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Evaluating Discrimination Indexes for Iron Deficiency Anemia among Children Aged Between 1-15 Years Old

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Abstract

Background: Iron Deficiency Anemia (IDA) is a massive health concern with a high frequency in Iran. Differentiating between IDA and other microcytic-hypochromic anemia like beta thalassemia minor requires demanding and money consuming tests. That is why this study aimed to assess well-suited and conclusive deferential indexes for IDA diagnosis among children aged between 1-15 years old

Methods: Blood samples were collected from outpatients aged between 1-15 years old. Consequently, Ferritin, Hemoglobin, Serum Iron, RBC count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), red cell volume distribution width (RDW), total iron binding capacity (TIBC) were determined. Furthermore, differential indexes including Mentzer, Shine and Lal and England-Frazer were measured and the data were analyzed using SPSS.

Results: Out of 100 children, 72 individuals were healthy and 28 had IDA. The average age was 3.6±2.9 years. The prediction value of the RBC indexes for the differentiation IDA were as follows: MCV (99%), HB (96%), Ferritin (95%), HCT (87%), MCH (79%), Serum Iron (71%), RBC count (51%), RDW (27%), and TIBC (26%). The prediction values of the formulas were as follows: Shine and Lal (96%), Mentzer (80%), and England-Frazer (79%).

Conclusion: According to the findings, it is possible to diagnose IDA by Complete Blood Count (CBC) test accompanied by differential indexes. A simple selective index such as Shine and Lal might be very beneficial for screening of IDA. This index is also useful for the diagnosis of microcytic anemia.

Key Words: Iron Deficiency Anemia, RBC indexes, Thalassemia.

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1- INTRODUCTION

IDA and β-Thalassemia trait (β-TT) are most frequent kinds of microcytic-hypochromic anemia and are still considered as a health concern around the world. It has been reported that approximately 30% of the global population suffer from IDA, specifically individuals who inhabit developing societies. Moreover, it has been estimated that about 1.5% of people are carriers for the β-Thalassemia gene, especially those who reside in Mediterranean districts (1).

Both IDA and β-Thalassemia are prevalent in diverse parts of Iran. It has been disclosed that there are 2-3 million β-Thalassemia carriers and approximately 25000 patients in Iran (2-4).

Malnourishment, famine, poverty, cereal-based diet and a couple of parasitic infections are the most common causes of IDA in developing communities (5). In the absence of inflammation, serum ferritin is the most sensitive and specific measurement for IDA diagnosis with 30 μg per liter cut-off. Serum ferritin declines in patients with IDA. Moreover, transferrin saturation below 16% indicates an inadequate iron supply for normal erythropoiesis. However, it is better to consider a whole picture, instead merely relying on a single test (6).

The diagnosis scheme for β-Thalassemia is based on clinical symptoms, Complete Blood Count (CBC) indexes, Hb electrophoresis, and sometimes genetic approaches (7).

Similar to IDA, β-Thalassemia is a kind of microcytic-hypochromic anemia. Definite and conclusive discrimination between IDA and β-TT can be done solely with regard to Hb electrophoresis, serum iron and ferritin measurement results (8); that is why, distinguishing between IDA and β-Thalassemia is complicated and causes immense social and financial burdens on patients and government.

There are a couple of methods, previously, introduced by Mentzer, Shine, Lal and England-Frazer (9-11). However, there are many controversial debates regarding the efficiency of these methods in the discrimination between IDA and other microcytic hypochromic anemia like β-thalassemia trait.

Thus, the current investigation as a pilot study aims to compare the prediction value of 12 of 28 different indexes and clarify which indexes are more dependable for IDA diagnosis.

2- MATERIALS AND METHODS

This cross sectional study was conducted on 100 outpatients (average age: 3.6 ± 2.9) who were admitted to an Amir Hospital in Semnan, Iran. Patient informed consent was obtained from the guardians of the contributing children. The study was conducted according to the Declaration of Helsinki.

The patients who had other background diseases like infectious diseases and major thalassemia as well as those whose brothers and sister suffered from such diseases were excluded from the study. Furthermore, the children detouring to iron supplementation, receiving iron replacement therapy for 3 months or more without clinical or laboratory improvement, and those who had stopped iron therapy for at least one month were also excluded.

Blood samples were collected in an EDTA anticoagulant tube from each individual aseptically according to standard procedures. Each sample went through the experiment process immediately and up to 3 hours after sample collection.

Hematological indices included RBC count, Hb, MCV, MCH and RDW measured using Sysmex KX-21N Automated Hematology Analyzer (NY, USA). Serum iron (SI) and TIBC were measured by colorimetric assay Hitachi

917 analyzer (Basel, Switzerland Roche). Ferritin was determined by the Human Ferritin Enzyme Immunoassay Test Kit (GenWay Biotech inc., CA.USA). Patients who had SI level <50 μg/dL, TIBC>450 μg/dL and Ferritin<12 μg/dL constituted the IDA group. Patients who had normal CBC, SI, TIBC and ferritin were considered as healthy individuals. With respect to these criteria, 28 people were confirmed to have IDA and 72 individuals were healthy.

Consequently, differential indexes including Mentzer, Shine and Lal and England-Frazer were calculated for each contributor chosen based on the following formula. Different RBC indices and their mathematical formulas are used to differentiate between β-TT and IDA (12).

a) Hematological index: Formula

b) Mentzer index (MI) (1973): MCV/RBC

c) RDWI (1987): MCV×RDW/RBC

d) Shine and Lal (S and L) (1977): MCV×MCV×MCH/100

e) Srivastava (1973): MCH/RBC

f) Green and King (G and K) (1989): MCV×MCV×RDW/Hb×100

g) Sirdah (2007): MCV−RBC−(3×Hb)

h) Ehsani (2005): MCV − (10 × RBC)

i) England and Fraser (E and F) (1973): MCV−(5×Hb)−RBC−3.4

j) Ricerca (1987): RDW/RBC

k) Mean density of Hb/lit; MDHL (1999): (MCH/MCV)×RBC

l) Mean cell Hb density; MCHD (1999): MCH/MCV

2-1. Data analysis

The data were analyzed using IBM® SPSS® Statistics. MCV, Hb, HCT, RBC, MCH, RDW, SI, TIBC and ferritin were compared between IDA and healthy group using Mann Whitney U test. P-values below 0.05 were considered statistically significant.

Area under curve (AUC) was calculated for each deferential index using backward logistic regression analysis and SPSS-Receiver Operating Characteristics (ROC) Curve.

3- RESULTS

In this investigation, 100 children (1-15 years) were included. Vein blood samples were collected from each individual and then hematological and biochemical indices including RBC count, Hb, MCV, MCH, HCT , RDW , SI and Ferritin were determined. With respect to these criteria, 28 children confirmed to have IDA according to the laboratory and clinical symptoms. Furthermore, 72 individuals were healthy.

MCV, MCH, and RDW, Hb, RBC and HCT indexes were indicated to be significantly lower in IDA patients in comparison to the control group (see **Fig. 1, Fig. 2** and **Tables 1 & 2**) and found as crucial factors for IDA diagnosis ($p < 0.05$).

The prediction value of each index was calculated using backward logistic regression and ROC software. Statistical calculations demonstrated that MCV among RBC indexes with a 99% prediction value is a gold standard. Among iron indexes, ferritin with a 95% prediction value is preferred to SI and TIBC determination. In the differentiation formula, Shin-lal with a 96% prediction value has a better prognostic value for IDA diagnosis, as compared to Mentzer (80%), and England & Frazer formula with a 79% prediction value (see **Table 2** and **Fig. 3**).

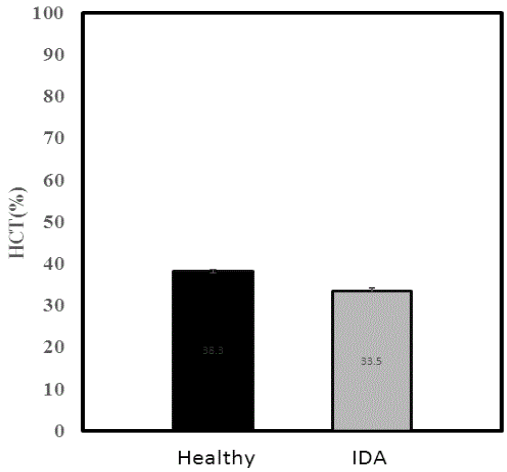

Fig.1: The mean percentage of HCT in the healthy (n=72) and IDA group (n=28)

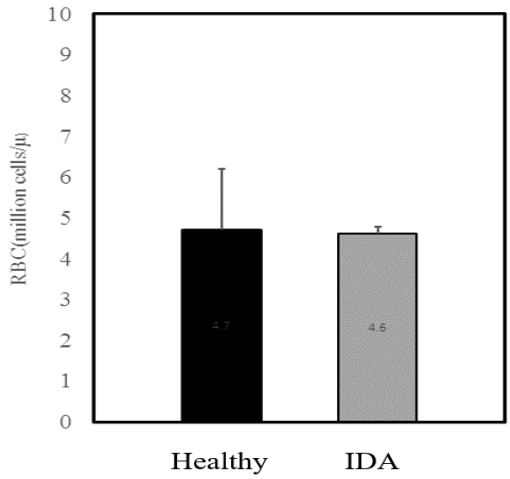

Fig. 2: The mean percentage of RBC in the healthy (n=72) and IDA group (n=28)

Table-1: Hematological indexes and biochemical data of the participants

Index	IDA(n=28)		Healthy group(n=72)	
	Range	Mean	Range	Mean
Age(year)	0.01 - 13	3.2±3.6	0.08 - 12	3.7±2.7
RBC(10^9/L)	1.9 - 6.1	4.6±0.94	3.6 - 5.9	4.7±0.43
Hb (mg/dl)	5.4 - 11.8	10.4±1.3	10.3 - 15.3	12.7±0.9
HCT (%)	17 - 38.9	33.5±4.1	31 - 45	38.3±2.8
MCV (fl)	53 - 70	63.9±3.9	69 - 87.7	80.3±3.6
RDW (%)	14.5 - 39.8	16.4±4.8	11.9 - 15.9	13.5±0.6
MCH (pg)	15.4 – 32.5	23.2±4	20.6 - 31.3	26.6±1.7
Ferritin (ng/ml)	18.5 - 175	30.6±28.4	24 - 285	98.3±329.9
SI (µ/dl)	15 - 250	62.6±43.7	25 - 180	78.2±28.2
TIBC (mg/dl)	290 - 387	538±656.8	180 - 500	358.3±61.5
Mentzer	9.1 - 32.6	14.4±4.4	11.7 - 23.6	16.9±2
Shine and Lal	816 - 2112	1493.2±303.9	1421 - 2660	2154.4±227.9
England-Frazer	6 - 29	3.2±6.7	0.4 - 28	8.7±5.7

Table-2: The prediction value of each index

Index	Area under curve
RBC (109/L)	0.51
Hb (mg/dl)	0.96
HCT (%)	0.87
MCV (fl)	0.99
RDW (%)	0.027
MCH (pg)	0.79
Ferritin (ng/ml)	0.95
SI (µ/dl)	0.71
TIBC (mg/dl)	0.26
Mentzer	0.80
Shine and Lal	0.96
England-Frazer	0.79

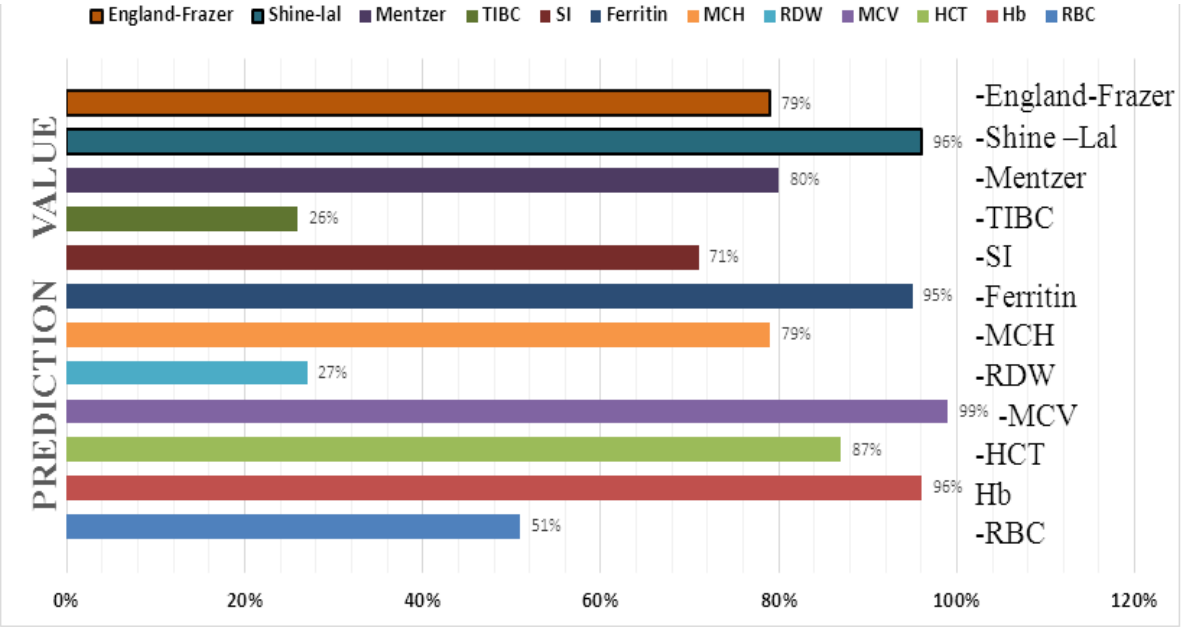

Fig. 3: The prediction value of each index

4- DISCUSSION

Mentzer, Shin-lal and England-Frazer introduced a couple of methods for IDA diagnosis. However, there are varied conflicting data about these indexes. Hence, the current investigation aimed to compare the prediction values of 12 out of 28 different indexes to find out which indexes are most reliable for IDA diagnosis (12, 13).

According to the findings, RDW, MCV and MCH were significantly lower in IDA cases as compared to the healthy controls, which coincides with the previous reports.(14) Moreover, this study showed that MCV followed by ferritin can be considered as the strongest index for the diagnosis IDA.

Melo et al. assessed a wide range of indexes in 2278 cases revealing that RDW is a robust index for IDA prediction (15).

On the other hand, Aysel Vehapoglu et al. evaluated diverse indexes in 290 1-16-year-old children and they showed that Menzer index is the most dependable index for IDA diagnosis (12).

Qurtom et al. evaluated RDW on 103 healthy, 69 IDA, 73 thalassemia children and 71 affected by other hemoglobinopathies. They found that RDW is the most reliable index in IDA and thalassemia (16).

In a study on Iranian population, by Jahangiri et al., 907 patients aged more than 18 years who were diagnosed with IDA or β thalassemia trait were selected to be involved in detecting the discriminating indices. The diagnostic performance of twenty-six previously known discrimination indices plus two new indices were introduced in order to discriminate between β thalassemia trait and IDA (13). It was suggested that performing cluster analysis in order to discriminate differential indices is useful with a similar diagnostic presentation. But in our study we have introduced simple and non-consuming time methods to diagnose IDA in children.

In another study in Egypt, 300 Egyptian pediatric patients with β-thalassemia trait or IDA were involved. The findings demonstrated that the Mentzer and Ehsani index had the highest diagnostic accuracy (100%) followed by Sirdah (97.5%), Sirvistava (95%), MDHL (92.5%), Green and King (90%), Recierca (90%), and Matos (70%) (17).

Our results were different from those of that study, since in that study beta thalassemia minor children were involved.

In our investigation, the prediction value of the RBC indexes for the differentiation IDA were as follows: MCV (99%), HB (96%), Ferritin (95%), HCT (87%) MCH (79%) Serum Iron (71%), RBC count (51%), RDW (27%), TIBC (26%). The prediction values of the formulas were as follows: Shine and Lal (96%), Mentzer (80%), and England-Frazer (79%). According to our data MCV and serum ferritin, being parallel to Shine and Lal, are useful and simple methods for the detection of iron deficiency anemia. Similar to our results, Shine and Lal index has been, previously, confirmed to have a great prediction value in detecting β-thalassemia carrier eminence in the broad-spectrum of population (18).

In this line, it has been revealed that amongst different indices, Shine and Lal has been found to have a sensitivity of 100% and has been recognized as the most sensitive index for screening of beta Thalassemia trait by some researchers (19).

Taking these findings together, we can suggest that a simple selective index such as Shine and Lal and serum ferritin might be very beneficial for screening IDA. These indexes can also be implemented in parallel for the diagnosis of Beta Thalassemia trait (19).

5- CONCLUSION

According to our findings, it is possible to diagnose IDA by a single CBC test accompanied by Ferritin measurement. Contemporary strategies for IDA diagnosis are expensive. Thus, it is valuable to change the strategies in the IDA diagnosis scheme and make it more affordable for patients specifically for those with financial constraints. This strategy may also be appropriate for the diagnosis of beta thalassemia trait.

6- COMPETING INTERESTS

None**.**

7- ACKNOWLEDGEMENT

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