

Thalassaemia in Indian Scenario and Newborn Screening: Mini Review

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Abstract

Haemoglobinopathies are important diagnostic challenge in newborn period. Diagnosis of Thalassaemia poses huge burden in medical, social, financial aspects of lives of the diseased. Newborn babies suffering from such diseases needs to be diagnosed at earliest period and with certainty. High Performance Liquid Chromatography (HPLC) and Iso Electric Focusing (IEF) are two most important diagnostic modalities in Thalassaemia.

Keywords: Thalassaemia; High Performance Liquid Chromatography (HPLC); Iso Electric Focusing (IEF)

Haemoglobinopathies

Hemoglobin is a tetramer consisting of 2 pairs of globin chains. Hemoglobinopathies results due to derangements in such structures. There are approximately 800 variant hemoglobins. The most common and useful clinical classification of hemoglobinopathies is based on nomenclature associated with alteration of the involved globin chain [1].

Thalassaemia

The thalassemias are an autosomal recessively inherited group of disorders of haemoglobin synthesis characterized by the absence or reduction in output of one or more of the globin chains of haemoglobin. Substitution of one or more amino acids in the globin chains results in structural abnormalities of the haemoglobin molecule [2]. The β thalassemias and their interaction with structural haemoglobin (Hb) variants like HbS and HbE are a major health problem in India. Children inheriting these β -thalassemia major syndromes most often have a severe disease and a transfusion dependent survival from early childhood. It is therefore important to accurately identify carriers of these disorders and offer the option of preventive measures by prenatal diagnosis to couples at risk of having a child with severe disease [3].

Indian Scenario

The severe and fatal form of α -thalassemia, Hb Bart's hydrops Fetalis is not seen in India. The commonest α gene defect in our population is a single α gene deletion. The carrier of this form of α -Thalassaemia usually get presumptively identified from the MCH, MCV and RBC count done on electronic counters, after exclusion of β -thalassaemia carriers and cases of iron deficiency anemia. However, few cases of Hb H disease have been reported where there is only one functional α gene [4]. These hereditary disorders of haemoglobin pose a massive health problem in many countries including India [5]. The distribution of specific disorders varies geographically and by community [6]. WHO figures estimate that 5% of the world population is carrier for haemoglobin disorders [7]. They cause moderate to severe haemolytic anaemia leading to high degree of morbidity and mortality. The frequency of β -thalassaemia in India ranges from 3.5

to 15% in general population. Every year 10,000 children with thalassaemia major are born in India, which constitutes 10% of the total numbers in the world [8]. The overall α gene deletion frequency is 0.05 to 0.98% but it is very high in India [9]. In west central Gujarat, it is as high as 95% [6].

The average frequency of haemoglobin S (Hb S) is 4.3% in India. The range varies from 0 - 44%. It is 0 - 18.5% in northeast zone, 0 - 33.5% in west zone, 22.5 - 44.4% in the central zone and 1 - 40% in the southern zone [6]. Sickle gene in India is mostly found amongst Dravidian and predravidian tribes [10]. Haemoglobin E (Hb E) is mostly present in the northeastern states of India [11]. Frequency of Hb E in Assam is 52%, 7% in Manipuri's and 3.33% in West Bengal [9,13]. Hb E has also been documented in people from Orissa, Uttar Pradesh, Rajasthan, Bihar and Punjab [13,14]. The frequency of Haemoglobin D (Hb D) has been reported to be 0.5 to 3.1% in different castes of Uttar Pradesh [15]. Hb D has also been reported from Bengal, Bihar, South India and Gujarat [16]. This condition was first described in a two and half year Bengali boy in the year 1938 [16]. It was realized later that a number of variant haemoglobins and/or interaction with β thalassaemia (bt) or α thalassaemia (at) can produce clinical pictures similar to β thalassaemia and the term "thalassaemia syndrome" was used to describe various conditions [17] the first abnormal haemoglobin (HbS) was first described in India in the tribal population of South India [18]. The next abnormal haemoglobin to be described was HbE in 1954 which is very commonly distributed in entire eastern India. The first description of HbE in India was made by JB Chatterjee [19]. Amongst Bengali and Assamese population. It has also been distributed in Tripura, Orissa and UP. The first survey of HbE carrier state was made amongst the Toto community Goalpara district and later a very high incidence was reported in the Thai Ahoi of Assam. High incidence has been described in Prodos of Assam, inheritance of Arunachal Pradesh. The coexistence of β and HbE gene makes the population of west Bengal vulnerable to get both β thalassaemia and HbE β thalassaemia. An impressive number of 796 cases of thalassaemic syndrome were investigated by JB Chatterjee in the School of Tropical Medicine. It was reported that 190 out of 796 (24%) cases had β thalassaemia, 526 (66%) had HbE β thalassaemia and 12 (1%) Hb- β -thalassaemia. So thalassaemia was the major public health problem in west Bengal. So recent data indicate that about 10% of the population is carrier of Hb disorder, commonly found in the heterozygous state of β -thalassaemia. Major form and symptomatic thalassaemia is Hb E β -thalassaemia.

Detection program

Most newborn screening programs employ High Performance Liquid Chromatography (HPLC) or Isoelectric Focusing (IEF) as the preferred first-line technique to make a presumptive diagnosis of a clinically significant hemoglobinopathy [6]. These methods are preferred over electrophoretic techniques such as cellulose acetate and citrate agar electrophoresis because they are more sensitive, less labour intensive and better suited for high-throughout population screening. In addition, HPLC permits quantification of Hb variants. While the sensitivity of HPLC and IEF are excellent, results and interpretation can be confounded by extreme prematurity or previous blood transfusion [6].

Conclusion

India is one of the most prevalent countries in the South-East Asia region regularly reporting Thalassaemic cases. Early detection is very important in overall management on such cases. HPLC and IEF are two most important diagnostic modalities for early detection of such hemoglobinopathies.

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