A Wide Spectrum Study of α-Globin Chain Variants: Cases from the UK

Khalil MSM, Timbs AT, Henderson SJ, Schuh A, El-Khawanky MM, Old JM.

Abstract:

ABSTRACT Over many years, cases of suspected α-globin chain variants were collected from different parts of the UK. The suspicion was based on the clinical picture, high performance liquid chromatography (HPLC) variant percentage, retention time (RT) and isoelectric focusing (IEF). DNA sequencing and the restriction enzyme EaeI were used for definitive diagnosis. One hundred and forty-eight variants were confirmed on one or both of the two α-globin genes (HBA2, HBA1). These cases were identified as 46 different α-globin chain variants. The most common variants were Hb J-Meerut [HBA2: c.362C>A (or HBA1)] (10.1%) and Hb Q-India (HBA1: c.193G>C) (8.1%), followed by Hb J-Paris-I [HBA2: c.38C>A (or HBA1)] and Hb Manitoba II (HBA1: c.309C>A) (7.4% for each). Other α variants were detected at lower frequencies. Two novel alleles were also detected: Hb Walsgrave [α116(GH4)Glu!Val (HBA2: c.350A>T)] and Hb Coombe Park [α127(H10)Lys!Glu (HBA2: c.382A>G)]. The majority of the ethnic origin was Indian. The positive predictive value for a variant identification by HPLC-RT analysis was 65.9%, 41.9% by IEF, and using both RT and IEF, the value was 72.1%. The number of variants was higher in HBA1 than in HBA2 genes and in exons 1 and 2 than in exon 3. There was no clustering of mutations in consecutive codons. This study, the characterization of a wide spectrum of α-globin chain variants, can facilitate the presumptive diagnosis of these variants prior to screening by a panel of amplification refractory mutation system-polymerase chain reaction (ARMS-PCR), and a definitive diagnosis by DNA sequencing.

Keywords:
a-Globin gene; α variants; DNA sequencing; hemoglobin (Hb) DOI: 10.1080/03630269.2020.1783288

Published In:

Hemoglobin. , 44(3), 195-200