Coinheritance of Beta Thalassaemia (β^0 Filipino) and Delta Variant (HbA_2 Deventer) in Sabahan Population: A Case Series

Yuslina Mat Yusoff[1], Syahzuwan Hassan[1], Nizmah Mahani Mokhri[2], Nur Aisyah Aziz[1], Faidatul Syazlin Abdul Hamid[1], Ezalia Esa[1], Rahimah Ahmad[1], Zubaidah Zakaria[1]

[1]Haematology Unit, Cancer Research Centre, Institute for Medical Research, Jalan Pahang, 50588 Kuala Lumpur, Malaysia
[2]Hospital Queen Elizabeth, Karung Berkunci No. 2029, 88586 Kota Kinabalu, Sabah, Malaysia

Mutations in the δ globin gene are not pathologically significant [1]. However, coinheritance of β and δ thalassaemia can mask the diagnosis of β thalassaemia trait as it causes HbA_2 level to be lowered [2,3]. Here, we reported 5 unrelated cases of compound heterozygous β^0 Filipino ~ 45 kb deletion and codon 67 (GTG>ATG) HbA2 Deventer in Sabahan population.

Cases of β°-thalassemia traits with unusual low HbA_2 were reviewed. These cases were initially referred to our laboratory for definitive diagnosis of β-thalassemia trait. Haematological parameters and Hb analysis were carried out at the referral hospital. Genomic DNA was extracted from the peripheral blood. Multiplex ARMS and Gap PCR were done to detect common point mutations and deletions for both alpha and beta globin genes. Sanger sequencing was performed to detect mutations in delta globin gene.

Patients' consist of 4 males and 1 female aged between 25-38 years old. All of them are indigenous Sabahan (2 Kadazans, 1 Murut, 1 Dusun and 1 Sungai). Their haemoglobin level ranges between 10.8 – 12.8g/dl. Hb analysis findings of HbA_2 and HbF level ranges between 2.9 – 4.0 and 2.2 – 9.4g/dl respectively. Molecular findings revealed heterozygous state of (β)°-thal, Filipino ~45Kb deletion, NG_000007.3:g.[66258_184734del];[66258_184734=] and heterozygous state of Codon 67 [GTG>ATG] Hb A_2-Deventer mutation, NG_000007.3:g.[63512G>A];[63512G=] (Figure 1 and 2).

Detection of 5 unrelated cases of HbA_2 Deventer may suggest that this delta variant is common among indigenous Sabahan. Since beta thalassaemia is also common in the population, more attention should be paid during diagnosis. Identification of delta variant in beta thalassaemia carrier is important because coinheritance of beta and delta thalassaemia results in a less

elevated HbA2 level. Therefore, molecular testing of thalassemia carrier state in the case of borderline HbA_2 is warranted to avoid misdiagnosis of beta thalassaemia carriers.

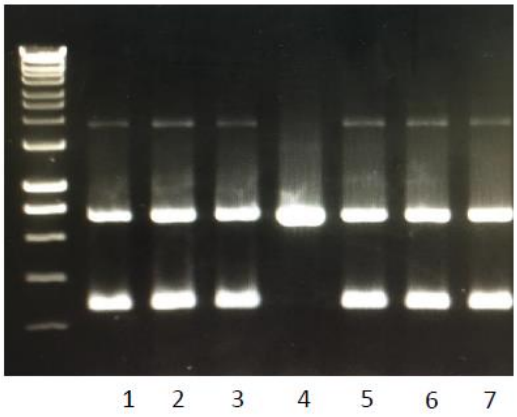

Fig. 1: Gel electrophoresis (lane 1-3 and 5-7) showing heterozygous β^0 Filipino deletion.

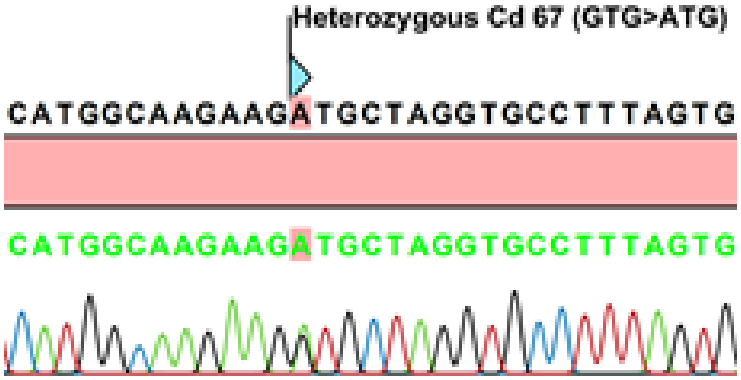

Fig. 2: Chromatogram of δ-globin gene sequencing showing heterozygous $\delta/\delta^{Cd67(GTG>ATG)}$

Keywords: coinheritance, delta variant, beta thalassaemia, β^0 Filipino, HbA_2 Deventer

***Correspondence:** yuslina@imr.gov.my

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