Sickling Erythrocytes: An Indian Perspective

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Since 2009, 19th June every year is marked as World Sickle cell day. As per World health organization (WHO), nearly 5% of world's population has haemoglobin disorders. Hemoglobin (Hb) is a heterotetramer with two alpha and two beta subunits. Major contributors of Hb disorders are sickle cell disease (SCD) and Thalessemia. HBB gene (Cytogenetic Location: 11p15.4) that codes for Hb beta subunit produces low levels of beta globin when mutated. This condition is known as beta thalessemia (1) while alpha thalessemia is a result of mutation in alpha subunit gene decreasing its protein levels. SCD is a group of disorders resulting from mutations of Hb beta subunit. One such mutation is a single base substitution, A to T, that causes sickle cell anaemia (SCA) which is most common SCD.

SCA is a homozygous recessive monogenic disorder with both alleles of beta hemoglobin gene harbouring the mutation at sixth amino acid (HbS) (Glu β6 Val). Valine being a hydrophobic residue exposes the hydrophobic patch of the protein thereby aggregating the protein into fibers making SCA a misfolding disease. This alters the erythrocytes making them sickle shaped which are prone to hemolysis and vasocclusion. Hemolysis reduces their numbers resulting in anaemia. Vasocclusion can block supply of oxygen to tissues resulting in tissue damage. Another serious complication seen in SCA patients is pulmonary hypertension (1).

SCD also comprises of equally severe hemoglobin SC disease where the two beta subunits are replaced by HbS and HbC (Glu β6 Lys). Yet another SCD is HbE disease (Glu β26 Lys). SCA and Thalessemia can coexist in an individual. Such a state is called as haemoglobin sickle-beta thalessemias (HbSBetaThal) (1).

In 1949, Linus Pauling and colleagues showed that HbS has altered electrophoretic mobility. This is one of the ways how SCA is diagnosed even today. They also defined SCA as a molecular disease. Eight years later in 1957, Venom Ingram discovered that HbS is an outcome of single amino acid substitution in normal Hb (2).

Earlier thought to be only spread in Africa, in 1952, Lehman and Cutbush first described SCA in Nilgiri Hills of Northern Tamil Nadu (3). SCA is spread to India, Africa, Mediterranean region, the Gulf region, Saudi Arabia. Sickle gene being an example of balanced polymorphism offer selective advantage in heterozygotes against Plasmodium falciparum malaria may be one of the reasons why its frequency is higher in these countries (~35% in some communities). Consanguinity is a further threat to increase in its frequency. In India, SCA occurs predominantly in Eastern Gujarat, Maharashtra, Kerela, Madhya Pradesh, Chhattisgarh, parts of Tamil Nadu and Odisha (4).

Africa being the first nation where it was first recognised, has devised ways for effective management of the disease. India has taken outreach programmes for better management of the disease since Indian subjects (Asian haplotype) differ from African people (benin haplotype) and same model of management will not work in this case. The sickle cell belt of India harbours a haplotype whose SCA is much milder than that of disease caused by benin haplotype (5).

In India, newborn screening by capillary electrophoresis, solubility test or high performance liquid chromatography (HPLC) are being adopted (5, 2). Exemplary image analysis of three year old Indian subject has been done by American society of hematology showing HPLC profile, sickling analysis and electrophoresis patterns (6). Extensive studies have been done in tribal populations in India in areas where its frequency is found to be high (~40%). These tribal populations also show HbSBetaThal, coinheritance of sickle gene with HbD Punjab and glucose-6-phosphatase deficiency (2). The Indian Council of Medical Research (ICMR) and the National Rural Health Mission have commenced numerous outreach programmes for better management and control of the disease in different states. ICMR, one of the oldest medical research council of India, has devised strategic framework of which one component is to work on development of data source for SCA among other important communicable and non-communicable diseases (7). It is still an ongoing project. Better insights can be obtained about the Indian population and a sure answer to why its spread is in a specified zone within the same country. We will get answers to what factors contain this disease in what is called the sickle cell belt of India.

In current Covid pandemic times, patients with comorbidities like diabetes, hypertension, liver disease and cancer show more complication of the disease. People with autoimmune conditions, SCD and thalessemias also are at higher risk. Patients with SCD have many cardiopulmonary comorbidity and have weakened immune system. COVID-19 that attacks the lungs is expected to make SCD patients even more prone to infection. Many countries have shared special care and management guidelines for SCD patients in this COVID pandemic (8). The same guidelines can be followed in all the countries to protect people with SCD who need extra care and protection.

References

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