International Journal of Health Sciences and Research
[Indexed, Peer-Reviewed Journal]
Volume 15; Issue: 2; February 2025
Website: www.ijhsr.org
Original Research Article *ISSN: 2249-9571*

Reliability Test of Different Red Blood Cell Discrimination Indices for Screening Iron Deficiency Anemia and Beta Trait Thalassemia in Pediatric Patients 6-59 Months of Age at Gema Santi Hospital, Nusa Penida, June 2023 - May 2024

I Kadek Jaya Santika[1]

[1]General Practitioner, Gema Santi Nusa Penida Hospital, Klungkung, Bali, Indonesia

Corresponding Author: I Kadek Jaya Santika

DOI: https://doi.org/10.52403/ijhsr.20250206

ABSTRACT

Introduction: Screening for iron deficiency anemia and thalassemia beta trait in hypochromic microcytic anemia in health facilities that do not have a complete examination is quite difficult. This study aims to determine the reliability of various indices against the Green and King index including the Mentzer index which is most used for screening. The results of the study can be used to determine whether the currently used indices are reliable enough to be used for patient screening.
Material and Methods: This study used a cross-sectional method with a sample of patients aged 6-59 months who came to the outpatient installation of RSUD Gema Santi Nusa Penida in June 2023 - May 2024. Various red blood cell discrimination indices that have high sensitivity and specificity such as Mentzer index, Mentzer with cut off 10.7 and Sirdah were compared with Green and King index using Cohen kappa ratio.
Results: Based on the results of the analysis, Mentzer index (-0.01) is not reliable, very low reliability on the Sirdah index (0.17) and moderate reliability on the Mentzer index with a cut off 10.7 when compared to the Green and King index.
Conclusions: The results stating that the Mentzer index is not reliable require further research on the sensitivity and specificity of various red blood cell indices including the Mentzer index which is often used in terms of screening to determine the best red blood cell index for use in areas with limited facilities such as the Nusa Penida region.

Keywords: hypochromic microcytic anemia, red blood cell discrimination index, cohen kappa ratio

INTRODUCTION

Anemia is a widespread health problem around the world, including among children. In 2016, approximately 41.7% of children under 5 years of age worldwide suffer from anemia.[1] This is also the case in Indonesia. Based on WHO (World Health Organization) data, the prevalence of anemia in children aged 6-59 months in Indonesia reached 43.9% in 2000 and 38.4% in 2019. A study in Jakarta, Indonesia, found that the prevalence of anemia in children aged 6-59 months in Indonesia in 2020 was 29.4%.[2] The American Academy of

Pediatrics (AAP) and WHO also recommend routine screening for anemia in children aged 12 months.[3]

Anemia is a condition in which hemoglobin levels are lower than normal. Normal hemoglobin levels vary depending on the age and sex of the patient. In children, anemia is defined as a hemoglobin level that is two standard deviations below age-appropriate normal.[3] Anemia can be classified by Wintrobe as microcytic, normocytic, and macrocytic.[4] The type of test that can be used to differentiate is a complete blood count. In adults, microcytic anemia occurs in people with mean corpuscular volume (MCV) levels below 80 fL.[4] These MCV levels are different from children, who have different hematologic normal intervals including MCV.[5]

Microcytic anemia is a disorder of hemoglobin synthesis. Iron deficiency due to deficiency or sequestration, thalassemia, or sideroblastic anemia can cause microcytosis.[4] The most common type of anemia in children is microcytic anemia due to iron deficiency anemia.[3] Iron is important for the neurological development of infants and children. Iron is required for nerve myelination, neurogenesis, and brain cell differentiation, which can affect sensory systems, learning, memory, and behavior. Iron deficiency anemia is associated with cognitive problems that can be treated by supplementation or increasing daily iron intake.[3]

Determining the state of iron deficiency anemia will be difficult in health care facilities that do not have or have limited access to iron profile testing and hemoglobin electrophoresis. There are several red blood cell indices that can be used to estimate whether a patient has iron deficiency anemia or thalassemia beta trait in patients with microcytic hypochromic anemia. These indices include the Mentzer index, Bessman index, Green and King index, Srivastava index, and Sirdah index.[6]

RBC indices generally use MCV, MCH, RBC, RDW and Hb values in various combinations. This is possible because in thalassemia, RBCs tend to be more microcytic and hypochromic than in iron deficiency conditions. This causes MCV and MCH to be lower in thalassemia than in iron deficiency anemia. Anisocytosis is also a consideration in the red blood cell index because in iron deficiency anemia there are different sizes of red blood cells in the peripheral blood. This is less common in thalassemia. This causes the tendency of the RDW to increase more in iron deficiency anemia compared to thalassemia.[6]

The most commonly used red blood cell index is the Mentzer Index.[3] Based on research by Shah et al, the Mentzer Index has a sensitivity of 93.2% and a specificity of 98.3% for detecting the thalassemia beta trait and a sensitivity of 98.3% and a specificity of 93.2% for detecting iron deficiency anemia.[7]

In the hospital where the study was conducted, which is a facility that does not have facilities for iron profile testing and hemoglobin electrophoresis, the Mentzer index is used to identify patients with iron deficiency anemia or thalassemia beta trait. The Mentzer index is also widely used in several regions in Indonesia to screen for these diseases in microcytic anemia because it has a relatively high sensitivity and specificity.[8]

Based on systematic review research examining various red blood cell indices, the types of indices that have high sensitivity and specificity are the Mentzer index (76.82%, 84.87%), Green and King index (79.37%, 82.54%), and Sirdah index (74.94%, 84.29%), with Youden index above 59% (61. 69%, 61.91% and 59.2%).[6]

In Indonesia, there was also a study in 2019 that compared different red blood cell indices with sensitivity and specificity results, namely Mentzer index (66%, 62.5%), Green and King (78.6%, 76.7%), Sirdah (64.2%, 64.1%) and Martos and Carvalho (27.7%, 25%).[9]

Different results were obtained in one of the studies in Indonesia that specifically examined the sensitivity and specificity of the Mentzer index in beta-thalassemia,

obtaining a rather low sensitivity of 36% with a specificity of 81%.[10] In one of the studies in Indonesia by Sari et al. obtained higher sensitivity and specificity on the Mentzer index using a cut-off value of 10.7 (81.6%, 28.6%) compared to 13 (60.5%, 28.6%).[8] Based on these considerations, the Mentzer Index, Mentzer Index with cut off of 10.7, Green and King and Sirdah were used as screening tools in this study by comparing the calculation results of the Green and King Index with other indices.

The purpose of this study is to determine whether various erythrocyte discrimination indices have a high degree of agreement with the index that has the highest sensitivity and specificity. These results can be used as baseline data to determine whether the Mentzer index, which has been used in screening, and other indices have a high level of agreement. The results of the study can also be used as baseline data to conduct further research on which indices have the highest sensitivity and specificity, the results of which can be used specifically in the area where the study was conducted.

MATERIALS & METHODS

This study used a cross-sectional method using patient medical record data for one year, from June 2023 to May 2024 at UPTD. RSUD Gema Santi Nusa Penida. The researcher used a total sampling method with samples that fell into the inclusion criteria, namely all patients aged 6 months to 59 months who came to the hospital outpatient facility and were diagnosed with anemia in the predetermined time frame. Patients underwent a complete blood count using the Sysmex XP-100. Of the total sample, patients with microcytic anemia with hemoglobin below the reference standard [5] were included in this study. The reference standards for hemoglobin and mean corpuscular volume (MCV) in each age group are shown in Table 1. Samples without a complete blood count in their medical records were excluded from the study.

Table 1. Reference standards for hemoglobin and MCV in each age range [5]

Age Range	Gender	Hemoglobin	MCV
6 months - 36 months	Male	10.4-12.5	75.6-83.1
	Female	10.8-12.6	76.7-83.2
36 months - 59 months	Male	11.4-14.3	77.2-89.5
	Female	11.4-14.3	77.2-89.5

Different types of indices were used in this study, namely the Mentzer, Green and King, and Sirdah indices. The score of each index was calculated for each sample using the results of hemoglobin, red blood cell, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and red cell distribution width (RDW) examinations as part of a complete blood count. The formula for each index and the cut-off value for each index are shown in Table 2.

Table 2. Formulas and cut-off values for each index

Index name	Formula	Cut-off value
Mentzer	MCV/RBC	<13
Mentzer with cut off 10.7	MCV/RBC	<10.7
Green and King	MCVxRDW/Hbx100	<65
Sirdah	MCV-RBC-(3xHb)	<27

The calculation results of each index were then classified into iron deficiency anemia and thalassemia beta trait according to the cut-off value in Table 2. If the value is below the cut-off value, it is classified as thalassemia beta trait, and if it is above the cut-off value, it is classified as iron deficiency anemia. The classification result for each index was calculated as the number

of iron deficiency anemia and thalassemia beta trait.

The results of each index were then compared with the Green and King index, which, based on the research of Sain et al. and Indrasari et al., has the highest sensitivity and specificity compared to other indices, using the Cohen kappa coefficient analysis.[6,9] The Cohen kappa coefficient < 0 indicates poor agreement, ≥ 0-0.2 indicates little agreement, coefficient > 0.2-0.4 indicates moderate agreement, coefficient > 0.4-0.6 indicates moderate agreement, coefficient > 0.6-0.8 indicates substantial agreement, coefficient > 0.8-1 indicates almost perfect agreement.[11]

RESULT

Based on the sample search results, there were 35 samples with anemia between the ages of 6 months and 59 months. Of these 35 samples, 26 samples (74.29%) had microcytic anemia. All samples were scored using the Mentzer, Green and King and Sirdah indices, the results of which are shown in Table 3.

Table 3. Distribution results of iron deficiency anemia and thalassemia beta trait in each index

Index name	Iron deficiency anemia N (%)	Thalassemia beta trait N (%)
Mentzer	17 (65.38)	9 (34.62)
Mentzer with cut off 10.7	25 (96.15)	1 (3.85)
Green and King	23 (88.46)	3 (11.54)
Sirdah	22 (84.62)	4 (15.38)

Table 4. Conclusion of reliability values between various indices compared to the Green and King index

Index Name	Cohen Kappa Value	Interpretation
Mentzer	-0.01	Poor agreement
Mentzer with cutoff 10.7	0.47	Moderate agreement
Sirdah	0.17	Weak agreement

DISCUSSION

In this study, different types of indices were compared with the Green and King index, which was shown to have the highest sensitivity and specificity. [6,9] The indices used for comparison included the Mentzer index, which is the most commonly used screening tool for iron deficiency anemia and thalassemia beta trait in Indonesia. Based on the analysis using the Cohen kappa coefficient, the Mentzer index had a poor agreement score (-0.01). This result was followed by the Sirdah Index (0.17), then the Mentzer Index with a cutoff of 10.7 had the highest agreement value (0.47).

From the results of the Mentzer Index calculation, it can be concluded that there is poor agreement between the Mentzer Index results and the Green and King Index results. Based on this, further research on the sensitivity and specificity of each index is needed to evaluate the reliability of the Mentzer index in screening and to consider the use of the Green and King index in screening for iron deficiency anemia and thalassemia beta trait. The Mentzer index with a cut-off value of 10.7 has moderate agreement with the Green and King index, which can be considered in screening compared to the traditional Mentzer index. The Sirdah index has low agreement with the Green and King index, which needs further evaluation if it is to be used as a screening tool.

In Indonesia, there is no standard reference for the range of normal hematological values in children, especially those aged 6 months to 59 months. This study used reference standards from the American Pediatric Association, which may have different conditions from those in Indonesia. This may affect the number of samples studied and the applicability of the research results to the population.

This study has limitations, namely the absence of further investigations such as iron profiles consisting of serum iron levels, total iron binding capacity (TIBC), and

ferritin and hemoglobin electrophoresis due to the lack of these facilities in the hospital where the study was conducted. This study could not distinguish between iron deficiency anemia and thalassemia beta trait in samples suffering from both at the same time. This resulted in samples suffering from both at the same time being included in one of the categories of either iron deficiency anemia or thalassemia beta trait. This study also used several indices that could not distinguish between thalassemia alpha and thalassemia beta major.

CONCLUSION

The study found that there was poor agreement between the Mentzer index and the Green and King index. This poor agreement can have a significant impact on patients because the index most commonly used to screen patients due to limited facilities, the Mentzer index, has poor agreement with the Green and King index, which has the highest sensitivity and specificity.

Further research is needed on the sensitivity and specificity of the Mentzer index compared to other indices using tests such as iron profile and hemoglobin electrophoresis to find the best index to be used as a screening tool for iron deficiency anemia and thalassemia beta trait in hospitals with limited facilities such as Gema Santi Nusa Penida Hospital.

Declaration by Authors

Ethical Approval: Approved

Acknowledgement: None

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Pasricha SR, Tye-Din J, Muckenthaler MU, Swinkels DW. Iron deficiency. Lancet [Internet]. 2021 Jan 1;397(10270):233–48. Available from: https://doi.org/10.1016/s0140-6736(20)32594-0
2. Sunardi D, Bardosono S, Basrowi RW, Wasito E, Vandenplas Y. Dietary determinants of anemia in children aged 6–36 months: a Cross-Sectional study in Indonesia. Nutrients [Internet]. 2021 Jul 13;13(7):2397. Available from: https://doi.org/10.3390/nu13072397
3. Wang M. Iron deficiency and other types of anemia in infants and children. PubMed [Internet]. 2016 Feb 15;93(4):270–8. Available from: https://pubmed.ncbi.nlm.nih.gov/26926814
4. Cascio MJ, DeLoughery TG. Anemia. Medical Clinics of North America/the Medical Clinics of North America [Internet]. 2017 Mar 1;101(2):263–84. Available from: https://doi.org/10.1016/j.mcna.2016.09.003
5. Soghier LM, Reyes C MD. Reference range values for pediatric care. 2019.
6. Sain A, Bhake A, Agrawal A, Thomas S. Discriminant red cell indices for microcytic hypochromic anaemia in distinguishing beta thalassaemia trait and iron deficiency anaemia: a Systematic review. Journal of Clinical and Diagnostic Research [Internet]. 2021 Jan 1; Available from: https://doi.org/10.7860/jcdr/2021/43521.14458
7. 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. PubMed [Internet]. 2023 Sep 8;21(1):99–102. Available from: https://pubmed.ncbi.nlm.nih.gov/37742157
8. Sari TT, Aliza N, Soedjatmiko S. Indeks Mentzer sebagai Alat Diagnostik Anemia Defisiensi Besi di Sarana Kesehatan dengan Fasilitas Terbatas: Perbandingan Berbagai Nilai Cut Off. Sari Pediatri/Sari Pediatri [Internet]. 2019 Nov 28;21(3):145. Available from: https://doi.org/10.14238/sp21.3.2019.145-51
9. Indrasari Y, Hernaningsih Y, Fitriah M, Hajat A, Dewa I, Ugrasena G, et al. Reliability of different RBC indices and formulas in the discrimination of ?-Thalassemia minor and iron deficiency Anemia in Surabaya, Indonesia. Indian Journal of Forensic Medicine and Toxicology [Internet]. 2021 Jan 7; Available from: https://doi.org/10.37506/ijfmt.v15i1.13543
10. Siswandari W, Rujito L, Indriani V, Djatmiko W. Mentzer Index Diagnostic

Value in Predicting Thalassemia Diagnosis. IOP Conference Series Earth and Environmental Science [Internet]. 2019 May 10; 255:012004. Available from: https://doi.org/10.1088/1755-1315/255/1/012004

11. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics [Internet]. 1977 Mar 1;33(1):159. Available from: https://doi.org/10.2307/2529310

How to cite this article: I Kadek Jaya Santika. Reliability test of different red blood cell discrimination indices for screening iron deficiency anemia and beta trait thalassemia in pediatric patients 6-59 months of age at Gema Santi Hospital, Nusa Penida, June 2023 - May 2024. *Int J Health Sci Res.* 2025; 15(2):49-54. DOI: *https://doi.org/10.52403/ijhsr.20250206*

******