The Burden of Haemoglobinopathies in India - Time to Wake Up?

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Haemoglobinopathies consist of thalassaemias and variant haemoglobins. Carriers of haemoglobinopathies are partially protected against morbidity and mortality of falciparum malaria and this has resulted in their higher prevalence in tropical countries. In India, they are responsible for the largest number of genetic disorders and hence are of great public health importance. Clinically important thalassaemic disorder in India is β-thalassaemia while α-thalassaemia, although more common in tribal population, is free from morbidity. Of the several abnormal haemoglobin molecules, three which are widely prevalent in India include: Hb S, Hb E and Hb D.

The cumulative gene frequency of haemoglobinopathies in India is 4.2%. With a population of over one billion and a birth rate of 28 per thousand, there are over 42 million carriers and over 12,000 infants are born each year with a major and clinical significant haemoglobinopathy. Out of these, β-thalassaemia major and clinically significant sickle cell disorders account for almost equal numbers.

β-thalassaemia is detectable in almost every Indian population, however, it is seen with highest frequency in north-west and far east. Sindhis, Gujaratis, Bengalis, Punjabis and Muslims account for most of β-thalassaemia. Carrier state for β-thalassaemia in India varies from 1-17% with an average of 3.2%.

α-thalassaemia is most widely prevalent in the tribal population with a frequency of 1-40% in Andhra Pradesh and Gujarat. Fortunately, the genotype of α-thalassaemia prevalent in India is α+, which is clinically silent both in the heterozygous as well as homozygous state. Hence, it is free from morbidity.

Lehman and Cutbush described the first case of Hb S from tribals of southern India in 1952. Subsequently, Hb S has been reported from various Indian states, communities and ethnic groups with an average frequency of 4.3% (range : 0-44%). Sickle gene in India is mostly found among Dravidian and pre-Dravidian tribes. However, with migration and mixing between the tribal and non-tribal, Hb S is now documented from most caste groups and states. Hb S is predominantly found in central India i.e. Vidarbh in Maharashtra, Madhya Pradesh, Orissa, Andhra Pradesh, Gujarat and to a lesser extent in Tamil Nadu, Karnataka, Kerala and Uttar Pradesh. It is rare in Bihar, West Bengal, north-eastern states, Punjab, Haryana, Himachal Pradesh, Rajasthan and Jammu & Kashmir.

Five distinct haplotypes of Hb S gene have been described with prevalence in specific geographical areas. Four of these i.e. Benin, Senegal, Bantu and Cameroon are the African haplotypes while the 5th one is the Saudi Arabia / Indian haplotype. As the name suggests, this is the haplotype which is prevalent in India. This haplotype is associated with higher levels of Hb F which ameliorates the clinical severity. High frequency of α-thalassaemia present in the state of Gujarat also helps in making the clinical severity of sickle cell disease milder. Unfortunately, the same does not apply to the sicklers of Vidarbh in Maharashtra where α-thalassaemia is rare. Thus, the clinical severity of sickle cell disease in India is milder with compare to Africa but highly variable within the country itself.

Hb E is widely distributed in north-eastern states of India. It was first reported amongst the Assamese with carrier rate of 23% among the totos. The Ahoms of Assam have the gene frequency of 46.4%, one of the highest for any abnormal haemoglobin reported from any population in the world. Interestingly, the prevalence of Hb E carrier state is below 1% in Mizoram. In West Bengal varies from 3-33% while it is almost non-existing in southern India.

Hb D is predominantly seen in Punjab, Uttar Pradesh, Gujarat and Jammu and Kashmir. It is most prevalent in Punjabi, Sikh and migrant Sindhi population. Fortunately, Hb D in both heterozygous and homozygous form is clinically asymptomatic. Even when co-inherited with β-thalassaemia, the presentation is similar to thalassaemia minor. The only clinically significant form of Hb D is when it is co-inherited with Hb S producing a severe sickle cell disease. Fortunately, no population in India has high frequency of both Hb D
and Hb S. The overall gene frequency of Hb D in India is below 1%.15,17,21

Several other rare types of thalassaemic disorders and haemoglobin variants have been sporadically reported from India. These include β-thalassaemia, hereditary persistence of foetal haemoglobin, Hb Lepore, Hb Q, Hb K, Hb J, Hb M, Hb Chandigarh, Hb Sunpraire, Hb Koyadora etc. Majority of these are rare and of not much clinical consequences.11

In this issue, Balgir RS from Divisional of Human Genetics, Regional Medical Research Centre (ICMR), Bhuvaneshwar, Orissa, have reported the spectrum of haemoglobinopathies in their state.24 This publication, once again, highlights a major public health problem of clinically significant haemoglobinopathies in central eastern part of India. The presence of thalassaemia and Hb E in the eastern costal part of Orissa and that of Hb S in the central, western and southern Orissa has great historical importance as it is based on the migration or flow of different population from different regions of India. The article also brings out that, at least in Orissa, sickle cell gene is prevalent even in general caste, unlike the reports from the other parts of the countries where the problem is chiefly confined to schedule tribes or castes.

What is the importance of this wealth of information to the clinicians? Amongst the widely prevalent nutritional anaemias, hidden is the problem of thalassaemia and abnormal haemoglobins. Poor infrastructure of medical laboratories in this country and the cost involved interfere with their diagnosis. Lack of knowledge regarding their prevalence, poor facilities for their diagnosis, inability to carry out genetic counseling and presence of only occasional centres for prenatal diagnosis have resulted in failure of community control of birth of these totally preventable dreadful genetic disorders. Funds and facilities do not permit effective treatment of thalassaemia and sickle cell disease. Cure by transplantation is available only to a handful. Against the bleak background, an informative article of this nature should help in reminding the clinicians and controlling agencies that a lot still remains to be done.

Unlike many other genetic disorders where couple at risk cannot be easily diagnosed, thalassaemia and abnormal haemoglobin give a tremendous opportunity for effective control of birth. There has to be only a political will to implement and achieve this. I hope, the concerned people wake up. The earlier the better.

REFERENCES


