DISTRIBUTION OF SICKLE CELL DISEASE IN AFRICA

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The term sickle cell disease includes a variety of pathological conditions resulting from the inheritance of sickle haemoglobin either in a homozygous state or the S gene in a heterozygous state with another abnormal haemoglobin e.g SS, SC, SD, S βthal, SO Arab, SD, SG.

The origin of the haemoglobin S (HbS) gene has been rather controversial. The HbS gene has often been regarded as an African ancestry because of its high frequency among blacks. Sickle cell anaemia is also prevalent in parts of Asia mainly the Arabian peninsula and the Indian subcontinent. It is seen in parts of Europe (mainly Greece and Sicily). It is also prevalent where people from the above areas have migrated. It is now prevalent in America including tropical America. It has recently been recognised in Southern Nepal. The S gene exists in all the three major "races" of human kind:- black, white and oriental.

Lehman proposed that the Arabian Peninsula was a fertile land but due to climatic conditions with conversion of this area to desert, people began to migrate and this explains the spread of this gene to India and equatorial Africa, but more recent work by Domique Labie has confirmed otherwise.

The HbS has spread so rapidly and increased so fast because of the enormous selective advantage the S gene has in the severe endemic falciparum malaria environment of tropical Africa. There is a strong association between HbS and malaria.

It has been postulated that there are two HbS mutations associated with 7.6kb fragment and 13.0kb fragment. The HbS gene associated with the 7.6kb fragment is prevalent in the Middle East, India, East Africa and is the major, variant in Coted'Ivoire, Gabon and Saudi Arabia. The gene associated with the 13.0kb fragment is assumed to be the West - African variant and is also found in high frequencies in Saudi Arabia, Algeria and Morocco.

Domique Labie worked in the Pasteur institute in Paris. She also worked in Dakar, Senegal, Republic of Benin and Bangui in Central African Republic. She found 3 different β^S haplotypes and named the different haplotypes after the places were she worked and discovered them.

Altogether five β^S haplotypes have been identified and designated Benin, Senegal, Cameroon, Kenya and Arabo - India.

The Kenya β^S haplotype is referred to as the Bantu (CAR-Central African Republic). This is associated with the severest form of SS Disease. The Arabo - Indian β^S haplotype is associated with the most benign form of SS disease and it is rare in Africa.

The Senegal β^S haplotype is also benign almost next to the Arabo -Indian type, while the Benin and the Cameroon types are in between. (Hence in severity → Kenya (Bantu, CAR is most severe), while Senegal and Arabo - Indian are mild clinically and have a high HbF).

However there is still no clear knowledge of the arrival of HbS gene in Tropical Africa. This is reflected in the absence of this gene from the more ancient inhabitants of the continent. These include the Nilotic peoples of Southern Sudan, the Nuer, Dinka and Shilluk, the Kru and Gagu people of South Eastern Liberia, Western Cote D'ivoire, some pygmy and Bantu peoples of the Congo and Gabon and the Bantu peoples of South Africa and Mozambique.

The Bantu (CAR -Central African Republic) have severe disease while the Saudi and Asiano have high HbF coupled with only a modest level of anaemia and a relatively mild disease.

The HbS gene is widely spread in East and Central Africa, to the North among the traditional hunters and agriculturists of Northern Uganda and Southern Sudan and amongst the pastoral Nilotics of Sudan.

There are population tribes in Eastern Liberia with high frequency of β thalassaemia now being replaced by HbS. The high frequencies and widespread distribution of HbS in Central and East Africa can be explained probably by the much greater Arab penetration into these areas compared to further North. The major ports of entry being along coasts of Kenya and Tanzania. It has been observed that the HbS in America West Indies have the West African β haplotypes while the HbS patents in Brazil have the CAR types. This can be due to movement of the slave trade.

There are also significant frequencies of the HbC gene variant in Central West Africa viz, in Upper Volta as well as Ghana, Togo and Benin. There are other haemoglobin variants notably the HbA_2 that tends to unite most African populations South of the Sahara.

The diffusion of the Hb variants has been determined to a great extent by ethnic migration. There is a decline of the S gene frequency from East to West Africa together with higher levels in the North compared to the South bank of the Zambesi, with the River having possibly acted as barrister to further Southern migration.

The prevalence of HbC trait reaches as high as 20% in West Africa. From this location, HbC was exported to the Caribbean and North America where the HbC trait now occur in 3.5 percent and 2 percent of the Black populations respectively. There is also a high prevalence of the HbC amongst the Bedouin tribe in Northern Israel. This might be a new mutation although the possibility of African ancestry can not be excluded.

Haemoglobin D Ibadan has been isolated. It causes a mild haemolytic anaemia.

The β Thalassaemia gene also occurs in areas where the sickle cell gene is common. In Nigeria a high prevalence of HbA_2 level occurs which is similar to what is observed in Jamaicans and Americans of West African origin with 0.2% prevalence in Nigeria, 1.3% in Southern Ghana and 1.7 percent in Northern Ghana. In Jamaicans the β^+ occurs in 1% of the population while the β^0 is 5% of the population.

There is little information on the distribution or prevalence of the gene in the rest of the African continent.

In South African there are also very low frequencies of HbS both in the Khoisans, the Bushmen, Hottentots and the Bantus. It is believed that these people had migrated South before the HbS gene was established in East Africa.

However an epidemic or endemic disease like malaria is

thought to have selected HbS variant in the African population.

Clinical relevance of Beta Globin Haplotypes

Currently there are differences between the Benin and Bantu Haplotypes. The Senegal haplotype has been claimed to be associated with increased levels of foetal haemoglobin in HbS. The homozygosity for the Senegal haplotype is infrequent in the Caribbean and the United States. It has been found that the α gene deletion increases the risk of osteonecrosis, mainly ischaemic necrosis of the femoral head whereas the Senegalese haplotype decrease the risk until age 30.

The Haemoglobin O Arab has been recognised in Israel, the Sudan, Kenya, Jamaica and the United States.

Though the β Thalassaemia gene is most common in the Mediterranean area, there is also a low prevalence of β Thalassaemia especially in areas where the sickle cell gene is common. Weatherall et al (1971) found a prevalence of 0.2 percent in Lagos Nigeria, 1.3 percent in Southern Ghana.

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REFERENCES

1. Serjeant Graham R. Sickle Cell Disease chapter 2 - Distribution of Sickle Cell Disease pp 13-24.
2. Kan., Y.W. and Dozy A.M. Evolution of the haemoglobin S and C genes in world populations, Science, 209, 388, 1980.
3. Stanley, H.M. In Darkest Africa Vol.2, Charles Scribner's Sons. New York 1980. 176.
4. Rachmilewtiz E.A., Levi and Huisman, T.H.J. High frequency of haemoglobin C in an Israel Bedouin tribe. Isr. J. Med. Sci., 10, 219, 1974.
5. Aluoch and Aluoch - Epidemilogy and β^s-Haplotypes of Sickle Cell disease in Africa (1999).