

Mentzer Index as a screening tool for differential diagnosis of Iron Deficiency Anaemia and Beta Thalassemia Trait

Dr Amita Gupta

¹Senior Resident, Department of Transfusion Medicine, Bhopal Memorial Hospital and Research Centre, Bhopal, Madhya Pradesh

Dr Manisha Shrivastava

²Professor, Department of Transfusion Medicine, Bhopal Memorial Hospital and Research Centre, Bhopal, Madhya Pradesh

Dr Divya Srivastava

³Assistant Professor, Department of Pathology, ASMC, Jaunpur, Uttar Pradesh.

Dr Anil Gupta

Assistant Professor, BIPMS, Jabalpur, Madhya Pradesh

Dr Seema Navaid

Senior Medical Officer, Department of Transfusion Medicine, Bhopal Memorial Hospital and Research Centre, Bhopal, Madhya Pradesh

Corresponding Author: Dr Anil Gupta

ABSTRACT

Introduction: Microcytic hypochromic anaemia is prevalent in India. Beta thalassemia and iron deficiency anaemia (IDA) is one of the important causes of microcytic hypochromic anaemia. High-Performance Liquid Chromatography Chromatography (HPLC) is currently the gold standard in diagnosing hemoglobinopathies which are only available in certain advanced laboratories. It is important to develop easily examined parameters that are useful to help in the diagnosis of thalassemia traits. In a resource-poor country, like India, HPLC may not be widely available, Mentzer's index can be used to differentiate IDA and thalassemia.

AIMS & OBJECTIVE:

1. To determine haemoglobin and other red cell indices on samples collected from patients with clinical symptoms of anaemia.
2. To differentiate between Iron deficiency anaemia and thalassemia.
3. To calculate Mentzer's index and study its sensitivity and specificity in differentiating iron deficiency anemia from thalassemia trait.

Material and Methods: This is a Cross-Sectional and Observational type of study conducted among 112 anaemic patients in the Department of Pathology in a Tertiary Care Teaching Hospital over a period of 1 year.

Results Out of 112 Patients who were included in our study, The blood indices of all the cases were studied and Mentzer index was calculated for all the cases of iron deficiency anaemia and beta thalassemia trait. Out of 57 patients with iron deficiency 54 (94.7 %) patients had Mentzer index more than 13 and 3 (5.3 %) had Mentzer index less than 13. While out of 55 patients with thalassemia trait 51 (92.7 %) patients had Mentzer index less than 13 and 4 (7.3 %) patients had Mentzer index of more than 13.

Conclusion: Iron deficiency anaemia and thalassemia have different effects on blood indices. In resource poor and developing countries like that of India it can be used as a screening tool. In doubtful cases the diagnosis can be confirmed by Hb Electrophoresis.

Mentzer index has low sensitivity and specificity; it can be used as a screening tool to differentiate between IDA and Thalassemia. In cases of fallacies and doubt to be confirmed by serum iron studies and HPLC.

Keywords: Mentzer Index, Iron Deficiency Anaemia, Beta Thalassemia Trait.

INTRODUCTION

Anaemia is a commonly encountered condition in India, wherein there is a decrease in the oxygen-carrying capacity of the blood. Anaemia can be due to many causes of which iron deficiency anaemia and haemoglobinopathies, notably thalassemia are most common. Microcytic hypochromic anaemia is characterised by decreased haemoglobin, PCV, MCV, MCH, MCHC and normal to increased RDW. Important causes of microcytic hypochromic anaemia include thalassemia, iron deficiency anaemia, sideroblastic anaemia and lead intoxication. [1] Sideroblastic anaemia and lead intoxication are relatively uncommon. While the diagnosis of beta thalassemia major usually becomes obvious within initial years of life because of progressive anaemia and need for repeated blood transfusion. It is children with beta thalassemia trait who pose a diagnostic dilemma. [2] Patients with beta thalassemia-Iron deficiency anaemia and thalassemia are some of the most common. Iron deficiency anaemia is an easily treatable condition usually requiring oral iron supplements or in severe cases parenteral iron therapy or blood transfusions.

Beta Thalassemia and Iron Deficiency Anaemia are the important causes of microcytic hypochromic anaemia and their differentiation is important because they not only require different management and treatment but also have different implications for the patient's family, community, or society. Beta Thalassemia requires pre-marriage counseling while iron deficiency anaemia needs assessment of nutritional status. Whereas thalassemia and thalassemia hemoglobinopathies are genetic disorders requiring lifelong blood transfusion support along with iron chelation therapy.

Thalassemia is an autosomal recessive inherited group of disorders of hemoglobin synthesis characterised by the absence or reduction of one or more of the globin chains of haemoglobin. The structural variants result from the substitution of one or more amino acids in the globin chains of the haemoglobin molecule. The only curative treatment of thalassemia and other haemoglobinopathies, is a HLA-matched hematopoietic stem cell transplant. Plethora of haemoglobin variants is prevalent in India owing to ethnic diversity of its population with minimal to major clinical significance. These diseases pose serious health problems leading to severe morbidity and mortality in the Indian population. It is therefore important to correctly diagnose the cause of anaemia as a correct diagnosis will help prevent the unnecessary iron loading of a thalassemia patient.

Differentiating iron deficiency anaemia from thalassemia carrier status is a frequently faced challenge in medical practice, in particular in subjects with mild or moderate iron deficiency anaemia and in regions where thalassemia is common. The differentiation between these two conditions can't be done on the basis of blood picture because both of these conditions present with decreased PCV, MCV, MCH, MCHC, and normal to increased RDW. Inability to differentiate between these two conditions on the basis of blood picture and unavailability and non-affordability of the tests like Hb electrophoresis and mutation analysis has led to some investigators utilizing various indices to differentiate between these two conditions. [3] These indices include Mentzer Index, England and Fraser Index, Srivastava Index, Green and King Index, Shine and Lal Index, red blood cell (RBC) count, red blood cell distribution width and red blood cell blood distribution width index (RDWI).

The aim of this study was to find out the diagnostic value of Mentzer index in differentiating between beta thalassemia trait and iron deficiency anaemia.

Mentzer index is calculated using the following formula

$$\text{Mentzer Index} = \frac{\text{MCV (in femtoliters per Cell)}}{\text{RBC Count in millions}}$$

An index of less than 13 suggests that the patient has thalassemia trait whereas greater than 13 suggests iron deficiency anaemia. We will also study the sensitivity and specificity of Mentzer's index in differentiating iron deficiency anaemia from thalassemia trait.

AIMS & OBJECTIVE

1. To determine haemoglobin and other red cell indices on samples collected from patients with clinical symptoms of anaemia.
2. To differentiate between Iron deficiency anaemia and thalassemia.
3. To calculate the Mentzer's index and study its sensitivity and specificity in differentiating iron deficiency anaemia from thalassemia trait.

Materials and Methods

This is a Cross-Sectional and Observational study conducted among 112 anaemic patients in the Department of Pathology in a Tertiary Care Teaching Hospital over a period of 1 year.

Inclusion criteria:

All patients who were found to have haemoglobin count low for their age/sex as per the WHO criteria for anemia

Children (6-59 months): less than 11.0 gm%.

Children (5-11 years): less than 11.5 gm%.

Children (12-14 years): less than 12 gm%.

Non-pregnant women: less than 12 gm%.

(15 yrs and above)

Pregnant women: less than 11gm%

Men: less than 13 gm%.

Exclusion criteria:

1. All patients having haemoglobin count greater than the cutoff values as per the WHO guidelines (mentioned above).
2. Coexistence of other haematological conditions like autoimmune hemolytic anaemia, aplastic anaemia or lead intoxication.
3. History of blood transfusion in the near past less than 3 months.

The complete blood count (CBC) was measured by an automated analyzer of all patients with anaemia (low Hb). Differentiation was done in between Iron Deficiency anaemia and Thalassemia by calculating Mentzer index as screening tool of all the patients belonging to each group to differentiate between beta thalassemia trait and iron deficiency anaemia.

Results

Total 112 patients with anaemia and falling under WHO guidelines were studied. Out of these iron deficiency anaemia or thalassemia traits was the cause of microcytic hypochromic anaemia in 55 patients. The diagnosis of microcytic hypochromic anaemia was done on the basis of anaemia along with decreased PCV, MCV, MCH, and MCHC. The diagnosis of iron deficiency was based upon iron studies and that of thalassemia trait was based upon increased Hb A2 on Hb electrophoresis (Figure 1).

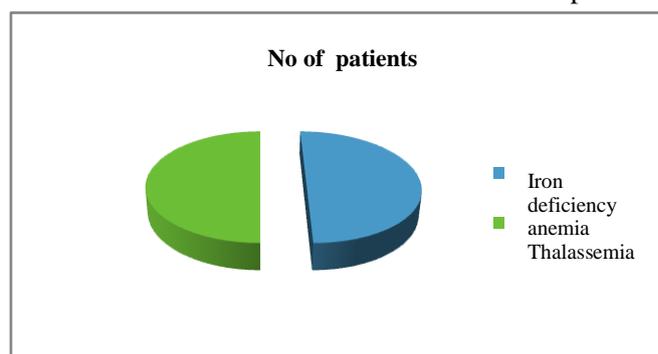


Figure 1: No of studied cases of thalassemia trait and iron deficiency anaemia.

RBC indices in Iron Deficiency Anaemia and Thalassemia.

In the study, the mean RBC indices in Thalassemia patients v/s patients with iron deficiency anaemia are as shown in the table.

It is seen that the normal RBC indices are:-

RBC count > 6.0 million/cumm; MCV, 82 femtoliter; MCHC, 33 grams/decilitre and MCH, 27 picogram. In our study, the RBC indices varied significantly in patients with Thalassemia compared to patients with Iron deficiency anaemia as shown in Table 3.

Abnormal haemoglobin indices (RBC count > 6.1 million/cumm; MCV <80 femtoliter /cell; MCHC < 33 g/dl and MCH < 27 picogram/ cell) was found in Thalassemic patients compared to non Thalassemic patients.

Mean values	Thalassemia	Iron deficiency anaemia	P value
RBC	5.23	4.56	1.0002
MCV	72.18	76.39	0.0022
MCH	20.78	22.05	0.134
MCHC	29.35	28.25	0.007

Figure 2: Mean RBC indices in Thalassemia patients v/s patients with iron deficiency anaemia.

The most common clinical features of the patients with iron deficiency were found to be fatigue (45%), anorexia (33.33%) breathlessness (30%), and irritability (25%) while the most patients with beta-thalassemia trait were asymptomatic some of them presented with fatigue (25%), anorexia (11.66%) breathlessness (13.33%) and irritability (13.33%).

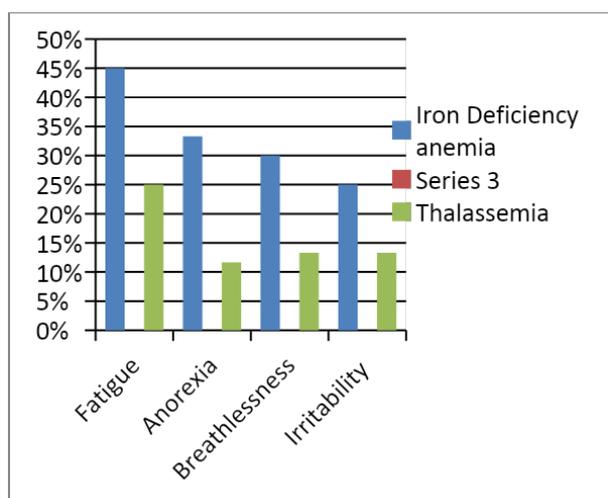


Figure 3: Clinical Features of patients

The blood indices of all the cases were studied and the Mentzer index was calculated for all the cases of iron deficiency anaemia and beta-thalassemia trait. Out of 57 patients with iron deficiency, 54 (94.7 %) patients had a Mentzer index of more than 13 and 3 (5.3 %) had Mentzer index of less than 13. While out of 55 patients with thalassemia trait 51 (92.7 %) patients had a Mentzer index of less than 13 and 4 (7.3 %) patients had a Mentzer index of more than 13.

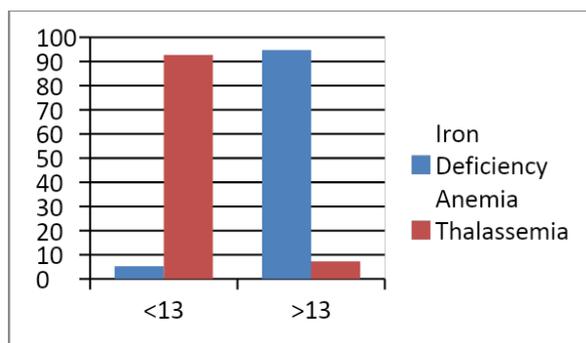


Figure 4 : Comparison of Mentzer index in Iron deficiency anaemia and Thalassemia

Discussion

Iron deficiency anaemia and thalassemia are important causes of microcytic hypochromic anaemia in the Indian population. Differentiating iron deficiency anaemia from thalassemia carrier status is a frequent issue in medical practice, in particular in subjects with mild or moderate iron-deficiency anaemia and in regions where thalassemia is common.

People are predisposed to iron deficiency because of dietary insufficiency, growth and helminthic infestations. On the other hand, beta-thalassemia trait is usually asymptomatic anaemia caused by a mutation in one beta-globin gene. The majority of the patients with thalassemia syndromes are found in Southeast Asia. They are also seen in the Mediterranean region, the Middle East, Southwest Europe, and Africa. In India, the communities in whom there is an increased risk of thalassemia due to the presence of traits in individual members are Sindhis, Gujratis, Punjabis, kachchis, Lohana, Prajapati, and Bengalis. [4]

It is not possible to distinguish both conditions using simple routine blood counts, as they are both associated with microcytic and hypochromic erythrocytes. However, in thalassemia RBCs do tend to be more microcytic, whereas iron-deficient RBCs are often more hypochromic. [5]

The clinical features of iron deficiency anemia and thalassemia traits are usually similar and consist of angular stomatitis, anorexia, irritability, pica, fatigue, and breathlessness. The diagnosis of iron deficiency anemia depends upon reduced PCV, MCV, MCH, and MCHC. The iron studies confirm the diagnosis of iron deficiency anemia. The classical findings seen in iron deficiency anemia are reduced serum ferritin and serum iron along with increased total iron-binding capacity. The diagnosis of thalassemia is dependent upon the demonstration of increased HbA2 levels in the blood (> 3.5%) on Hb electrophoresis and mutation analysis.

Though the definitive tests for iron deficiency anaemia and thalassemia are iron studies and Hb electrophoresis respectively it is always not possible to do these tests in all patients having microcytic hypochromic anaemia. It is for this reason that various indices have been studied to differentiate between iron deficiency anaemia and thalassemia traits. The commonly used indices are given below. [6]

Originally described by Mentzer in 1973, the Mentzer index is useful to differentiate between iron deficiency anaemia and thalassemia traits. Mentzer index can be calculated using MCV and RBC count and can be used to differentiate between beta thalassemia trait and iron deficiency anemia. Many studies have found it to be one of the most reliable indices to differentiate between these 2 conditions. Differentiating these conditions is important because of the obvious implications such differentiation may have on the management of the patients. [7-15]

Conclusion

Beta thalassemia trait and iron deficiency anemia are conditions causing microcytic hypochromic anemia. Mentzer index can be used as an economically efficient screening tool to advise further

advanced tests like HPLC, Hb electrophoresis, or Iron studies. Though the definitive diagnosis depends upon iron studies and Hb electrophoresis. In doubtful cases, confirmation of diagnosis by iron studies and Hb electrophoresis must be done.

References

1. Moy RJ, Early AR. Iron deficiency in Adults. *Journal of the Royal Society of Medicine*. 1999;92(5):234-236.
2. Yates AM, Mortier NA, Hyde KS, Hankins JS, Ware RE. The Diagnostic Dilemma of Congenital Unstable Hemoglobinopathies. *Pediatric blood & cancer*. 2010;55(7):1393-1395.
3. Eldibany MM, Totonchi KF, Joseph NJ, Rhone D. Usefulness of certain red blood cell indices in diagnosing and differentiating thalassemia trait from iron-deficiency anemia. *Am J ClinPathol*. 1999 May;111(5):676-82. Erratum in: *Am J ClinPathol* 1999 Sep;112(3):428. (5)
4. Demir A, Yarali N, Fisgin T, Duru F, Kara A. Most reliable indices indifferntiation between thalassemia trait and iron deficiency anemia. *PediatrInt*. 2002 Dec;44(6):612-6.
5. Lafferty JD, Crowther MA, Ali MA, Levine M. 1996. The evaluation of various mathematical RBC indices and their efficacy in discriminating between thalassemic & non - thalassemic microcytosis. *Am J Clin Pathol*, 106:2015.
6. Eldibany MM, Totonchi KF, Joseph NJ, Rhone D. Usefulness of certain red blood cell indices in diagnosing and differentiating thalassemia trait from iron-deficiency anemia. *Am J ClinPathol*. 1999 May;111(5):676-82. Erratum in: *Am J ClinPathol* 1999 Sep;112(3):428.
7. Eldibany MM, Totonchi KF, Joseph NJ, Rhone D. Usefulness of certain red blood cell indices in diagnosing and differentiating thalassemia trait from iron-deficiency anemia. *Am J ClinPathol*. 1999 May;111(5):676-82. Erratum in: *Am J ClinPathol* 1999 Sep;112(3):428
8. Karimi M, Cohan N, De Sanctis V, Mallat NS, Taher A. Guidelines for diagnosis and management of Beta-thalassemia inter-media. *Pediatr Hematol Oncol*. 2014Oct; 31(7):583-96.
9. Patel AG, Shah AP, Sorathiya SM, Gupte SC. Hemoglobinopathies in South Gujarat population and incidence of anemia in them. *Indian Journal of Human Genetics*. 2012;18(3):294-298.
10. Brancaleoni V, Di Pierro E, Motta I, Cappellini MD. Laboratory diagnosis of thalassemia. *Int J Lab Hematol*. 2016 May;38Suppl 1:32-40.
11. Zaghoul A, Al-Bukhari TA, Bajuaifer N, Shalaby M, Al-Pakistani HA, Halawani SH, Teama SH, Wassif GA. Introduction of new formulas and evaluation of the previous red blood cell indices and formulas in the differentiation between beta thalassemia trait and iron deficiency anemia in the Makkah region. *Hematology*. 2016 Jul;21(6):351-8.
12. El-Agouza I, Abu Shahla A, Sirdah M. The effect of iron deficiency anaemia on the levels of haemoglobin subtypes: possible consequences for clinical diagnosis. *Clinical and Laboratory Haematology*. 2002;24(5):285-289.
13. Ntaios G, Chatzinikolaou A, Saouli Z, et al. Discrimination indices as screening tests for β -thalassemic trait. *Annals of Hematology*. 2007;86(7):487-491
14. Rahim F, Keikhaei B. Better differential diagnosis of iron deficiency anemia from beta-thalassemia trait. *Turkish Journal of Hematology*. 2009;26(3):138-145.
15. Ghafouri M, Mostaan Sefat L, Sharifi L. Comparison of cell counter indices in differentiation of beta thalassemia trait and iron deficiency anemia. *The Scientific Journal of Iranian Blood Transfusion Organization*. 2006;2(7):385-389.