Received: 6 January, 2025 Accepted: 22 January, 2025 Published: 27 January, 2025 ISSN: 3007-1208 | 3007-1216 Volume 3, Issue 1, 2025

-----

### DIAGNOSTIC ACCURACY OF HEMATOLOGICAL INDICES FOR DIFFERENTIATION OF BETA THALASSEMIA TRAIT AND IRON DEFICIENCY ANEMIA – A CROSS SECTIONAL STUDY

Dr Hajra Javed<sup>1</sup>, Dr Sughra Wahid<sup>2</sup>, Dr Amber Latif<sup>3</sup>, Dr Maliha Akhtar Qureshi<sup>4</sup>, Dr Irshad Hussain<sup>5</sup>, Dr Anam Zafar<sup>6</sup>

1,2,3,4,5,6 KRL Hospital, Rawalpindi

#### **DOI:** https://doi.org/10.5281/zenodo.14750371

#### ABSTRACT

**Objective:** To check diagnostic accuracy of reliable hematological indices for differentiation between beta thalassemia trait and iron deficiency anemia in pediatric patients

**Methodology:** This Cross-sectional study was conducted at Department of Pediatric, KRL Hospital, Islamabad Pakistan during July 2024 to December 2024. Children of age 2-12 years with microcytic anemia (Hb < 12.0 md/dL and low MCV < 74 fL) presenting to Pediatric OPD or admitted in pediatric wards were included. Blood complete picture for hemoglobin, MCV, RBC count, serum ferritin levels and Hb electrophoresis advised in all children. Diagnostic accuracy metrics of hematological indices including Mentzer index (MI), RBC count, RDW index, Srivastav Index (SI), Sirdah index, Ehsani Index (EI), England and Fraser index (EFI) and Ricerca Index (RI) were checked for detecting and differentiating type of anemia.

**Results:** From 377 children with microcytic anemia, 240 (63.7%) were confirmed to have iron deficiency anemia (IDA) while 137 (36.3%) were confirmed as having Beta Thalassemia trait (BTT). The mean Hb of IDA and BTT children were  $9.23 \pm 0.83$  and  $9.62 \pm 0.83$  respectively (p=0.652), whereas MCV was  $63.08 \pm 4.37$  and  $58.23 \pm 5.20$  fL, respectively (p=0.011). Statistically significant difference was noted in RBC count and serum ferritin levels between IDA and BTT diagnosed children (p<0.005). The sensitivity ranged from 68.75% (Srivastav Index) to 95.83% (Ricerca Index), while specificity varied between 43.79% (Ricerca Index) and 76.64% (Ehsani and Sirdah Indices) with the Ehsani Index demonstrating the highest accuracy (79.56%).

**Conclusion:** Ricerca Index had highest sensitivity 95.83% whereas Ehsani and Sirdah Indices had highest specificity of 76.64%.

**Keywords:** Hb electrophoresis, Iron deficiency Anemia, Mentzer Index, Ricerca Index, Thalassemia

#### INTRODUCTION

Iron deficiency anemia (IDA) and thalassemia are common hematological disorders of red blood cells in pediatric age groups and remains a global public health concern for developing countries.<sup>1</sup> As normal human hemoglobin (Hb) consists of two alpha and two beta hemoglobin chains, defective synthesis of one or more globin chains of hemoglobin results in Thalassemia, which is an inherited disorder of red blood cells

(RBCs).<sup>2</sup> It includes alpha thalassemia due to defect in one or more alpha chains and beta thalassemia due to defective synthesis of one or more beta globin gene. B-thalassemia trait (BTT) or thalassemia carrier is absence or reduction of one beta chain leading to mild anemia with no or minimal symptoms.<sup>3</sup> According to published data, the overall prevalence of beta thalassemia trait in Pakistan is 5.0-7.0% with more than 10 million carriers across the country.<sup>4</sup> Thalassemia is suggested by the presence of microcytic anemia with anisopoikilocytosis with nucleated RBCs on peripheral film and confirmed by reduction or absence of hemoglobin A (HbA) and increased hemoglobin A<sub>2</sub> (HbA<sub>2</sub>) on electrophoresis.<sup>5</sup>

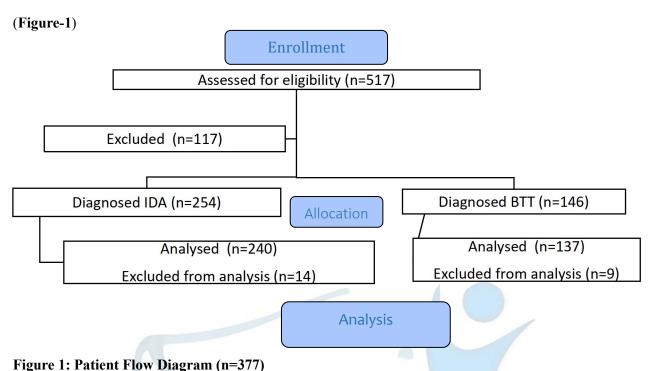
Iron is one of the essential components for hemoglobin production and deficiency of iron due to dietary deficiency, absorption impairment or increase body demand leads to anemia which is microcytic like thalassemia.<sup>6</sup> Iron deficiency anemia (IDA) is most common hematological disorder with overall prevalence of 39.8% in developed countries and up-to 48.1-70% in developing countries like Pakistan in pediatric age group.<sup>7</sup> According to National Nutritional Survey of Pakistan (2018-2019), the prevalence of IDA in pediatric age group was 28.9%.<sup>8</sup>

BTT and IDA are similar in clinical presentation and morphology but differ in terms of management and prognosis.<sup>9</sup> Blood indices including MCV, MCHC, Red blood cell count (RBC count), Red cell distribution width (RDW) index, serum ferritin levels, total iron binding capacity (TIBC), Mentzer index (MI), Srivastav Index (SI), Ehsani Index (EI), England and Fraser index (EFI) and Hb electrophoresis are among the most common hematological indices to evaluate and differentiate between IDA and BTT.<sup>10</sup>

Beta thalassemia trait and IDA being common but different disorders in terms of treatment, therefore, screening and differentiation of these two is deemed important, as these require long-term management and monitoring. To the author's knowledge, there are limited data available on local population in differentiating IDA and BTT. Hence, the rationale of this study was to observe different hematological indices and ascertain most reliable indices to differentiate accurately between IDA and BTT to further plan care and management strategies by doctors and parents both.

#### Methodology

It was a Cross-Sectional Study, done in the Department of Pediatrics, KRL Hospital, Rawalpindi, Pakistan, from july 2024 to Dec 2024 over period of 6 months following approval of the Ethical committee of KRL Hospital Islamabad. The sample size 377 was calculated using the WHO sample size calculator taking a confidence interval of 95%, a margin of error of 5%, and a reported prevalence of microcytic anemia in developing countries like Pakistan of 57% in a study by Lubna et al in Zia-u-din Hospital Karachi.<sup>11</sup>Consecutive non-probability sampling technique was used. Total 517 children with anemia reported to pediatric OPD and ward during study period and 400 children fulfilling inclusion criteria were included in study after scrutiny. Total 377 patients were included in final analysis as during course of admission and data collection, 23 patients were either needed iron therapy or diagnosed to have bleeding disorder were excluded.



#### 5

#### Inclusion Criteria:

Patients of age group 2-12 years with anemia (Hb < 11.0 md/dL) on complete blood picture with low MCV presenting to Pediatric OPD or admitted in pediatric wards were included.

#### Exclusion Criteria:

All patients of age below 2 or above 12 years, macrocytic anemia with high MCV and MCH, bleeding disorder, admitted due to surgical cause or had recent surgical intervention, patients on oral or IV iron replacements, or history of recent blood transfusion were excluded. Patients found to have any other form of Hemoglobin defect such as alpha thalassemia, carrier state for Hemoglobin C disease, Sickle cell disease or Hemoglobin SC on electrophoresis were excluded from the study.

All patients were advised blood complete picture including peripheral blood film and Hb electrophoresis. Hematological indices including Mentzer index (MI), RBC count, RDW index, Srivastav Index (SI), Sirdah index, Ehsani Index (EI), England and Fraser index (EFI) and Ricerca Index (RI), Hb electrophoresis for HbA<sub>2</sub> and HbF were noted for all patients. Results of all indices were compared in reference to baseline cut off values (**Table-I**) in all patients to differentiate BTT from IDA reliable on hematological index.<sup>12</sup>

#### **Hematological Indices** BTT **IDA** RBC Count (in Millions) > 5.5 $\leq 5.5$ RDW Index: MCV x RDW/RBC < 220 > 220 Serum Ferritin (ng/mL) > 15 ≤15 Mentzer Index (MI): MCV/RBC < 13 > 13 Srivastav Index (SI): MCH/RBC < 3.8 > 3.8 Ricerca Index (RI): RDW/RBC >4.4 $\leq 4.4$ Sirdah Index MCV-RBC-(3 x Hb) <27 >27

#### Table-I Different Hematological Indices to differentiate IDA and BTT

Ehsani Index: MCV – (10 x RBC)	≤17	> 17
England and Fraser Index (EFI):	$\leq 0$	> 0
$MCV - (5 \times Hb) - RBC - 3.4$		

Data were entered in Statistical Package for Social Sciences version 25 (SPSS v25) for analysis. Variables including age, gender, Hb levels, MCV, RBC count, RDW index, serum ferritin levels, Mentzer index (MI), Srivastav Index (SI), Ricerca Index (RI), Ehsani Index (EI), England and Fraser index (EFI) and Hb electrophoresis for HbA<sub>2</sub> and HbF were analyzed. Categorical variables were presented as frequencies and percentages whereas continuous variables as mean  $\pm$  SD. The sensitivity and specificity of hematological indices to reliably differentiate between BTT and IDA was also calculated. The statistical significance was checked using independent samples t-test and p-value of  $\leq 0.05$  was taken as statistically significant.

#### **Results:**

Total 377 children with microcytic anemia were included in among which based on the gold standard tests i.e. Serum ferritin and Hb electrophoresis, 240 (63.7%) were confirmed to have iron deficiency anemia (IDA) while 137 (36.3%) were confirmed as having Beta Thalassemia trait (BTT). The mean age of IDA and BTT children was  $5.91 \pm 3.50$  years and  $5.65 \pm 2.32$  years respectively (p=0.402). The mean Hb of IDA and BTT children were noted as  $9.23 \pm 0.83$  g/dL and  $9.62 \pm 0.83$  g/dL respectively (p=0.652), whereas MCV was  $63.08 \pm 4.37$  fL and  $58.23 \pm 5.20$  fL in IDA and BTT children respectively (p=0.011). Statistically significant difference was noted in RBC count and serum ferritin levels between IDA and BTT labelled children (p<0.005) as shown in table-II.

Parameter	Iron Deficiency	Beta Thalassemia	p-value
	Anemia (IDA)	Trait (BTT)	
	(n=240)	(n=137)	
Age (mean years $\pm$ SD)	$5.91 \pm 3.50$	$5.65 \pm 2.32$	0.402
<b>Hemoglobin</b> (mean $g/dL \pm SD$ )	$9.23\pm0.83$	$9.62 \pm 0.83$	0.652
MCV (mean $fL \pm SD$ )	$63.08 \pm 4.37$	$58.23 \pm 5.20$	0.011
<b>RBC Count</b> (mean x $10^6/L \pm SD$ )	$4.33 \pm 0.55$	$6.01 \pm 0.70$	< 0.005
<b>Ferritin</b> (mean $ng/mL \pm SD$ )	$28.91 \pm 10.70$	$101.95 \pm 26.30$	< 0.005

#### Table-II: Basic Parameters of Studied Patients (n=377)

Eight hematological indices were calculated for all patients to check diagnostic accuracy metrics for differentiating IDA and BTT. The frequencies of true positive and negative patients in comparison to gold standard has been summarized in table-III.

Table-III: Comparison of True Positive and Negative (TP & TN) and False Positive and Negative (FP
& FN) for each Index (n=377)

Hematological In	ndex	ТР	FN	TN	FP	p-value
Mentzer Index	IDA	184 (76.7%)	56 (23.3%)	99 (72.3%)	38 (27.7%)	0.064
	BTT	99 (72.3%)	38 (27.7%)	184 (76.7%)	56 (23.3%)	
<b>RDW Index</b>	IDA	177 (73.8%)	63 (26.3%)	103 (75.2%)	34 (24.8%)	0.539
	BTT	103 (75.2%)	34 (24.8%)	177 (73.8%)	63 (26.3%)	
<b>RBC Count</b>	IDA	181 (75.4%)	59 (24.6%)	97 (70.8%)	40 (29.2%)	0.058
	BTT	97 (70.8%)	40 (29.2%)	181 (75.4%)	59 (24.6%)	
Srivastav Index	IDA	165 (68.8%)	75 (31.3%)	93 (67.9%)	44 (32.1%)	0.730
	BTT	93 (67.9%)	44 (32.1%)	165 (68.8%)	75 (31.3%)	
Ehsani Index	IDA	194 (80.8%)	46 (19.2%)	105 (76.6%)	32 (23.4%)	0.059
	BTT	105 (76.6%)	32 (23.4%)	194 (80.8%)	46 (19.2%)	

England &	IDA	179 (74.6%)	61 (25.4%)	86 (62.8%)	51 (37.2%)	< 0.005
Fraser Index	BTT	86 (62.8%)	51 (37.2%)	179 (74.6%)	61 (25.4%)	
Sirdah Index	IDA	188 (78.3%)	52 (21.7%)	105 (76.6%)	32 (23.4%)	0.453
	BTT	105 (76.6%)	32 (23.4%)	188 (78.3%)	52 (21.7%)	
<b>Ricerca Index</b>	IDA	230 (95.8%)	10 (4.2%)	60 (56.2%)	77 (43.8%)	< 0.005
	BTT	60 (56.2%)	77 (43.8%)	230 (95.8%)	10 (4.2%)	

The ability of different indices to identify IDA or BTT correctly were evaluated. The sensitivity ranged from 68.75% (Srivastav Index) to 95.83% (Ricerca Index), while specificity varied between 43.79% (Ricerca Index) and 76.64% (Ehsani and Sirdah Indices). The Ehsani Index demonstrated the highest accuracy (79.56%), followed closely by the Sirdah Index (78.14%) and the Ricerca Index (78.05%). The diagnostic accuracy metrics of different indices have been summarized in the Table-IV.

Table-IV Diagnostic Accuracy Metrics (%) of different Hematological Indices to differentiate IDA and BTT (n=377)

Hematological Indices	Sensitivity	Specificity	PPV	PV	Accuracy
	(%age)	(%age)	(%age)	6age)	(%age)
Mentzer Index (MI)	76.66	72.26	82.88	.89	76.64
RDW Index (RDWI)	73.75	75.18	83.88	.06	75.04
<b>RBC Count Index</b>	75.41	70.80	81.88	.18	74.00
Srivastav Index (SI)	68.75	67.88	78.94	.37	69.86
Ehsani Index (EI)	80.83	76.64	85.85	.51	79.56
<b>England and Fraser Index</b> (EFI)	74.58	62.77	77.83	.50	72.24
Sirdah Index	78.33	76.64	85.46 .90	78.14	
Ricerca Index (RI)	95.83	43.79	74.91 .7	78.05	

#### Discussion

Iron deficiency anemia (IDA) and beta thalassemia trait (BTT) are two most commonly clinical presentation of microcytic anemia and differentiation between these two are significant because both are different in terms of etiology, evaluation, medical as well as dietary management, and genetic counselling. The hematological indices have diagnostic importance for differentiating IDA from BTT, hence diagnostic performance of eight hematological indices for such purpose was assessed in this study. It was observed that the sensitivity ranged from 68.75% (Srivastav Index) to 95.83% (Ricerca Index), while specificity varied between 43.79% (Ricerca Index) and 76.64% (Ehsani and Sirdah Indices). The Ehsani Index demonstrated the highest accuracy (79.56%), followed closely by the Ricerca Index (78.05%) and the Sirdah Index (78.14%). In a similar study by Vehapoglu et al it was observed that England and Fraser index showed highest specificity of 85.3% followed by Mentzer Index 82.3%.<sup>13</sup>

In our study, Mentzer index correctly diagnosed IDA with sensitivity of 76.7% and specificity of 72.3%. In a study by Abbas et al demonstrated that Mentzer index correctly diagnosed 90.24% children as having IDA and 9.75% had BTT. Also Ehsani index diagnosed 95.1% children with IDA and 4.9% with BTT.<sup>14</sup> In our study, RDWI index had sensitivity and specificity of 75.2% and 72.3% respectively. Similarly in a study by Jameel et al, RDWI was reported as a useful index for IDA and BTT differentiation with sensitivity and specificity of RDWI 89% and 94% respectively.<sup>15</sup>

The Ricerca Index achieved the highest NPV (85.71%), and the Ehsani Index exhibited the highest PPV (85.85%), highlighting their potential clinical utility in identifying BTT and ruling out IDA, respectively. Bhargava et al concluded three best indices for IDA and BTT differentiation including Ricerca index, Green and King index followed by Mentzer index. He also explained that Mentzer index is considered to be a reliable index however Ricerca index has better diagnostic accuracy for said purpose.<sup>16</sup> Similar findings were noted in a study by Dunzenli et al in which RDWI and RBC count showed highest sensitivity and specificity

for differentiation between IDA and BTT followed by England and Fraser Index, Sirdah index and Srivastav index.17

Hoffman et al demonstrated the diagnostic accuracy of hematological indices with Index26 having having highest specificity (92.9%) followed by Ehsani index (89.1%), England and Fraser index (86.6%), Mentzer index (86.2%) and Ricerca index (82.8%).<sup>18</sup> However, in our study Ehsani index and Sirdah index found to have highest specificity of 76.6%. Similar results were found in another study by Nerune et al in which it was concluded that RDWI had highest sensitivity of 90% with 77 % specificity followed by England and Fraser index that was noted to have sensitivity and specificity of 85% and 80% respectively.<sup>19</sup> Mukhtar et al concluded England and Fraser index being best discriminative mathematical index for IDA versus BTT with Youden index of 0.91 followed by Ricerca index and RDW index.<sup>20</sup>

Noulsri et al explained in his study that Shine and Lal index being the best hematological index to differentiate between IDA and BTT with sensitivity and specificity of 86.2% and 83.2% respectively, followed by Srivastava index having sensitivity of 80.6% and specificity of 74.1%. He also observed that Ehsani index had 74.6% sensitivity and 80.6% specificity and Mentzer index being lowest among these four indices with sensitivity of 73.13%.<sup>21</sup> The findings of our study were in accordance with other published studies and data, which actually underscore the variable performance of hematological indices and the importance of selecting the most appropriate metric for clinical decision-making.

#### Conclusion

It was observed that no hematological index is 100% accurate to differentiate between IDA and BTT but Ricerca Index had highest sensitivity 95.83% whereas Ehsani and Sirdah Indices had highest specificity of 76.64%. In addition, Ehsani Index demonstrated the highest accuracy (79.56%) for correctly differentiating between IDA and BTT. Gold standard laboratory investigations are necessary to diagnosis and differentiate between IDA, BTT and other types of anemia in association with hematological indices.

#### Limitations

Conducting the study at a single center and a limited sample size are amongst the major limitations of the study. The effects of other causes of microcytic anemia were excluded from current study. The results therefore cannot be generalized to other demographics.

lhe

#### Acknowledgement

Research of Medical Science Review Authors extend their sincere appreciation to all the colleagues for assistance in data collection and analysis.

We also acknowledged the help of consultants, colleague registrars, nursing staff and laboratory staff to help in data collection, patient care and authentic laboratory tests.

**Conflict of Interest** None

Funding Nil

#### **Author's Contribution:**

The authors confirm the contribution to the paper as follows:

Dr Hajra Javed : Concept and study design, Data Acquisition, Manuscript writing, Analysis & interpretation. Dr Sughra Wahid: Concept and study design, Analysis & interpretation, critical review & final approval. Dr Amber Latif: Data Acquisition, Manuscript writing, critical review & final approval.

Dr Maliha Akhtar: Concept and study design, Analysis & interpretation, critical review & final approval. Dr Irshad Hussain: Concept and study design, Analysis & interpretation, critical review & final approval Dr Anam Zafar: Data Acquisition, Manuscript writing, Analysis & interpretation, critical review.

#### REFERENCES

- 1.Habib A, Kureishy S, Soofi S, Hussain I, Rizvi A, Ahmed I, et al. Prevalence and Risk Factors for Iron Deficiency Anemia among Children under Five and Women of Reproductive Age in Pakistan: Findings from the National Nutrition Survey 2018. Nutrients. 2023;15(15):3361. <u>https://doi.org/10.3390/nu15153361.</u>
- 2.E Y, Vasudevan S, Sonti S, Kannan K, Srinivasan C. Exploring the Clinical and Hematological Characteristics of Beta-Thalassemia Trait: A Comprehensive Analysis in a Tertiary Care Hospital Setting. Mav [cited Cureus. 2024 26 2024 Sep 117: Available from: https://www.cureus.com/articles/244345-exploring-the-clinical-and-hematological-characteristicsof-beta-thalassemia-trait-a-comprehensive-analysis-in-a-tertiary-care-hospital-setting. https://doi.org/10.7759/cureus.61093
- 3.Ali S, Mumtaz S, Shakir HA, Khan M, Tahir HM, Mumtaz S, et al. Current status of beta-thalassemia and its treatment strategies. Molec Gen & amp; Gen Med. 2021;9(12):e1788. https://doi.org/10.1002/mgg3.1788.
- 4.Khaliq S. Thalassemia in Pakistan. Hemoglobin. 2022;46(1):12–4. https://doi.org/10.1080/03630269.2022.2059670
- 5.Munkongdee T, Chen P, Winichagoon P, Fucharoen S, Paiboonsukwong K. Update in Laboratory Diagnosis of Thalassemia. Front Mol Biosci. 2020;7:74. <u>https://doi.org/10.3389/fmolb.2020.00074.</u>
- 6.Kumar A, Sharma E, Marley A, Samaan MA, Brookes MJ. Iron deficiency anaemia: pathophysiology, assessment, practical management. BMJ Open Gastroenterol. 2022;9(1):e000759. https://doi.org/10.3389/fmolb.2020.00074
- 7.Moscheo C, Licciardello M, Samperi P, La Spina M, Di Cataldo A, Russo G. New Insights into Iron Deficiency Anemia in Children: A Practical Review. Metabolites. 2022;12(4):289. <u>https://doi.org/10.3390/metabo12040289</u>
- 8.Sherali A, Ahad A, Tikmani SS, Sohail S. Screening of Iron Deficiency Anemia in Children Using Mentzer Index in Pakistan: A Cross Sectional Study. Global Pediatric Health. 2023;10:2333794X2211309. <u>https://doi.org/10.1177/2333794X221130986</u>
- 9.Jahangiri M, Rahim F, Malehi AS. Diagnostic performance of hematological discrimination indices to discriminate between βeta thalassemia trait and iron deficiency anemia and using cluster analysis: Introducing two new indices tested in Iranian population. Sci Rep. 2019;9(1):18610. <u>https://doi.org/10.1038/s41598-019-54575-3</u>
- 10.Sun A, Chang JYF, Jin YT, Chiang CP. Differential diagnosis between iron deficiency anemia and thalassemia trait-induced anemia. Journal of Dental Sciences. 2023;18(4):1963–4. https://doi.org/10.1016/j.jds.2023.07.036
- 11.Lubna et al. Anemia among Hospitalized Children A Study Based on Occurrence, Morphology and Associated Factors. PJMD [Internet]. 2021 Jul 31 [cited 2024 Sep 14]; Available from: https://pjmd.zu.edu.pk/volume-10-issue-3/anemia-among-hospitalized-children-a-study-based-on-occurrence-morphology-and-associated-factors/. https://doi.org/10.36283/PJMD10-3/006
- 12.Shah TP, Shrestha A, Agrawal JP, Rimal S, Basnet A. Role of Mentzer Index for Differential Diagnosis of Iron Deficiency Anaemia and Beta Thalassemia Trait. J Nepal Health Res Counc. 2023;21(1):99– 102. <u>https://doi.org/10.33314/jnhrc.v21i1.4479.</u>
- 13.Vehapoglu A, Ozgurhan G, Demir AD, Uzuner S, Nursoy MA, Turkmen S, et al. Hematological Indices for Differential Diagnosis of Beta Thalassemia Trait and Iron Deficiency Anemia. Anemia. 2014;2014:1–7. <u>https://doi.org/10.1155/2014/576738</u>
- 14.Abbas S, Khurrum S, Zamir T. Application of Hematological Indices for the Differential Diagnosis of Beta Thalassemia Trait and Iron Deficiency Anemia. <u>http://hdl.handle.net/123456789/6581</u>
- 15.Jameel TA, Baig M, Ahmed I, Hussain MB, Doghaim Alkhamaly MB. Differentiation of beta thalassemia trait from iron deficiency anemia by hematological indices. Pak J Med Sci [Internet]. 2017[cited

2024 Dec 11];33(3). Available from: http://pjms.com.pk/index.php/pjms/article/view/12098. https://doi.org/10.12669/pjms.333.12098

- 16.Bhargava M, Kumar V, Pandey H, Singh V, Misra V, Gupta P. Role of Hematological Indices as a Screening Tool of Beta Thalassemia Trait in Eastern Uttar Pradesh: An Institutional Study. Indian J Hematol Blood Transfus. 2020;36(4):719–24. <u>https://doi.org/10.1007/s12288-020-01282-z.</u>
- 17.Düzenli Kar Y, Özdemir ZC, Emir B, Bör Ö. Erythrocyte Indices as Differential Diagnostic Biomarkers of Iron Deficiency Anemia and Thalassemia. Journal of Pediatric Hematology/Oncology. 2020;42(3):208–13.<u>https://doi.org/10.1097/MPH.000000000001597</u>
- 18.Hoffmann JJML, Urrechaga E. Verification of 20 Mathematical Formulas for Discriminating Between Iron Deficiency Anemia and Thalassemia Trait in Microcytic Anemia. Laboratory Medicine. 2020;51(6):628–34. <u>https://doi.org/10.1093/labmed/lmaa030</u>
- 19.Nerune SM, Rao H. R. S, Pallavi K, Lavate AP, Das SK, Pagi S. Optimizing the Diagnosis of Microcytic Hypochromic Anemia: A Comparative Evaluation of Erythrocyte and Reticulocyte Parameters. Cureus [Internet]. 2024[cited 2024 Dec 11]; Available from: https://www.cureus.com/articles/294837-optimizing-the-diagnosis-of-microcytic-hypochromicanemia-a-comparative-evaluation-of-erythrocyte-and-reticulocyte-parameters. <u>https://doi.org/10.7759/cureus.69244</u>
- 20.Mukhtar Z, Valente S, Masi L, Lakos G, Papa F. Clinical utility of Abbott Alinity hq extended red blood cell parameters in differentiating β-thalassemia trait and iron deficiency anemia. Int J Lab Hematology. 2021;43(6):1635–43. <u>https://doi.org/10.1111/ijlh.13663</u>
- 21.Noulsri E, Lerdwana S, Palasuwan D, Palasuwan A. Diagnostic Performance of 10 Mathematical Formulae for Identifying Blood Donors with Thalassemia Trait. Laboratory Medicine. 2023;54(6):593–7. <u>https://doi.org/10.1093/labmed/lmad011</u>

