Frequency and type of newly diagnosed haemoglobin variants in Northern Italy

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Haemoglobinopathies are the most common single gene disorders in humans[1]. Most structural haemoglobin variants typically result from a point mutation in a globin gene that produce a single amino acid substitution. Although some of these disorders are of limited clinical significance, a few important subtypes have been identified with some frequency. Homozygous HbC and HbS (sickle cell disease) produce significant clinical manifestations, whereas HbE and HbD homozygotes may be mildly symptomatic[1]. The accurate diagnosis of haemoglobinopathies and haemoglobin quantification are crucial to enable the most appropriate treatment and to preventing at-risk marriages through genetic counselling[2].

European countries have undergone a major transformation over the past decades, shifting from being emigrant nations to immigrant destinations. Immigrants in Italy come from many different areas, but in recent years there has been a rapid increase in immigration from North Africa and South-East Asia. As the number of immigrants continues to increase, disorders of haemoglobin chains will be increasingly prevalent, thus requiring more efficient diagnosis and triage. Since it is advisable to inform carriers and at-risk couples of their risk and the options for reducing it, screening for haemoglobin disorders should be part of basic health services in countries in which haemoglobin variants are widespread, but it should also be considered in those countries in which immigration trends are likely to increase the frequency of such variants substantially[2]. Accordingly, it is important to initiate or continue to monitor national trends, and to identify those haemoglobin variants which are more likely to be diagnosed.

We searched the database of our Laboratory Information System at the Clinical Chemistry Laboratory of the University Hospital of Verona to retrieve data on haemoglobin variants collected during a large screening programme of the general population before marriage during the period January 2006-May 2009. Venous blood from outpatients referred to our laboratory for this population screening was routinely collected in the morning after overnight fasting. Screening for haemoglobin variants was performed by ion exchange high performance liquid chromatography (HPLC) on HLC-723 G7 (Tosoh), a fully automated HPLC system using reagents and conditions specifically designed to separate and quantify HbA_2 and HbF in a 7.5-min run. The instrument also allows the presumptive identification of three of the most frequent haemoglobin variants, i.e., HbS, HbC and HbD, by assigned retention time windows[3,4]. In the presence of a haemoglobin variant, a definitive diagnosis of the disorder was established in accordance with the guidelines of the British Society of Haematology[2].

Overall, 806 patients (432 Caucasians, 296 Africans and 78 Asians) underwent the screening during the study period. Among these, 33 (4.1%) haemoglobin variants were identified, as shown in Figure 1. The most prevalent haemoglobin variant was HbS (2.8%), followed by HbC (0.7%) and HbE (0.4%), which is in agreement with the increasing migratory flux from Central Africa and Asia towards Italy. The frequency of newly diagnosed HbS was remarkably high in Africans (19/296, 10%), whereas HbE was confined to Asian subjects (3/78, 4%).

According to a global epidemiological database, haemoglobin disorders represent a significant health

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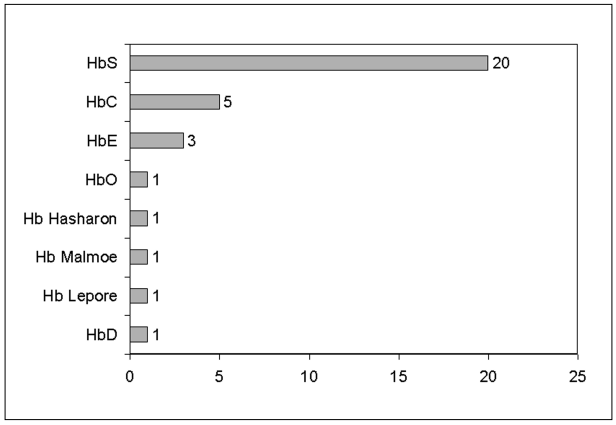

Figure 1 - Relative frequency of haemoglobin variants identified in 806 patients referred for screening before marriage in Northern Italy.

problem in 71% of 229 countries, which include 89% of all births worldwide[5]. Over 330,000 affected infants are born annually (83% with sickle cell disorders, 17% with thalassaemias). Globally, around 7% of pregnant women carry HbS, C, D Punjab or E, and over 1% of couples are at risk[5]. In this comprehensive epidemiological database, however, the frequency of haemoglobin variants in Italy was much lower than that observed in our study (0.2% versus 2.5% for HbS, <0.05% for HbC and HbE versus 0.4% and 0.1%, respectively)[5]. The results of our epidemiological investigation thereby attest that haemoglobin variants are relatively common among a population referred to our laboratory for screening before marriage, being as high as 4.1%. Closely mirroring the trend of immigration, haemoglobin variants widespread in central Africa (HbS and HbC) were those more frequently diagnosed in our laboratory. We, therefore, conclude that structurally abnormal haemoglobins constitute a significant public health problem in Italy, and that their increasing frequency is very unlikely to be reversed in the very next future due to the persistent immigration from North Africa and South-East Asia.

Key Words: haemoglobin disorders, haemoglobin variants, screening, epidemiology.

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