S, Xie J, Chen X, Xu Y, Mao P: **Detection of erythrocytes in patients with iron deficiency anemia using atomic force microscopy.** Scanning 2012; 34(4):215–220.

19. Sharma A, Sharma M, Sharma V. **Evaluation of red cell distribution width in the diagnosis of iron deficiency anemia.** Int J Res Med Sci 2016; 4:3733-6.

20. Saroja CN, Alapaty S, Jeyan M. **Efficacy of red cell distribution width (RDW) as a screening test for diagnosing children with iron deficiency anaemia.** Sch J App Med Sci 2014; 2(6):3412-5.

21. Chaudhary M, Sharma D, Shekhawat DS, Dabi D. **Significance of red cell distribution width in the diagnosis of iron deficiency anemia: an observational study from India.** J Pediatr Neonatal Care 2015; 2(6):00102.

22. Jadhav MN, Agarwal SA, Kadgi NV, Khedkar SS. **Utility of automated RBC parameters in evaluation of anemia.** Int J Healthcare Biomed Res 2015; 3(3):170-181.

23. Khatri A, Kavatkar A, Puranik S. **Evaluation of red cell distribution width (RDW) and other indices in microcytic anemias.** Medical J Western India 2013; 41(1):76-80.

24. Pandya AN, Agarwal M, Dave D. **Red cell distribution width as a screening tool in classifying microcytic hypochromic anemias.** J Evolution Med Dent Sci 2014; 3(23):6559-65.

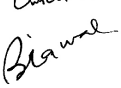
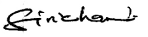
25. Aulakh R, Sohi I, Singh T, Kakkar N. **Red cell distribution width (RDW) in the diagnosis of iron deficiency with microcytic hypochromic anemia.** Indian J Pediatr 2009; 76 (3):265-7.

26. Nesa A, Tayab A, Sultana T, Khondker L, Rahman Q, Karim A, et al. **RDWI is better discriminant than RDW in differentiation of iron deficiency anemia and beta thalassaemia trait.** Bangladesh J Child Health 2009; 33(3):100-3.

27. Suri V, Solanki S, Ahi RS, Maheshwari A, Gupta A, Roychoudhury AK. **RDW- A discriminative index in differentiation of microcytic hypochromic anemia in children below five years.** Int`l J Sci Res 2017; 6 (6):73-76.

28. Chaudhary M, Sharma D, Shekhawat DS, Dabi D. **Significance of red cell distribution width in the diagnosis of iron deficiency anemia: an observational study from India.** J Pediatr Neonatal Care 2015; 2(6):00102.

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Nathumal Maheshwari	Literature review, Materials handling, compilation of results, statistical analysis, Manuscript write up, Proof reading, Correspondence.	
2	Omperkash Khemani	Concept Mainterials handling, Interpretation lab investigations, Manuscript write up, Proof reading.	
3	Bilawal Hingorjo	Concept, Materials handling, Collection of materials, compilation of resutls, statistical analysis,manuscript write up.	
4	Mehmood Shaikh	Literature review, Concept, Materials handling, Interpretation lab investigations, Manuscript write up, Proof reading.	
5	Sirichand	Concept materials handling, Interpretation lab investigations, Manuscript write up Proof reading.	
6	Anjum Rehman	Concept, materials handling, collection of materials compilation of resutls, statistical analysis, manuscript.