Alpha-thalassaemia trait as a cause of unexplained microcytosis in a South African population

To the Editor: I read the article by Loonat et al.[1] with interest. In the early 1980s a study was undertaken at Red Cross War Memorial Children’s Hospital, Cape Town, South Africa (SA), to assess the frequency with which a low red cell mean corpuscular volume (MCV) was associated with the presence of thalassaemia or an abnormal haemoglobin.[2] Between January 1979 and December 1980, 730 patients with an MCV of ≤60 fl were investigated. Forty-six (6.4%) were found to carry a β-thalassaemia gene and 20 (2.7%) had an abnormal haemoglobin, most commonly Hb E. The prevalence of thalassaemia was highest in individuals of mixed ethnic origin, and abnormal haemoglobins were found exclusively in this population, although the numbers of white and black patients were much smaller in comparison. Alpha-thalassaemia was not tested for, as the technology was unavailable at the time owing to cost constraints. Nevertheless the findings confirmed that patients with persistent unexplained microcytosis/hypochromia should be screened for thalassaemia and haemoglobin variants.

A further survey of blood donors of mixed racial origin was undertaken to determine the prevalence of inherited haemoglobin disorders in this population more accurately.[3] Globin synthesis studies and DNA analyses were performed in donors with microcytosis or hypochromia or both associated with normal ferritin, Hb A, and Hb F levels. DNA was analysed by Southern blotting and hybridisation with an α-globin complementary DNA probe and a γ-globin genomic probe. In 989 donors screened, Hb S and E were the commonest structural variants detected, each with a prevalence of 1%. Hb C was detected in just 1 donor. Seven donors had β-thalassaemia trait (0.8%) and 2 had hereditary persistence of fetal haemoglobin. A total of 45 donors had DNA analyses. Thirty-three were documented as having α-thalassaemia, the majority (n=24) of whom were heterozygous for the α (–α/) haplotype, with an observed frequency of 0.023.

I am not clear whether other haemoglobin variants, in particular Hb E, were screened for in the study by Loonat et al.[1] Hb E was first described in Thailand and is common in South-East Asia. Many South-East Asians who were brought to the Cape in the early years of settlement were from Indonesian islands, and presumably this accounts for the presence of Hb E in the mixed-race population of the Western Cape. The heterogeneous and homozygous states for Hb E are benign conditions clinically, but individuals often have red cell microcytosis and/or hypochromia.[4] The βE gene results in inefficient synthesis, as borne out by studies that show decreased βE globin chain synthesis,[5] and there is also evidence that the βE messenger RNA is smaller in comparison.[6,7] Nevertheless the findings confirmed that patients with persistent unexplained microcytosis/hypochromia should be screened for thalassaemia and haemoglobin variants.

However, in patients with persistent unexplained microcytosis and/or hypochromia following a thorough haematological assessment, a full investigation for the presence of a haemoglobinopathy is warranted. Haemoglobinopathies are not the most common monogenic disorders in SA, but from the data summarised above it is clear that they do occur at significant frequencies in high-risk minority groups, and when detected appropriate genetic counselling can be offered. It is also important that these patients are identified, since they may receive inappropriate chronic therapy such as iron medication.

A R Bird
Western Province Blood Transfusion Service, Cape Town, South Africa
arbird27@gmail.com

6. Traeger J, Wood VG, Clagg JR, et al. Defective synthesis of Hb E is due to reduced levels of βE mRNA. Nature 1980;288(5790):497-499. DOI:10.1038/288497a0

A R Bird Western Province Blood Transfusion Service, Cape Town, South Africa
arbird27@gmail.com

6. Traeger J, Wood VG, Clagg JR, et al. Defective synthesis of Hb E is due to reduced levels of βE mRNA. Nature 1980;288(5790):497-499. DOI:10.1038/288497a0