

Evaluation of Thalassaemia Screening Tests in the Antenatal and Non-Antenatal Populations in Singapore

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Abstract

Introduction: Haemoglobinopathy testing is performed for carrier screening and evaluation of microcytic anaemia. We evaluated the effectiveness of thalassaemia screening tests at our institution and suggest ways of improving the testing algorithm. **Materials and Methods:** A total of 10,084 non-antenatal and 11,364 antenatal samples with alkaline gel electrophoresis (AGE), capillary electrophoresis (CE), haemoglobin H (HbH) inclusion test, mean corpuscular haemoglobin (MCH) and mean corpuscular volume (MCV) were retrospectively reviewed. A subgroup of 187 samples with genetic testing was correlated with HbH inclusions and MCH/MCV. The effect of iron deficiency on percentage haemoglobin A2 (HbA2) was studied. **Results:** HbH inclusion test showed low sensitivity of 21.43% for α -thalassaemia mutations but higher sensitivity of 78.95% for $-\text{SEA}$ deletion. By receiver operating characteristic (ROC) analysis, MCH ≤ 28 pg or MCV ≤ 80 fl for non-antenatal samples and MCH ≤ 27 pg or MCV ≤ 81 fl for antenatal samples had $>98\%$ sensitivity for HbH inclusions. Above these thresholds, the probability that HbH inclusions would be absent was $>99\%$ (negative predictive value [NPV] $>99\%$). MCH ≤ 28 pg had 100% sensitivity (95% CI 95.63%-100%) for α -thalassaemia mutations and 97.68% calculated NPV in the antenatal population. Detection of haemoglobin variants by CE correlated highly with AGE (99.89% sensitivity, 100% specificity). Severe iron deficiency reduced HbA2 in haemoglobin E ($P < 0.001$) and α -thalassaemia ($P = 0.0035$), but not in β -thalassaemia. **Conclusion:** MCH/MCV thresholds have adequate sensitivity for α -thalassaemia in the antenatal population, and genotyping plays an important role as HbH inclusion test shows low sensitivity. CE without AGE, may be used as initial screening for haemoglobin variants. Our study provides contemporary data to guide thalassaemia screening algorithms in Singapore.

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Key words: Haemoglobinopathy, Mean corpuscular haemoglobin, Mean corpuscular volume

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