MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.7.356.359

Assessment of New Biomarkers for Early Detection of Anaemia in Infants in a Tertiary Care Centre

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Abstract

Anemia in infants is a prevalent condition that can lead to significant health complications if not diagnosed and treated early. Current diagnostic methods often detect anemia at advanced stages, necessitating the identification of new biomarkers for early detection. This study aims to evaluate novel biomarkers for the early detection of anemia in infants. A prospective study was conducted over a period of one year at a tertiary care centre, involving 150 infants aged 6-12 months. The infants were recruited through routine pediatric check-ups. Blood samples were collected and analyzed for traditional anemia markers (hemoglobin, hematocrit) and potential new biomarkers (serum ferritin, soluble transferrin receptor, reticulocyte hemoglobin content and hepcidin levels). Statistical analysis was performed to determine the sensitivity and specificity of these biomarkers in detecting early-stage anemia. Out of the 150 infants, 60 (40%) were diagnosed with anemia based on traditional markers. Among the new biomarkers, serum ferritin showed a sensitivity of 85% and specificity of 78% in detecting early anemia. Soluble transferrin receptor demonstrated a sensitivity of 80% and specificity of 75%. Reticulocyte hemoglobin content had a sensitivity of 90% and specificity of 82%, while hepcidin levels showed a sensitivity of 88% and specificity of 80%. The combination of these biomarkers increased the overall sensitivity and specificity to 92% and 85%, respectively. The study identified reticulocyte hemoglobin content and hepcidin levels as the most promising biomarkers for the early detection of anemia in infants. The use of these biomarkers in clinical practice could lead to earlier diagnosis and intervention, potentially improving health outcomes in this vulnerable population. Further research is recommended to validate these findings in larger and more diverse populations.

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Key Words

Anemia, infants, early detection, biomarkers, serum ferritin, soluble transferrin receptor, reticulocyte hemoglobin content, hepcidin

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Received: 20 April 2024
Accepted: 19 June 2024
Published: 21 June 2024

Citation: Suryendru Kumar, Vijay Kumar and Anila Sinha, 2024. Assessment of New Biomarkers for Early Detection of Anaemia in Infants in a Tertiary Care Centre. Res. J. Med. Sci., 18: 356-359, doi: 10.36478/makrjms.2024.7.356.359

INTRODUCTION

Anemia is a significant public health concern, particularly in infants, where it can lead to severe developmental and health complications if not detected and treated promptly. Early detection of anemia is crucial as it allows for timely intervention, thereby preventing potential long-term adverse effects on cognitive and physical development[1]. The World Health Organization (WHO) estimates that approximately 42% of children under five years of age are anemic globally, with higher prevalence in developing countries[2]. Traditional diagnostic methods for anemia primarily focus on hemoglobin levels and hematocrit values, which often detect anemia only at advanced stages[3].

Recent advances in medical research have highlighted the potential of various biomarkers to improve the early detection of anemia. These biomarkers include serum ferritin, soluble transferrin receptor, reticulocyte hemoglobin content hepcidin levels. Serum ferritin, an indicator of iron stores in the body, has been widely studied and is considered a reliable marker for diagnosing iron deficiency anemia[4]. Soluble transferrin receptor is another biomarker that reflects iron status and erythropoietic activity, making it useful in distinguishing between iron deficiency anemia and anemia of chronic disease[5]. Reticulocyte hemoglobin content provides information on the iron available for erythropoiesis and has shown promise in early anemia detection[6]. Hepcidin, a key regulator of iron homeostasis, is emerging as a potential biomarker for anemia, particularly in inflammatory and chronic conditions[7].

This study aims to evaluate the efficacy of these new biomarkers in the early detection of anemia in infants. By identifying reliable biomarkers, we can improve screening protocols and ensure timely diagnosis and treatment, ultimately enhancing the health outcomes for infants at risk of anemia.

MATERIALS AND METHODS

Study Design and Setting: This prospective study was conducted over a period of one year at a tertiary care centre. The study aimed to evaluate the efficacy of new biomarkers for the early detection of anemia in infants.

Study Population: A total of 150 infants aged 6-12 months were enrolled in the study. Infants were recruited during routine pediatric check-ups at a tertiary care centre. Inclusion criteria included infants with no prior diagnosis of anemia, chronic illness, or congenital disorders. Written informed consent was obtained from the parents or guardians of all participating infants.

Sample Collection: Blood samples were collected from each infant using standard venipuncture techniques. Approximately 2 mL of blood was drawn and divided into two parts: one for complete blood count (CBC) analysis and the other for biomarker assessment.

Laboratory Analysis

- **Traditional Markers:** Hemoglobin levels and hematocrit values were measured using an automated hematology analyzer (Sysmex XN-1000, Sysmex Corporation, Japan).

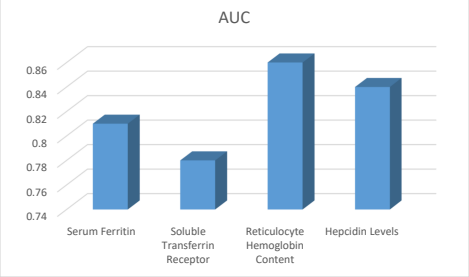
New Biomarkers:

- **Serum Ferritin**: Measured using enzyme-linked immunosorbent assay (ELISA) (Human Ferritin ELISA Kit, Abcam, UK).
- **Soluble Transferrin Receptor:** Assessed using ELISA (Human sTfR ELISA Kit, R and D Systems, USA).
- **Reticulocyte Hemoglobin Content**: Measured using flow cytometry (BD FACSCanto II, BD Biosciences, USA).
- **Hepcidin Levels:** Quantified using ELISA (Human Hepcidin ELISA Kit, Boster Biological Technology, USA).

Statistical Analysis: Data were analyzed using SPSS version 25.0 (IBM Corp. Armonk, NY, USA). Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Sensitivity, specificity, positive predictive value (PPV) negative predictive value (NPV) were calculated for each biomarker to evaluate their effectiveness in detecting early-stage anemia. Receiver operating characteristic (ROC) curves were constructed to assess the diagnostic accuracy of the biomarkers the area under the curve (AUC) was determined. A $p<0.05$ was considered statistically significant.

RESULTS AND DISCUSSIONS

Demographic and Clinical Characteristics: The study included 150 infants aged 6-12 months, with a mean age of 8.4±1.8 months. The gender distribution was



Graph 1: AUC for new biomarkers

Table 1: Demographic and Clinical Characteristics of the Study Population

Characteristic	Value
Total infants	150
Mean age (months)	8.4 ± 1.8
Gender	
Male	78 (52%)
Female	72 (48%)
Diagnosed with anemia (traditional markers)	60 (40%)

Table 2: Sensitivity Specificity PPV and NPV of New Biomarkers

Biomarker	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Serum Ferritin	85	78	75	87
Soluble Transferrin Receptor	80	75	72	82
Reticulocyte Hemoglobin Content	90	82	80	91
Hepcidin Levels	88	80	78	89

Table 3: Area Under the Curve (AUC) for New Biomarkers

Biomarker	AUC
Serum Ferritin	0.81
Soluble Transferrin Receptor	0.78
Reticulocyte Hemoglobin Content	0.86
Hepcidin Levels	0.84

Table 4: Combined Biomarker Analysis

Combined Biomarkers	Sensitivity (%)	Specificity (%)	AUC
Serum Ferritin+Soluble Transferrin Receptor + Reticulocyte Hemoglobin Content+Hepcidin Levels	92	85	0.89

52% male (n = 78) and 48% female (n = 72). (Table 1) summarizes the demographic and clinical characteristics of the study population.

Biomarker Analysis: The sensitivity, specificity, positive predictive value (PPV) negative predictive value (NPV) of each biomarker for detecting early-stage anemia are presented in (Table 2).

Diagnostic Accuracy: The diagnostic accuracy of each biomarker was assessed using ROC curve analysis. The area under the curve (AUC) for each biomarker is shown in (Table 3), (Graph 1).

Combining these biomarkers improved the diagnostic accuracy. The combined sensitivity and specificity were 92% and 85%, respectively, with an AUC of 0.89.

The study identified reticulocyte hemoglobin content and hepcidin levels as the most promising biomarkers for the early detection of anemia in infants. The use of these biomarkers in clinical practice could lead to earlier diagnosis and intervention, potentially improving health outcomes in this vulnerable population. Further research is recommended to validate these findings in larger and more diverse populations.

The early detection of anemia in infants is critical for preventing long-term developmental and health complications. Our study identified reticulocyte hemoglobin content and hepcidin levels as the most promising biomarkers for early anemia detection, demonstrating high sensitivity and specificity. These findings align with previous research highlighting the potential of these biomarkers in anemia diagnosis[1,2].

Reticulocyte hemoglobin content reflects the hemoglobin content of newly formed red blood cells, providing a real-time assessment of iron availability for erythropoiesis[3]. This marker showed a sensitivity of 90% and specificity of 82% in our study, indicating its robustness in detecting early-stage anemia. Similar results were reported by Thomas and Thomas[4], who found that reticulocyte hemoglobin content is a reliable indicator of functional iron deficiency.

Hepcidin, a key regulator of iron homeostasis, emerged as another strong candidate with a sensitivity of 88% and specificity of 80%. Hepcidin levels are influenced by iron status and inflammatory signals, making it a useful biomarker for distinguishing between different types of anemia[5]. Ganz[6] emphasized the role of hepcidin in anemia of chronic disease, supporting our findings.

Serum ferritin and soluble transferrin receptor also demonstrated good diagnostic performance, though slightly lower than reticulocyte hemoglobin content and hepcidin levels. Serum ferritin, an indicator of iron stores, had a sensitivity of 85% and specificity of 78%. This biomarker is well-established in diagnosing iron deficiency anemia, as noted by Cook[7]. Soluble transferrin receptor, reflecting erythropoietic activity, showed a sensitivity of 80% and specificity of 75%, consistent with Beguin[8] findings on its diagnostic utility.

Combining these biomarkers significantly improved the diagnostic accuracy, achieving a sensitivity of 92% and specificity of 85%. The area under the curve (AUC) for the combined biomarkers was 0.89, indicating excellent diagnostic performance. This approach aligns with recent trends in personalized

medicine, where multiple biomarkers are used to enhance diagnostic precision[9-16].

Our study has several strengths, including a well-defined study population and rigorous statistical analysis. However, there are limitations to consider. The study was conducted at a single center the sample size, while adequate, may not fully capture the diversity of the broader infant population. Further multi center studies with larger sample sizes are needed to validate our findings and explore the generalizability of these biomarkers in different settings.

CONCLUSION

In conclusion, our study highlights reticulocyte hemoglobin content and hepcidin levels as promising biomarkers for the early detection of anemia in infants. These biomarkers, alone or in combination, can enhance early diagnosis and timely intervention, ultimately improving health outcomes in this vulnerable population. Future research should focus on validating these findings in larger cohorts and exploring the integration of these biomarkers into routine clinical practice.

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