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Editorial Open Access

Screening for Beta Thalassaemia Carriers: A Relook

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Editorial

Thalasssaemia is an inherited disorder of haemoglobin synthesis. It is characterised by absence or reduced synthesis of one or more globin chains of human haemoglobin. Public health concern about carrier detection is not only confined to the geographical areas with high disease prevalence but becomes a global issue because of population migration [1]. The majority of carriers are not aware of their status. The homozygous state of β0-thalassaemia results in transfusion dependent thalassaemia.

In the past, screening for thalassaemia involved methods such as osmotic fragility of red blood cells, followed with estimation of Hb subtypes by Hb electrophoresis, cutting and elution. Both these techniques are obsolete and may miss identification of thalassemia in the populations studied. Osmotic fragility tests depend upon the integrity of the salt solutions and Hb subtyping on operator skills.

Current screening of thalassaemia carriers require a multistep approach that encompasses the acronym, BHES+F: B, blood counts, blood indices, blood film; H, haemoglobin (Hb) subtypes; E, electrophoresis; S, Stability; and F, functional characteristics. In screening of classical beta-thalassaemia carriers, the first 2 steps are informative [2]. In a classical beta-thalassaemia carrier, the Hb is normal or mildly reduced, erythrocytosis occurs, red blood cells are hypochromic / microcytic and the HbA2 level is raised.

Automated blood counters are instruments commonly seen in a laboratory. The red cell indices generated on the automated blood counter is the first line for screening of thalasaemia. A mean corpuscular volume (MCV) less than 80 fl and a mean corpuscular Hb (MCH) less than 27 pg warrants further investigation for thalassaemia and a common condition iron deficiency anaemia. The MCV has been found not useful in stored samples as it gradually increases with storage. MCH however remains stable and is used in population and family screening of thalassaemia [3]. In classical carriers of beta thalassaemia, the MCV is less than 75 fl and MCH less than 25 pg respectively.

Accurate determination of HbA2 is critical for the presumptive identification of a beta thalassaemia carrier. Automated methods are available for this. Two automated methods are extensively used: cation-exchange high performance liquid chromatography (CE-HPLC) and capillary zone electrophoresis (CZE). Both these methods produce accurate and precise results in HbA2 estimation. Duplicate values in measurement of HbA2 should be within 0.2%. The estimated HbA2 level in normal persons is 2-3.4%. In classical beta-thalassaemia trait, the HbA2 is 4.1-6.3% with HbA2 level greater than 7% uncommon. In moderate and severe iron deficiency anaemia, the Hb A2 level is normal or reduced as globin chain synthesis is reduced. In screening for beta thalassaemia it is important to repeat Hb subtyping when iron replete [4]. The grey area in beta- thalassaemia carrier identification are levels 3.5-3.9%. In addition, the carriers with mild beta thalassaemia mutations such as poly A mutation (AATAA to AATAGA) may have normal HbA2 levels. It is important to confirm presence or absence of alpha and beta thalassaemia with DNA studies in those with HbA2 levels between 3.5-3.9%. In a carrier with concurrent alpha and beta thalassaemia, the MCV is 75 fl and above and MCH 25 pg and above respectively [5]. However, the Hb A2 level remains elevated.

Hb electrophoresis is now available by 2 automated techniques that incorporate cellulose acetate and gel in alkaline and acidic media. Hb electrophoresis is not used to quantify Hb subtypes. In beta-thalassaemia carrier identification, it plays a role to alert the presence of a beta-thalassaemia haemoglobinopathy. The H-inclusion test including the heat test may be informative for screening of alpha thalassaemia and presence of abnormal haemoglobins. Functional test s for abnormal haemoglobins is done in research laboratories [6].

Currently automated analysers are available for qualitative measurement of red blood cells, red blood cell indices and haemoglobin subtyping. Measurement of variables are accurate and precise with availability of validation criteria incorporating controls, reference materials and calibrated instruments. Quality control procedures including participation in external quality assurance programs have led to improved screening of beta-thalassaemia carriers.

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