Neglecting borderline HbA₂ (3.2–3.9%) may impede prevention program for thalassemia

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Carrier screening and counselling for prevention of marriage between carrier couples is cost-effective and simple way to diminish the incidence of common monogenic disorders such as sickle cell anemia and thalassemia. Mohanty et al., 2022 performed screening in tribes of Rajasthan state by solubility and NESTROFT test for the preliminary screening of Sickle cell and beta thalassemia respectively followed by the confirmatory test by Cation Exchange-High performance liquid chromatography (BioRad variant II using β -thal short program).¹ Authors have used HbA₂ > 4.0% as cutoff value for the confirmation of β -thalassemia trait and reported a very high prevalence of beta thalassemia trait (7.25%).¹ It has been seen at several instances that the beta thalassemia trait cases, having β^+ or β^{++} mutation, have HbA₂ in the range of 3.2–3.9%.² Beta thalassemia case with borderline HbA₂ is common in population with high prevalence of beta thalassemia. Therefore, several laboratories have revised the cut off value of HbA₂ to 3.5% or even 3.2% for diagnosis of beta thalassemia trait.³ Colaco et al., 2021 reported that 35.4% of individuals having borderline HbA₂ carry a molecular defect⁴ which warrants the necessity to investigate these cases at a molecular level, particularly if the partner is a carrier of beta-thalassemia. Furthermore, Indian tribes have high prevalence of alpha thalassemia (up to 97%).⁵ Beta thalassemia traits when co-inherited with alpha thalassemia may have low HbA₂ levels. Therefore, using a cut off value of HbA₂>4.0% for screening of beta thalassemia, a significant number of beta thalassemia traits can be missed.

Detection of all beta thalassemia trait cases is central to prevention program for thalassemia and therefore all cases having borderline HbA₂ must be correlated with red cell indices (RBC count, MCV, MCH and RDW) and molecular analysis of beta globin gene for confirming the status of beta thalassemia trait.

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Declaration of competing interest

None.

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References

1. Mohanty SS, Parihar S, Huda RK, Toteja GS, Sharma AK. Prevalence of sickle cell anemia, β -thalassemia and glucose-6-phosphate dehydrogenase deficiency among the tribal population residing in the Aravali hills of Sirohi region of Rajasthan state. *Clin Epidemiol Global Health*. 2022;13:100916.
2. Mosca A, Paleari R, Ivaldi G, Galanello R, Giordano PC. The role of haemoglobin A(2) testing in the diagnosis of thalassaemias and related haemoglobinopathies. *J Clin Pathol*. 2009;62(1):13–17.
3. Old J, Hartevelde CL, Traeger-Synodinos J, Petrou M, Angastiniotis M, Galanello R. *Prevention of Thalassaemias and Other Haemoglobin Disorders*. vol. 2. Laboratory Protocols. Nicosia (Cyprus): Thalassaemia International Federation; 2012, 2012.
4. Colaco S, Nadkarni A. Borderline HbA(2) levels: dilemma in diagnosis of beta-thalassemia carriers. *Mutat Res Rev Mutat Res*. 2021;788:108387.
5. Mukherjee MB, Surve RR, Ghosh K, Colah RB, Mohanty D. Clinical diversity of sickle cell disease in western India - influence of genetic factors. *Acta Haematol*. 2000;103(2):122–123.

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