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LETTER TO THE EDITOR

Auto-analyzer based screening of microcytic hypochromic ratio to differentiate thalassaemia and non thalassemic microcytosis

This cross sectional analytic study by auto analyzer, performing M/H ratio, helps as a screening tool for thalassaemia trait in Bangladeshi population. Among total of 150 subjects, 50 known obligate carrier of beta-thalassaemia trait and 100 patients with hypochromia and microcytosis were included. In our study, the sensitivity, predictive value and diagnostic accuracy of the M/H ratio for the beta thalassaemia trait were 96%, 90.4% and 90.4%. Thus M/H ratio is an easy, reliable and sensitive index for mass screening of beta-thalassaemia population where iron deficiency anemia is also prevalent.

Twenty percent world's population is iron deficient[1]. In our population there is a high prevalence of iron, vitamin B_{12} and folic acid deficiencies along with high incidence of Beta-thalassaemia trait[1]. WHO estimates that at least 6.5% of the world populations are carriers of different inherited disorders of Haemoglobin and in Bangladesh about 3.0% of populations are carriers of Beta thalassaemia and 4.0% are carriers of Hb-E with approximately six thousands thalassaemic children born each year[2,3]. This Auto-Analyzer Based Screening of M/H Ratio study helps to picked up all cases of Beta-thalassaemia trait with iron deficiency anaemia[4-6].

This was a cross sectional analytic study. 150 subjects of both sexes above 12 years were referred to the Department of Pathology, BICH, Dhaka and Department of Haematology, BSMMU, from 1st January 2003 to 31st December, 2005. Group I comprised of 50 subjects from 18 to 55 years (median 24 years) of known obligate carrier of beta-thalassaemia trait diagnosed by HbA_2. They have normal serum ferritin level and male to female ratio was 1.5:1. Group II was composed of 100 patients with hypochromia and microcytosis diagnosed by cell counter and peripheral blood film. HBA_2 and serum ferritin level was done among this study subject. Although we use Group I and Group II, the results were seen as an observatory manner and Group II was divided into four groups by the observation of HbA_2 and serum ferritin level. The age of Group II subjects ranged from 12-60 years (median 35 years) and male to female ratio of 1.3:1. The parents of 56% were first cousins and of 11% were related but not first cousins. The parents of 33% had no previous relationship. The haematological parameters are obtained from cell counter (Advia, USA). In our study, M/H ratio has been calculated as: M/H ratio= % of Microcytosis/% of Hypochromia[6,7]. The sensitivity, predictive value and diagnostic accuracy of M/H ratio for Beta-thalassaemia trait was calculated according to the method of Galen and Gambino[4-10].

The results are presented in Table-I and in Table-II. The M/H ratios have been implemented to identify all the cases of BTT and BTT with IDA. There were 9 false positive which actually belonged to true IDA category. The sensitivity and predictive value of M/H ratio for BTT was 96% and 90.4% respectively found from the above calculation. The diagnostic accuracy was 90.4% using this calculation. Six cases belonged to the miscellaneous (unclassified group) with normal levels HbA_2 and serum ferritin. These cases could be of α-thalassaemia trait or $\delta\beta$-thalassaemia but the exact cause could not be identified.

Table I: Haematological parameters and diagnostic tests of Group I (obligate carrier of beta-thalassaemia trait) and Group II (% Hypocromic and % microcytic)

Parameters & Diagnostic tests	Group I (n=50)	Group II (n=100)
Hb (gm/L)	125 ± 18.50	113 ± 2.35
TRBC (10^{12}/L)	5.8 ± 1.80	5.1 ± 0.85
MCV (fl)	65.3 ± 4.30	66.0 ± 7.30
MCH (pg)	20.0 ± 1.50	21.40 ± 3.20
Serum ferritin (ng/ml)	88.0 ± 5.50	85.6 ± 4.80
HbA_2	4.8 ± 0.80	3.7 ± 0.80
% Hypochromia	17.6 ± 12.0	18.0 ± 10.0
% Microcytosis	32.0 ± 15.80	27.5 ± 14.80

Table II: On the basis HBA_2 and serum ferritin level Group II (n=100) were divided into four groups. All the Haematological parameters of these groups were shown in this table.

Parameters & Diagnostic tests	BTT (n=67)	BTT + IDA (n=18)	IDA (n=09)	Misc. (n=06)
Hb (gm/L)	11.70±1.45	9.25±2.86	7.90±1.48	12.30±2.35
RBC (10^{12}/L)	5.10±0.90	4.90±0.45	4.10±0.50	5.0±0.90
MCV (fl)	66.5±3.90	63.20±7.50	66.0±4.35	83.0±7.50
MCH (pg)	22.0±2.40	18.5±3.40	20.8±2.90	28.85±2.90
Serum Ferritin (ng/ml)	117.0±10.90	6.10±2.95	2.60±3.90	85.0±7.50
HbA_2	5.10±0.90	4.0±0.40	2.25±0.60	2.90±0.40
%Microcytosis	28.60±16.80	29.80±14.80	28.10±6.60	7.80±5.90
%Hypochromia	17.6±9.80	19.20±12.60	30.3±7.10	8.40±5.90

Study with the Advia series Siemens 2120 analyzer showed, M/ H ratio as a reliable index[6,7]. Mean % microcytosis was much more increased in thalassemia (36.5%) than in IDA (28.8%; p-0.05),

while mean % hypochromacia demonstrated an opposite trend (thalassemia 3.4%, IDA 20.4%; p-0.001) with Advia. Here, mean MH ratio was higher in thalassemia (15.1) than in IDA (4.6; p-0.001)[6,7]. With a Youden index of 76.3% and a sensitivity of 99.2%, an M/H ratio value higher than 3.7 is a highly suspicious feature of beta thalassemia trait, so HbA2 must be quantified to confirm the presence of the disease. Although the specificity is 77.1%, due to its high sensitivity, less false negative results obtained when patients have a mild anemia. According to Demir, RBC count and RDWI are the most reliable discrimination indices in differentiation between BTT and IDA[8]. Our M/H ratio showed similarity to Urrechaga E study, with a Youden index of 76.3%[6,7]. The sensitivity, predictive value and diagnostic accuracy of this index for Beta-thalassaemia trait was found to be 96%, 90.4% and 90.4% respectively which almost match by d'Onfrio, Khattaak, M. Saleem and M-H index of Sysmex XE 5000 analyzer[6-10]. Thus proved as a cost effective and sensitive screening tool for detection of beta thalassaemia traits.

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