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Transfusion-Dependent Thalassemia in Northern Sarawak: A Molecular Study to Identify Different Genotypes in the Multi-Ethnic Groups and the Importance of Genomic Sequencing in Unstudied Populations

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Abstract

Background: Although thalassemia is a genetic hemoglobinopathy in Malaysia, there is limited data on thalassemia mutations in the indigenous groups. This study aims to identify the types of globin gene mutations in transfusion-dependent patients in Northern Sarawak.

Methods: Blood was collected from 32 patients from the Malay, Chinese, Kedayan, Bisayah, Kadazandusun, Tagal, and Bugis populations. The α- and β-globin gene mutations were characterized using DNA amplification and genomic sequencing.

Results: Ten β- and 2 previously reported α-globin defects were identified. The Filipino β-deletion represented the majority of the β-thalassemia alleles in the indigenous patients. Homozygosity for the deletion was observed in all Bisayah, Kadazandusun and Tagal patients. The β-globin gene mutations in the Chinese patients were similar to the Chinese in West Malaysia. Hb Adana (HBA2:c.179G>A) and the −α3.7/αα deletion were detected in 5 patients. A novel 24-bp deletion in the α2-globin gene (HBA2:c.95 + 5_95 + 28delGGCTCCCTCCCCTGCTCCGACCCG) was identified by sequencing. Co-inheritance of α-thalassemia with β-thalassemia did not ameliorate the severity of thalassemia major in the patients.

Conclusion: The Filipino β-deletion was the most common gene defect observed. Homozygosity for the Filipino β-deletion appears to be unique to the Malays in Sarawak. Genomic sequencing is an essential tool to detect rare genetic variants in the study of new populations.