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Diagnostic Test Validity of MCV for Determination of Thalassaemia Carrier in Bangladesh

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Abstract

Background: Mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) of red blood cell is the useful diagnostic test which is performed during routine blood examination. **Objective:** The purpose of the present study was to measure the diagnostic test validity of MCV for the determination of thalassaemia carrier. **Methodology:** This analytic cross-sectional study was carried out in the Department of Pediatrics and Department of Medicine at MAG Osmani Medical College Hospital, Sylhet, Bangladesh from September 2007 to January 2009 for a period of one year and five months. Siblings and cousins of beta Thalassemia major and Hb- E -beta Thalassemia satisfying the selection criteria were enrolled. The detailed history and thorough physical examination were done meticulously. Five (5) mL blood was drawn from each case and control for determination of MCV and Hb-Electrophoresis. **Result:** Total 63 were enrolled as cases and total 65 were enrolled as controls. Sensitivity, specificity, positive and negative predictive value of MCV in determination of thalassemic carriers were 92%, 89.2%, 89.2% and 92% respectively. The area under the curve value was 0.094 (0.035 to 0.152). **Conclusion:** In conclusion the diagnostic test validity of MCH and MCH is high in determination of Thalassemic carrier. [Journal of National Institute of Neurosciences Bangladesh, 2016;2(2): 94-97]

Keywords: Diagnostic test; validity; mean corpuscular volume; mean corpuscular haemoglobin

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Introduction

Hemoglobinopathies are a major health problem in many areas of the world[1]. Two of the most prevalent hemoglobinopathies are sickle hemoglobin (HbS) and beta thalassemia. Thalassemia is a molecular abnormality with underproduction of one of the globin chains[2]. In Bangladesh 7% population is thalassemic carrier[3]. Determination of Thalassemic carrier is the mainstay of prevention.

Red cell indices provide valuable tool for preliminary screening of thalassemia traits[4]. Thalassemic traits in general have reduced mean corpuscular volume (MCV) and reduced mean corpuscular hemoglobin (MCH) with normal mean corpuscular hemoglobin concentration (MCHC). Specific cut off points for each index varies from laboratory to laboratory. Some laboratories

concentrate on both reduced MCV and MCH and some on MCV or MCH alone[5]. The purpose of the present study was to determine sensitivity, specificity, positive & negative predictive values of MCV in the determination of thalassemic carrier like beta thalassemia major and haemoglobin E beta thalassemia.

Methodology

This present study was designed as analytical cross-sectional study. This study was carried out in the Department of Pediatrics and Department of Medicine of Sylhet MAG Osmani Medical College Hospital, Sylhet, Bangladesh from September 2007 to January 2009 for a period of one year and four months. The siblings and cousins of diagnosed cases of beta thalassaemia major and Hb E beta thalassaemia with the age group of 1 to 20 yrs who were presented with the HbA2 level more than 3.5% were selected as case group and those who were presented with HbA2 less than 3.5% were selected as control group. Iron deficiency anemia diagnosed clinically by moderate to severe pallor, angular stomatitis, smooth tongue, koilonychias, hepatomegaly and subjects below 1 year were excluded from this study. Both case and control groups were selected by systematic random sampling by choosing every 2nd case. Siblings aging more than l year, first degree cousins of the patient diagnosed as beta thalassemia, E-beta thalassaemia by Hb-Electrophoresis were interviewed and detailed history was taken and thorough physical examination were done; 5ml blood was taken for MCV measurement and Hb-electrophoresis. Two (2) mL was introduced into automated cell counter in haematology laboratory of private diagnostic centre in Sylhet (Medinova Medical Service Ltd., Sylhet and Popular Diagnostic Center Ltd., Sylhet) for MCV & MCH and three (3) mL anti-coagulated blood was sent to Dhaka in two private diagnostic laboratories (Medinova Medical Service Ltd., Dhanmondi, Dhaka and Popular Diagnostic Center Ltd., Dhanmondi, Dhaka) by air incubated in freeze for Hb electrophoresis. MCV test was carried out by SYSMEX XT1800i cell counter. Hemoglobin electrophoresis is carried out by Serbia Automated System on agarose gel (Hydragel). Controls were also investigated for MCV and Hb-Electrophoresis. Sensitivity, Specificity, positive and negative predictive values were calculated. Data were collected by a structured questionnaire were analyzed and interpreted duly using computer software SPSS 20.0. Informed written consent was taken before data collection. Permission from the local Ethical committee of SMAGMOC was taken.

Results

A total number of 128 subjects were recruited for this study of which 63 subjects were in case group and the rest 65 subject were in control group. MCV in cases and control group were 68.2±2.3 fl and 86.2±3.2 fl respectively. There was no significant difference between case & control group in MCV (p=0.995) (Table 1).

Table 1: Mean Values of MCV among the Study Population (n=128)

Variables	Group		P value
Mean±SD)	Case	Control	
MCV (fl)	68.2±2.3	86.2±3.2	0.995

fl= femtolitre,

Among the 63 cases MCV was positive in 58(92.1%) cases and negative in 5(7.9%) cases. Again, among 65 control group MCV was positive and negative in 7(10.8%) cases and 58(89.2%) cases respectively. The association between these two group was statistically significant (p=0.0001) (Table 2).

Table 2: Comparison of MCV and Hb-Electrophoresis for Detection of Thalassaemia Carriers (n=128)

MCV	Case	Control	Total	P value
Positive	58(92.1%)	7(10.8%)	65(50.8%)	
Negative	5(7.9%)	58(89.2%)	63(49.2%)	0.0001
Total	**63(100.0%)**	**65(100.0%)**	**128(100.0%)**	

Sensitivity and Specificity of MCV in the diagnosis of thalassemic carriers were found 92% and 89.2% respectively & were high. The Positive predictive value and Negative predictive value of MCV in the diagnosis of thalassemic carriers were found 89.2 % and 92% respectively (Table 3).

Table 3: Diagnostic Test Validity of MCV for Detection of Thalassaemia Carriers

Variables	Values	95% CI
Sensitivity	92.0%	82.4 to 97.4%
Specificity	89.2%	79.1 to 95.6%
Positive Predictive Value	89.2%	80.4 to 94.4%
Negative Predictive Value	92.0%	83.3 to 96.4%
Accuracy	90.6%	85.5 to 95.7%

*95% CI=95% Confidence Interva

Discussion

It is very difficult task to detect the thalassemic carrier by screening test[6]. These are related to the heterogeneity of beta thalassaemia. The absence of a

single test is still a scarcity to cover all beta-thalassemia variants. It has been well established that the most accurate tests for the detection of thalassemic carriers are genetic detection and globin chain determination[7]. Both of which are either very expensive or not available for screening programs in third world countries like Bangladesh[8].

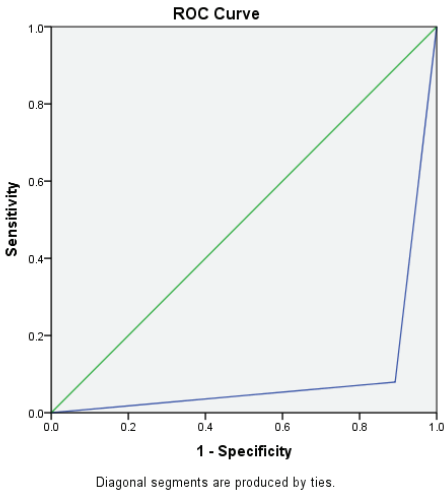

Figure I: The ROC curve for MCV value for Detection of Thalassaemia Carriers

Carrier diagnosis involves the accurate measurement of MCV, MCH, HbA2 and HbF values[9]. Thalassemic traits in general have reduced mean corpuscular volume (MCV). MCV is used in determination of thalassemic carrier in high rate[10]. The present descriptive study showed that MCV alone was 92% sensitive, 98.2% specific, positive predictive value was 89.2% and negative predictive value was 92% for determination of thalassemic carriers which is considered high. A similar study was performed on 1286 antenatal women in India using MCV (<77fl) for determination of thalassemic carrier, where sensitivity and specificity was 98% and 92% respectively[11]. The increased sensitivity in this study group is probably due to large sample size and selective study group (women). The result of this study supports the result of current study.

During the past few years, several new discoveries mostly arising from human patients or mouse models have highlighted the implication of iron metabolism. Components in hereditary microcytic anemia are transported from intestinal absorption to its final inclusion into heme[12]. Degree of reduction of MCV and MCH in iron deficiency tends to parallel the severity of the anemia which contrasts with most cases of heterogygous thalassemia in which the MCV and MCH are disproportionately low[13]

Table 4: Value of Area Under the Curve of MCV value for Detection of Thalassaemia Carriers

Area	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
		Lower Bound	Upper Bound
0.094	0.0001	0.035	0.152

*The test result variable(s): MCH_MCV has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased; a. Under the nonparametric assumption; b. Null hypothesis: true area = 0.5

However, it may be recalled that another method of carrier detection is NESTROFT (Naked eye single tube red cell osmotic fragility test). In a recent survey in India on 1048 antenatal women sensitivity specificity, positive and negative predicative values of NESTROFT were 91.0%, 95.0%, 55.0%, 99.0% respectively[14]. The result of this study has similar result with the current study. A hospital based descriptive study was performed where sensitivity, specificity, positive and negative predictive values of NESTROFT were 94.3%, 88.6%, 89.1% and 94.0%; these findings are in conformity with the result of current study[15].

This present study has some limitations. Study was carried out in Sylhet where Hb electrophoresis facility is not available. Transportation of blood sample might cause some alteration of result. Sample was selected from hospital relation and sample size was small. Furthermore, iron deficiency anemia can't be excluded by laboratory test by RDW due to more financial burden on the study. The study includes cousins and siblings of both beta thalassemia major and Hb-E- beta thalassemia. Hb-E electrophoresis facility is not available in Sylhet, available only in Dhaka city of Bangladesh during the study period.

Conclusion

In conclusion sensitivity, specificity and predictive values of MCV is high in detection of thalassemic carriers like beta thalassemia major and Hb-E beta thalassemia in the age range of 1 year to 20 years. Further large scale study should be carried out to see the real scenario of the validity of the test.

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