Original Article
Utilization of Mentzer Index to Discriminate Between Beta Thalassemia Minor and Anemia of Iron Deficiency, Followed by HPLC

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Abstract
Objective: Aim was to evaluate the sensitivity and specificity of Mentzer index in differentiating beta thalassemia minor from anemia of iron deficiency.

Materials and Methods: A cross-sectional study conducted in Hematology unit of Hayatabad Medical Complex. Sampling was done non-consecutively. A total of 860 cases with value of Hemoglobin less than 11 Gm/DL were counted. In all the selected cases full blood count were checked and Mentzer Index (mean corpuscular volume [MCV] per RBCs count) was calculated. Value of <13 suggests the diagnosis of beta Thalassemia minor/trait while a value >13 is more indicative of iron deficiency anemia (IDA). Confirmation of diagnoses was made by hemoglobin study using HPLC. Values for specificity and sensitivity for Mentzer Index were calculated for the two differentials of microcytic hypochromic anemia presenting with microcytosis and hypochromia.

Results: Mean hemoglobin level of patients was 9.01±0.85. Minimum and maximum hemoglobin value was 2.90 and 11 g/dl. Mean RBC count was 4.66±4.59 minimum and maximum RBC count was 1.07 and 136. Mean MCV value was 63.89±9.01. Minimum and maximum MCV value was 39.40 and 92.10 respectively. Men Mentzer index was 15.70±7.68. Minimum and maximum Mentzer index value was 7.80 and 10.7 respectively. Based on Mentzer index criteria 489(56.86%) patients had iron deficiency anemia and 371(43.14%) patients had higher suspicion of beta thalassemia.

Conclusion: It was concluded that for differentiation among Beta thalassemia minor and anemia of iron deficiency, Mentzer Index can be beneficial to discriminate with a high sensitivity as well as specificity percentage and thus through a cost effective way, only suspected cases of beta thalassemia trait/minor can be further confirmed by Hb Electrophoreses.

Keywords: Mentzer Index, iron deficiency Anemia, beta Thalassemia minor

Introduction
Anemia is the most common hematological condition, especially in children and infants, due to insufficient iron to synthesize hemoglobin. Decreased hemoglobin with reduction in the indices of Erythrocytes (RBCs) including, Mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), mean hemoglobin concentration (MCH), hematocrit (HCT) are characteristic of Hypochromic microcytic anemia.

Conditions presenting with anemia of microcytic and hypochromic blood morphology includes anemia due to iron deficiency, thalassemias, sidoblastic anemia and lead poisoning with IDA and thalassemia being the commonest causes while sidoblastic anemia and lead poisoning are less common causes. Due to progressive anemia and the need for repeated blood transfusions, patients with beta thalassemia major are usually diagnosed at an early age. Pediatric patients with carrier state of beta thalassemia are creating confusions in diagnosis.

Since the presentation of anemia of iron deficiency anemia and beta thalassemia trait is common as microcytic hypochromic anemia, it is of vital to differentiate them from each other because they both need a different plan of treatment and further management and also differ in implication for the patients, their families as well as the society. Fortunately, IDA (iron deficiency anemia) is a benign and reversible condition by treatment with oral iron supplements and only in very severe conditions parenteral iron replacement therapy is adopted while on the other hand patients with beta thalassemia are asymptomatic but still require premarital counseling. While thalassemia and hemoglobinopathies are genetic diseases and patients with these conditions depend on lifelong transfusion along with an iron chelating agent.

Globally, 30% of the population suffers from IDA. However, it has been estimated that the prevalence of the beta-thalassemia trait is 1.5% worldwide. Ansari SH et al conducted a study and reported estimated the beta thalassemia trait carrier rate of 5.7% of the total population. According to another study the prevalence of beta thalassemia trait is 7.96% (5).

Distinguish IDA from the beta-thalassemia trait often addressed in medical practice, particularly in individuals having iron deficiency anemia and in the region of high frequency of thalassemia. The differentiation between these two conditions cannot be made on the blood picture as in these both two conditions presentation is with reduced packed cell volume, mean corpuscular volume, mean hemoglobin concentration and mean cell hemoglobin concentration and red cell distribution width is either normal or elevated. The difficulty in diagnosis among the two disorders is based on its mimicking blood morphology and also the non-accessibility and high cost of diagnosis confirmatory tests such as Hemoglobin studies and genetic mutation tests, has led to the development of various methods utilizing red cell indices to provide clues in easy way of differential diagnosis of these two conditions.

These include the Mentzer index, the Srivastava index, the Shine and Lal index, the Green and King index, the RBCs distribution width, England and the fastest RBCs index.

Keeping in view the high prevalence of beta thalassemia as well as iron deficiency anemia in our population, it is of vital significance to develop a cost effective single test method that can be performed at the district health center, which can filter the cases of these two mimicking conditions primarily. Among the discriminatory parameters, that can be considered for differentiation of beta thalassemia trait is the Mentzer index.

The Mentzer Index is a calculation of the ratio between MCV and red cells count, where if patients has a value <13 are diagnosed with a thalassemia trait while a value >13 is found in patients with anemia of iron deficiency.

Material and Methods
A cross-sectional study conducted in Hematology unit of Hayatabad Medical Complex sampling was done as Non-consecutively. A total of 860 cases with value of Hemoglobin less...
than 11 Gm/DL were counted. In all the selected cases full blood count were checked and Mentzer Index (mean corpuscular volume [MCV] per RBCs count) was calculated. Value of <13 suggests the diagnosis of β Thalassemia minor/trait while more than 13 value is more indicative of Iron deficiency anemia (IDA). Confirmation of diagnoses was made by hemoglobin study using HPLC. Values for specificity and sensitivity for Mentzer Index were calculated for the two differentials of microcytic hypochromic anemia presenting with microcytosis and hypochromia

RESULTS

Table 1: Hematological profile of patients

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hemoglobin</th>
<th>RCB</th>
<th>MCV</th>
<th>Mentzer Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>860</td>
<td>860</td>
<td>860</td>
<td>860</td>
</tr>
<tr>
<td>Mean</td>
<td>8.78</td>
<td>4.66</td>
<td>63.89</td>
<td>15.70</td>
</tr>
<tr>
<td>Median</td>
<td>8.95</td>
<td>4.56</td>
<td>63.25</td>
<td>13.69</td>
</tr>
<tr>
<td>SD</td>
<td>1.85</td>
<td>4.59</td>
<td>9.01</td>
<td>7.68</td>
</tr>
<tr>
<td>Min</td>
<td>2.90</td>
<td>1.07</td>
<td>39.40</td>
<td>7.80</td>
</tr>
<tr>
<td>Max</td>
<td>12.90</td>
<td>136</td>
<td>92.10</td>
<td>107</td>
</tr>
</tbody>
</table>

Mean hemoglobin level of patients was 9.01±1.85 Gm/dl. Minimum and maximum hemoglobin value was 2.90 and 11.00 Gm/dl. Mean RCB count was 4.66±4.59 minimum and maximum RCB count was 1.07 and 136 million/dl. Mean MCV value was 63.89±9.01. Minimum and maximum MCV value was 39.40 and 92.10 fl respectively. Mean Mentzer index was 15.70±7.68. Minimum and maximum Mentzer index value was 7.80 and 107 respectively.

Figure 1: Diagnosis of Patients based on

As per patients diagnosis 516(60%) of the patients had iron deficiency anemia and the remaining 344(40%) patients had beta thalassemia trait.

Based on Mentzer index criteria 469(56.86%) patients had iron deficiency anemia and 371(43.14%) patients had higher suspicion of beta thalassemia.

Table 2: Diagnostic Accuracy of Mentzer Index

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mentzer Index</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDA</td>
<td>&gt;13</td>
<td>103</td>
</tr>
<tr>
<td>Beta Thalassemia Trait</td>
<td>&lt;13</td>
<td>241</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>489</td>
</tr>
</tbody>
</table>

Mentzer index’s Sensitivity and specificity was 74.81% and 70.06%. Positive and Negative predictive values were 78.94% and 64.96% respectively. Diagnostic accuracy of Mentzer index was 72.91%.

Table 3: Comparison of Mentzer Index value in patients with IDA and Beta Thalassemia Trait

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Lower - Upper 95% CIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>75.41%</td>
<td>(72.74, 78.91)</td>
</tr>
<tr>
<td>Specificity</td>
<td>70.06%</td>
<td>(65.02, 75.10)</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>79.69%</td>
<td>(75.1, 84.3)</td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>64.46%</td>
<td>(59.97, 69.04)</td>
</tr>
<tr>
<td>Diagnostic Accuracy</td>
<td>72.91%</td>
<td>(69.84, 75.77)</td>
</tr>
</tbody>
</table>

Mean value of Mentzer index was significantly higher for patients with Beta thalassemia trait. i.e 17.39 vs. 13.16, p-value<0.001

DISCUSSIONS

In this study, calculated values of Sensitivity and specificity of Mentzer index was 74.81% and 70.06%. Positive predictive value and negative predictive value was 78.94% and 64.96% respectively. Diagnostic accuracy of Mentzer index was 72.91%. Mean value of Mentzer index was significantly higher for patients with Beta thalassemia trait, i.e. 17.39 vs. 13.16, p-value<0.001

Thalassemia, is a condition caused due to reduced or absent production of either single or more globin chain and is the commonest hereditary condition worldwide and as per WHO 05% of the population are thalassemia trait, anemia of Iron deficiency anemia and carrier state of β thalassemia both lead to anemia with microcytosis and hypochromia. (9)Discrimination of anemia due to iron deficiency and trait state of β thalassemia is of paramount importance and has significant clinical implications because each one of them has its own clinical course, prognosis and treatment.(9) The diagnosis of IDA is confirmed by serum Ferritin level and Iron studies including TIBC (Total Iron Binding Capacity), serum Iron level, serum Transferrin saturation etc., which are costly and time consuming investigations, and Mentzer index can predict the differentiation of β thalassemia trait from hypochromic microcytic anemia due to iron deficiency by a simple complete blood count.(10)

Mentzer WC et in Turkey did a study on assessed 290 children between 1-16 years of age and utilized the RBC count, Red cell distribution width and Mentzer index (MCV/RBCs count ratio) for differentiating between carrier state of β thalassemia and IDA. It was found in these studies that Mentzer index is a trustable discriminatory index, with a very high sensitivity (98.7%) and with specificity (82.3%). In a study conducted by Ehsani et al, it was found that the reliable most index to differentiate was Mentzer index. According to Youden’s criteria (90.1%), Ehsani et al index (85.5%) was the next to follow. Mentzer and Ehsani et al, in their studies, diagnosed accurately 94.7% and 92.9% of cases,
respectively. (11) Ghafari et al. found similar conclusions of 90.9% sensitivity and 80.3% specificity in their study.

Batebi et al. came to a conclusion that the sensitivity and specificity of the Mentzer index is quite high with figures of 86.3% and 85.4% respectively. There are few studies in which lower sensitivity has been concluded of 67% while some studies have reported a index of 82-95%. These conclusions signify that this measure is suitable to be utilized for predicting thalassemia trait with quite certainty minimizing the chances of misdiagnosis.

(12) An index to discriminate among the described conditions of hypochromic microcytic anemia, it must be reliably high sensitive as well as specific. When excluding cases with thalassemia minor, high sensitivity is required while exclusion of cases with anemia developed due to only iron deficiency, high specificity is mandatory.

The strengths of this study was it novelty and feasibility in the context of conducting a difficult research with ease. Since this was a cross sectional study there will always be a problem generalizing these results to other population.

CONCLUSION
It was concluded that Mentzer Index values are considerably reliable for differentiation between carrier /trait status of Beta thalassemia and anemia of iron deficiency, Mentzer Index can be trusted to be used as a primary filtration test and is highly sensitive and specific and above all cost effective. Only suspected cases of beta thalassemia trait/minor can be further confirmed by Hb Electrophoreses.

REFERENCES