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Editorial

World Sickle Cell Day: Lessons for India

At the plenary session of the 63rd General Assembly of the United Nations on December 22, 2008, a resolution recognized 'sickle cell anaemia as a public health problem' and urged the Member States and United Nations organizations to raise awareness of sickle cell anaemia - among the world's foremost, and at times most lethal, genetic diseases - at national and international levels on June 19 of each year. The first Sickle Cell Day was celebrated on June 19, 2009.

A genetic condition occurring when abnormal haemoglobin genes are inherited from both parents, the disease was first recognized in a dental student from the island of Grenada in the West Indies[1]. Three more cases were reported over the next 12 years, and reviewing the features of these four cases, Mason[2] noted that all were of African origin. This gave rise to the common misconception that the disease was confined to the peoples of African origin, but it is now clear that other racial groups are also involved around the Mediterranean, the Gulf region, especially Saudi Arabia, and across India. The frequency of the AS genotype in the Arab-India region predicts that nearly 49,000 or 17 per cent of global births with homozygous sickle cell (SS) disease would be born in the Arab-India region[3], of which the great majority would be in India. These calculations may be influenced by the heterogeneous distribution of haemoglobin S (HbS) in the Indian subcontinent and the relative frequency of consanguinity in the affected communities; however, with the high birth rate, it seems likely that India will account for a progressively greater proportion of the global SS population.

Regarding clinical features and management of the disease, most of the knowledge comes from the US, Caribbean and Western Europe and so has been in patients of African origin. Advances include pneumococcal prophylaxis[4], prevention of deaths from acute splenic sequestration (ASS)[5], prevention of strokes[6], better management of the bone pain crisis and increasing use of hydroxyurea[7]. Since several of these interventions require implementation early in life, newborn screening for the disease is now universal throughout the US, the UK and increasingly in Europe and is a vital component of the models of care.

India has not been left behind and from the early work on the distribution of the HbS gene conducted by the Anthropological Survey of India[8], many expert groups have focussed on molecular aspects and clinical features of the disease, producing a valuable body of clinical information. It has been shown that the Indian sickle cell gene has a flanking DNA structure that is different from that seen in African populations and both India and the Gulf area share the Asian haplotype which is probably an independent occurrence of the HbS mutation[9]. It has also occurred against a genetic background of high frequencies of alpha thalassaemia and high levels of foetal haemoglobin[10], both of which modify the expression of Indian sickle cell disease. The disease in India occurs predominantly in a central belt stretching from Eastern Gujarat, Maharashtra, Madhya Pradesh, Chhattisgarh, to Western Odisha with a smaller focus in the Nilgiri Hills of northern Tamil Nadu and Kerala in southern India. This distribution coincides with much of the tribal population leading to the belief that the disease is confined to tribal peoples, but it is now recognized to affect all groups in these areas including the 'Other Backward Classes'[11]. The Indian scene now presents major challenges and opportunities. Documentation of Indian sickle cell disease is required for the development of locally appropriate methods of care, exploring the role of genetic counselling and whether traditional tribal social pattern may be used

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to prevent the disease and mechanisms to harness the great reservoirs of clinical experience in India.

It is true that there is abundant knowledge on the management of the disease in populations of African origin, but it cannot be automatically assumed that this model of care is optimal for Indian subjects. As we learn more about sickle cell disease in India, we realize that there are many differences from the disease in peoples of African origin. Some of these differences may derive from the frequently associated alpha thalassaemia and high levels of foetal haemoglobin, both of which inhibit sickling and may contribute to the persistence of splenomegaly and probably splenic function. If true, this could change the natural history of splenic-related pathologies such as pneumococcal septicaemia and ASS. The latter occurs in Indian patients but we do not know its frequency or natural history. Regarding pneumococcal sepsis, there is no evidence from the literature or from personal contacts with paediatricians that this occurs, and although it is feasible that it has escaped diagnosis because of death before clinical presentation or a failure of culture, it seems that the implementation of expensive and difficult pneumococcal prophylaxis in Indian patients should rest on better evidence. These questions could be resolved by close follow up of cohorts diagnosed at birth, and it is important that appropriate protocols are in place to collect these data.

Sickle cell disease is readily preventable if one parent has a normal AA haemoglobin genotype. Following the success of voluntary premarital screening in Bahrain[12], screening has been mandatory in the Kingdoms of Bahrain and Saudi Arabia[13] since 2004 and has reduced the births affected by sickle cell disease. In Jamaica, early experience in senior school students suggests that knowledge of the genotype may not influence the choice of partner[14] largely because of reluctance of the male to be tested. In Indian tribals, there was some success in acceptance of genetic counselling[15] and work is needed to determine whether this information can successfully prevent births with sickle cell disease.

There is no shortage of research opportunities in India. It is important to examine the role of alpha thalassaemia and of high levels of HbF in modifying the clinical features of the disease. Documenting the clinical course in cohorts of SS disease followed from birth will provide the data needed for locally appropriate models of care. At the population level, genetic counselling should be integrated into the health services and to determine any effect on the prevalence of affected births. Indian healthcare personnel have huge experience in managing the disease; however, unless this experience is published and available to others, it will be lost. There is a need to find the methods to provide time and resources for experienced doctors, nurses, medical technologists and paramedical personnel to share their experiences with colleagues.

With the goodwill and resources available to State sickle cell control programmes, the careful design of research protocols, their implementation which must include statistical and other technical resources and time for research or possible specific research posts may begin to address this problem.

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