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Evaluation of the sensitivity and specificity of MCH and MCV for screening of Beta thalassemia minor

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ABSTRACT

Introduction: Beta thalassemia minor (BTM) is a hypochromic and microcytic anemia that is determined by reduced mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH). The important screening methods for this disease are lack of patient recovery after 2 months of iron therapy and increased Hemoglobin A2 (HbA_2). In this study, we evaluated the sensitivity and specificity of MCH and MCV for diagnosis of BTM.

Methods: This cross-sectional study was performed among patients with BTM. CBC samples were taken and hematological parameters were measured. Two months of iron therapy and measurement of HbA_2 were carried out for definitive diagnosis of beta-thalassemia. After definitive diagnosis, the specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV) for MCV and MCH were calculated. To investigate the relationship between HbA_2 and hematological parameters (MCV and MCH), the linear regression test was performed using the SPSS18 software.

Results: From 300 patients, 154 (51.3%) were men and 146 (48.7%) women. According to the results, the highest sensitivity was associated with MCH with 90% sensitivity and specificity, respectively. Linear regression analysis showed the negative correlation -0.53 and -0.51 between HbA_2 and MCV, and MCH, respectively.

Conclusion: According to the results, using parameters like MCH are more appropriate than time consuming and expensive HbA_2 measurements for diagnosis of BTM. However, none of the aforementioned parameters showed 100% specificity and sensitivity.

Introduction

Thalassemia is one of the most common single gene disorders in the world, and about 1.5 percent of the world's population are living with this disease (1, 2). It is caused by a defect in the synthesis of globulin which is results in decreased hemoglobin synthesis and congenital hemolytic anemia (3). Various types of thalassemia depend on the involved chain. It is reported that alpha and beta thalassemia are the most common types. Based on the degree of impairment in the beta chain gene, three phenotypes of thalassemia are observed, including : Thalassemia major or Cooley's anemia, also called Mediterranean anemia, Thalassemia intermedia and Thalassemia minor or Thalassemia carrier which is a beta thalassemia trait (4). BTM is a mild form of thalassemia in which only one of the beta chains is defective, and the symptoms are mild: some cases are asymptomatic and only havelaboratory demonstrations. In this type of thalassemia, peripheral blood smear shows microcytic- hypochromic anemia with anisocytosis, poikilocytosis, tear drop cells with sharp projection and sometimes nucleated red blood cell (RBC)(5). Quatification and detection of hemo-

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globins are often examined by cellulose acetate electrophoresis and DE-52 microchromatography or HPLC. Molecular diagnosis of beta thalassemia often includes PCR-based techniques. Important methods used for these purpose are Reverse Dot Blotting method and Primer-Specfic-Amplification (PSA). If the examination does not determine the type of mutation, beta gene sequencing could be used to detect mutations (6-8). Prenatal diagnostic methods are amniocentesis which is usually done around 15-18 weeks of pregnancy, or examination of chorionic villus in week 11. Fetal cells and fetal DNA analysis could be useful for diagnosis (9). Prevalence of BTM was reported about 4% in Iran which is higher than the prevalnce of BTM-related gene (1.5%). The prevalence of BTM in the province of Mazandaran, Sistan and Baluchestan, Hormozgan and Kerman was high, and the lowest rate was in four provinces of Tehran, Khorasan, Hamedan and Yazd (10). MCV and MCH are the blood parameters representing the average size of RBCs and hemoglobin in RBCs, that are both reduced in BTM and cause microcytic hypochromic anemia. HbA_2 is one of the human hemoglobin types that is normally 1.5 to 3.5 percent, and consists of two β and δ chains. In patients with defects in the construction of the beta chain, the amount of this hemoglobin increases. The current study was done to assess the specificity and sensitivity of MCH and MCV for diagnosis of BTM, and also evaluate the association of HbA_2 with MCV and MCH.

Methods

Patients

In this cross-sectional study, 300 BTM patients referring to Sina laboratory in Sanandaj were included. According to the previus studies, the BTM criteria included hypochromic-microcytic anemia with MCV<80 and MCH<26.5 (11, 12). Definitive diagnosis was based on the lack of response to iron therapy for two months and increased HbA_2.

Sampling and measurement of hematological parameters

Blood samples were taken from patients and CBC was performed by cell counter device (Mindray, China). MCV and MCH parameters were extracted, and the data were entered into the software for analysis. Measurement of HbA_2 was done by electrophoresis for definitive diagnosis of BTM. Sensitivity, specificity, PPV, NPV and Youden's index of MCV and MCH in the diagnosis of BTM was calculated.

$$Sensitivity = \left[\frac{true\ positive}{(true\ positive + false\ negative)}\right] \times 100$$

$$Specivity = \left[\frac{true\ negative}{(true\ negative + false\ positive)}\right] \times 100$$

$$PPV = \left[\frac{true\ positive}{(true\ positive + false\ positive)}\right] \times 100$$

$$NPV = \left[\frac{true\ negative}{(true\ negative + false\ negative)}\right] \times 100$$

$$Youden's\ index = (Sensitivity + specificity) - 100$$

Statistical analysis

Data were analysed by the SPSS 18 software using the t-test and regression test.

Results

From 300 patients, 154 (51.3%) were men and 146 (48.7%) women. Table 1 shows the results of hema-

Table 1. Hematological findings of BTM patients

	MCV	HbA_2	MCH	Age
Mean	68.7	4.32	21.5	38.26
Std. Error	0.40	0.08	0.15	0.61
Std. Deviation	7.05	1.46	2.7	1.05
Variance	49.71	2.14	7.3	112.16

Table 2. Sensitivity, specificity, PPV, NPV and Youden's index of formulas

	Sensivity	specificity	PPV	NPV	Youden's index
MCV	87.71	44.44	83.33	53.33	32.15
MCH	90.58	58.44	86.32	68.18	49.02

tological parameters of BTM patients. MCH had the highest sensitivity and specificity in the diagnosis of BTM. Evaluation of MCV and MCH sensitivity and specificity showed that MCV was more sensitive and specific than MCH, with 90% sensitivity and 58% specificity, versus 88% and 44% (Table 2).

Discussion

The best diagnostic method for BMT, which is a hypochromic-microcytic anemia, is measurement of HbA_2 and mutation in beta globin gene, but these tests are time consuming and expensive. Therefore, using other hematological parameters reported in CBC results, seems to be more effective and economic (13). Results of this study showed 90.58% and 87.71% sensitivity, and 58.44% and 44.44% specificity for MCH and MCV, respectively; in MCH=26.5 pg and MCV=80 fl cut-off point. Thus, unlike sensitivity, the specificity of MCH and MCV is low for Screening BTM. Many studies have been conducted in this regard. In our previous study, we evaluated the formulae based on RBC indices in differentiating between iron deficiency anemia and beta thalasemia minor, and suggested the King-Green formula (K and G)= MCV×RDW/Hb×100 for differentiating between them, because of its high sensitivity (14). In the present study, it was shown that the use of MCH and MCV can be helpful due to their high sensitivity in screening BTM, although, their sensitivity is not 100%. In a study by Karimi and colleagues (11), the highest sensitivity for MCH was reported similar to our study,but they reported 98.5% sensitivity for MCH in the diagnosis of BTM unlike our result which was 91%. This contrast may be due to differences in sample size and patients. In the study of Pranpanus and colleagues which was carried out on pregnant women, 95.6% sensitivity in the diagnosis of BTM was reported for MCH (12), that was consistent with our result. The advantage of our study was using proven cut off points for MCH and MCV based on previous studies, while in many studies it was calculated based on common values of sensitivity and specificity. Measurement of MCV and MCH could be helpful in the diagnosis of BTM without measuring HbA_2.

Conclusion

In conclusion, using MCH could be beneficial in the diagnosis of BTM because of its high sensitivity, low cost and easy measurement.

Ethical disclosure

All the data were extracted from the records.

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Author contributions

All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Conflict of interest

The authors declare that they have no conflict of interest.

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