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VALIDITY OF MENTZER INDEX AS A SCREENING TOOL FOR β-THALASSEMIA

Hematology

Dr. Prafulkumar C K* Pathology Resident, Department Of Pathology, GIMS, Gadag *Corresponding Author

Dr. Basavaraj P Bommanahalli Professor And Head, Department Of Pathology, GIMS, Gadag

Dr. Shakunthala S Aramani Associate Professor, Department Of Pathology, GIMS, Gadag

Dr. Sushmitha S Assistant Professor, Department Of Pathology, GIMS, Gadag

ABSTRACT

Hemoglobinopathies are most common monogenic hereditary disorders. β-thalassemias and their interaction with hemoglobin E (Hb E) and hemoglobin S (Hb S) are a considerable health problem in India. Hemoglobinopathies are diagnosed by HPLC based on the fractions of normal and aberrant hemoglobin variants. It is a costly setup and available in only few referral centers. **Objectives:** To assess predictive value of Mentzer index in identification of thalassemia. **Material And Methods:** A cross-sectional study was conducted at the GIMS, Gadag from December 2020 to may 2022. A total number of 1070 patients with anemia were included in present study. **Results:** In the present study the mean age of patients with anemia was 25.8 years. 80.8% were females and 19.2% were males. 95.2% of patients with anemia showed absence of abnormal hemoglobin variant and 2.4% of the patients had BTT, 2.9% of other hemoglobinopathies. **Conclusion:** Hemoglobinopathies are public health issues and can have patients from pediatric/adolescent to adult care. HPLC is the gold standard to quantify normal and aberrant hemoglobin fractions. Various discriminant indices add value in identifying the patients with anemia in whom HPLC is indicated for detection of hemoglobinopathies.

KEYWORDS

Hemoglobinopathies, β-Thalassemia, HPLC, Discriminant indices.

INTRODUCTION

Iron deficiency anaemia (IDA) and β-thalassemia trait(βTT) are most common cause of microcytic hypochromic anaemia, former is due to lack of adequate iron required to synthesise haemoglobin (Hb), seen approximately in 30% of global population, latter is genetic mutation leading to decreased β-globin chain synthesis[1].

Thalassemia is most common inherited disorder in the world. WHO reported that 5% of world's population is thalassemia carriers, found in different ethnicity population due to migration and intermarriage[2]. In India the prevalence rate of thalassemia is 3.3%, which is alarming and major health problem. Thalassemia carriers are usually asymptomatic with mild anaemia, unaware of their carrier status unless they have undergone testing [3].

Recognition of β-thalassemia trait is important because a major disease in progeny can be prevented by genetic counselling and spouse screening. Often βTT is mistaken for iron deficiency anaemia and has implications for genetic counselling [4,5].

As IDA and βTT conditions present with different blood indices in haematological investigations. The red blood cell counts (RBC) and derived indices are extremely important in the screening of beta thalassemia traits. A number of formulas and indices have been proposed to differentiate iron deficiency anaemiafrom beta thalassemia traits [6].

Thalassemia traits have high RBC count, while mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) are markedly reduced.[7]. RBC discriminants indices like Mentzer's index (MI) is found reliable, with sensitivity and specificity of 89% and 87.9% respectively [3]. Mentzer index is calculated by formulae MI = MCV ÷ RBC Count; <13 is indicative of βTT, whereas >13 is suggestive of IDA diagnosis is confirmed by HPLC (High performance based liquid chromatography) [8].

This discriminating index being able to calculated by CBC parameters serves as a feasible screening tool in resource limited regions. Though Hb-chromatography and Hb-electrophoresis can differentiate IDA and βTT, these testing facilities are unavailable in most of the health care centres[3]. This study is taken up to correlate Mentzer index and HPLC in patients of microcytic hypochromic anaemia to evaluate reliability of Mentzer index as preliminary screening tool for detection of β-thalassemia traits.

MATERIAL AND METHODS

A Hospital based Prospective cross-sectional Study. Undertaken in Gadag Institute of Medical Sciences (GIMS) Teaching hospital. From December 2020 to May 2022. All patients of various age groups attending the Hematology Department of GIMS, Gadag for evaluation of anemia were included in the study. Sample size : 1070 patients.

Inclusion Criteria

All cases of anemia diagnosed as per WHO criteria were included in the present study.

Table No : WHO Criterion For Consideration Of Anemia.[11]

Population	WHO criteria
Children 6 - 59 months of age	<11.0 gm/dl
Children 5 - 11 years of age	<11.5 gm/dl
Children 12 - 14 years of age	<12.0 gm/dl
Non-pregnant women (15 years of age and above)	<12.0 gm/dl
Pregnant women	<11.0 gm/dl
Men (15 years of age and above)	<13.0 gm/dl

Exclusion Criteria

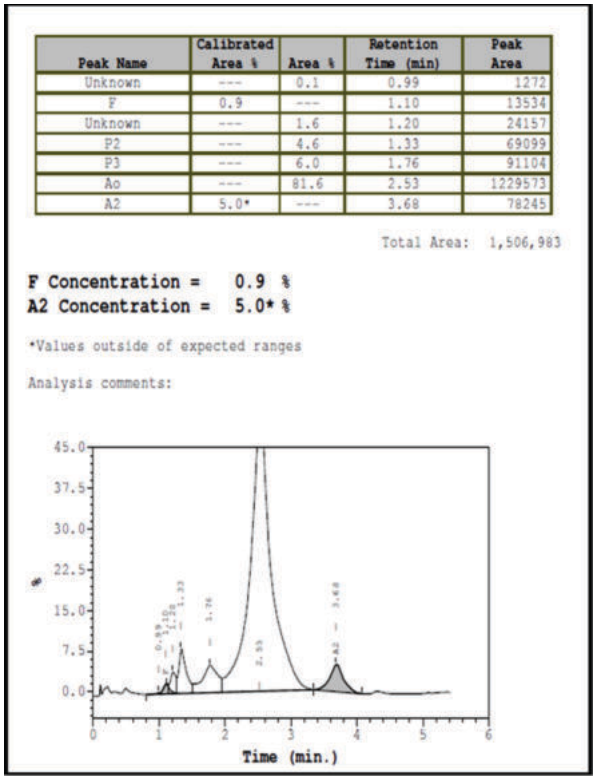
- Patients with history of blood transfusion within past 3 months.
- Infants less than 6 months of age are deferred to avoid interference with fetal Hemoglobin.

RESULTS

The present study included screening of 1070 patients with anemia. Youngest patient in the series was 1 year of age and oldest patient was 75 years of age. The mean age of presentation was 25.8 years. 80.8% were females and 19.2 were males. Male to female ratio was 1:4.2

Means of various blood parameters for study population were RBC count: 3.8million cells/µl, Hb: 10.3 g/dl, MCV: 83.4 fl, MCH: 24.9 pg, MCHC: 29.3 g/dl and RDW-CV: 18.08%. Majority of the patients showed microcytic anemia (34.1%) and 27.3% of the patients showed normocytic, 10.3% showed macrocytic and 28.3% showed dimorphic anemia.

Majority of the patients with BTT(92.3%), showed microcytic anemia on peripheral smear. The association between haemoglobinopathies and red cell morphology was statistically significant ($p<0.001$).



Peak Name	Calibrated Area %	Area %	Retention Time (min)	Peak Area
Unknown	---	0.1	0.99	1272
F	0.9	---	1.10	13534
Unknown	---	1.6	1.20	24157
P2	---	4.6	1.33	69099
P3	---	6.0	1.76	91104
Ao	---	81.6	2.53	1229573
A2	5.0*	---	3.68	78245

Total Area: 1,506,983

F Concentration = 0.9 %
A2 Concentration = 5.0* %

*Values outside of expected ranges

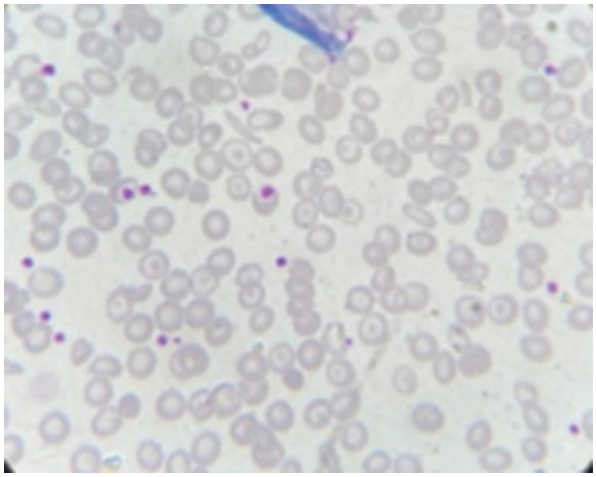
Analysis comments:

Choramtograph Of A β Thalassemia Trait Patient.

95.2% of patients with anemia showed absence of abnormal hemoglobin variant. About 4.9% of the patients had a hemoglobinopathy. In addition to thalassemias, the hemoglobin variants like HbE, HbD, and HbS were observed with varying frequencies. Beta Thalassemia trait was the most common hemoglobinopathy observed in our study. Heterozygous beta thalassemia carriers have persistently increased HbA2 levels, which range from 3.5 to 7% with a mean of 4.8%.

DISCUSSION

In the present study, the mean Hb in BTT cases was 8.8±3.1g/dL. Hb was considerably lower in BTT cases compared to other studies. This may be due to concomitant nutritional deficiency among the BTT cases. However it has to be confirmed by further investigating for the nutritional deficiency anemia.



Peripheral Smear Of Patient With Beta Thalassemia Trait Showing Microcytic Hypochchromic RBC's With Target Cells (Leishman Stain X 40x)

According to Nishi Madan, Meera Sikka, and colleagues, the mean RBC count in BTT cases was $5.67 \pm 0.76 \times 10^{12}$/L ($p<0.0001$).[3] And mean RBC count of $5.45 \pm 0.71 \times 10^{12}$/L in BTT cases was reported by Mohamed M. et al.[09] The mean RBC count among BTT cases in the study by Das Gupta et al.,[10] was $5.6\pm0.7 \times 10^{12}$/L. $5.9\pm1.0 \times 10^{12}$/L was reported by KhinEi Han et al.[11] The mean RBC count in the present study was $4.78 \pm 1.3 \times 10^{12}$/L in BTT, which is a lower when compared to other studies but an increased count for the observed mean hemoglobin.

In BTT cases, Nishi Madan, MeeraSikka, and colleagues reported a mean MCV count of 64.7±4.8fl ($p<0.0001$).[80] According to Mohamed M et al., the average MCV count in BTT was 64.81±4.72fl.[09] The average MCV count in the Das Gupta et al study was 64.53.7fl in BTT.[10] According to KhinEi Han et al., the mean MCV count in BTT was 62.71±2.1fl.[11] The average MCV count in the current study was 67.3±10.5fl in BTT. This observation is similar to that made by KhinEi Han et al.[11]

In a 1999 study of 337 BTT cases and 40 healthy controls, Nishi Madan, MeeraSikka, and colleagues discovered that the mean MCH value in BTT was 20.6±3.6pg ($p<0.0001$).[80] Mohamed M. et al.,[09] studied 382 BTT patients and 78 controls in 1999 and discovered that the mean MCH value in BTT was 20.75±1.64 pg.[09] In 1994, Das Gupta et al.,[10] studied 56 cases of BTT and 50 cases of controls and discovered that the mean MCH value in BTT was 20±1.2pg.[10] In 1992, KhinEi Han et al.,[11] studied 133 BTT and 30 controls and discovered that the mean MCH count in BTT was 19.9±3.5pg.[85] The mean MCH value in the present study was 19.3±3.6pg in BTT. This observation is similar to that made by KhinEi Han et al.[11]

Ehsani et al. observed Mentzer index as the best discriminatory index with the highest YI (90.1) with accuracy of 97.71% (269/284)[13] compared to 89% (259/291) achieved by d'Onofrio et al. at a cut-off of 14.[13] Batebi et al. obtained sensitivity, specificity, and YI of 86.3%, 85.4%, and 71.7, respectively at a cut-off of 13.[11] Niazi et al. obtained accuracy, sensitivity, specificity, and YI of 86.85% (2nd to RDWI), 89%, 81%, and 70, respectively.[12] In the present study, Mentzer index achieved sensitivity and specificity of 57.6% and 90% respectively.

CONCLUSION

Mentzer index add value in identifying the patients with anemia in whom HPLC is indicated for confirmation of hemoglobinopathies. Considering red cell indices alone for screening of hemoglobinopathies will be misleading because in liver disease, zidovudine therapy, or in vitamin B12 and folic acid deficiency there will be elevated MCV & MCH, leading to false negative interpretation.

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