Sickle Cell Disease in Central India - Need for Micro Level Planning

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Abstract

Haemoglobinopathies in form of sickle haemoglobin and β -thalassaemia are common in Central India and are important from clinical and disease burden point of view. These disorders are more common in Scheduled Tribes and Scheduled Castes as compared to other endogamous groups of Central India. There is heterogeneity in the distribution of these deleterious genes in the area. In some endogamous groups like Jharia, Mehra in Scheduled Caste group and Pradhan. Panika, Barela, Bhilala in Scheduled Tribe group, sickle haemoglobin has high prevalence and β -thassaemia is very low or absent. In some primitive tribes like Saharia, Hill Korba, Kamar sickle haemoglobin is either absent or with low prevalence but β -thalassaemia is common. The distribution of the ethnic (caste & tribe) groups is also uneven in the various pockets of Madhya pradesh and Chhattisgarh. For examples Jhabua, Dhar, Badwani and Mandla districts of Madhya Pradesh and Bastar, Surguja and Narayanpur districts of Chhattisgarh has high (>60%) proportion of tribes whereas in many districts the proportion of tribal population is less than 20 percent. Both these states need micro level planning to develop the infra-structural facilities, based on the type of abnormal gene and population size of STs and SCs, to diagnose manage and prevent the disease in the area.

Introduction

Sickle haemoglobin (HbS) is a first molecular disease known to man. It is structural variant of haemoglobin in which glutamtic acid, an amino acid, at position No.6 of b-globin chain of haemoglobin is replaced by valine. This happens due to change of nucleotide, adenine to thymine (GAG®GTG) of codon 6 of β -globin gene, located on the short arm of chromosomes 11. This substitution of amino acid changes the net charge of haemoglobin, oxygen affinity and three-dimensional structure of haemoglobin thus rendering it as unstable haemoglobin. Sickle haemoglobin gets polymerized at low oxygen tension and deforms the red blood cell from discoid shape to sickle like form (Fig. 1). It is commonly found among people of tropical countries and transmitted as autosomal recessive character. It is the most common single genetic mutation in man and reported from a large part of the world i.e. Africa, Mediterranean countries, Middle East and parts of South American countries, India and others parts of the globe where people originating from these countries have settled. If a person receives only one gene responsible for sickle haemoglobin from either of parent, the condition is called carrier or trait. If one inherits two defective genes, one from each parent, the condition is called sickle cell disease. As the carrier state is stated to provide protection against mortality against malaria, it has attained high frequency in many parts of the tropical world (Serjeant and Serjeant, 2001). The DNA analysis of sickle haemoglobin gene prevalent in various parts of the world including India revealed that the gene got mutated at least five times in the different parts of the world though every time mutation was the same but other linked gene were quite different from each other to give rise to five different haplotypes. (Kulozik et.al.1986; Gupta et.al. 1991). In India the sickle cell belong to the same haplotype and is stated to have evolved independently. Clinically and haematologically

also the sickle cell disease prevalent in India is different from rest of the world (Oner et.al,1992).

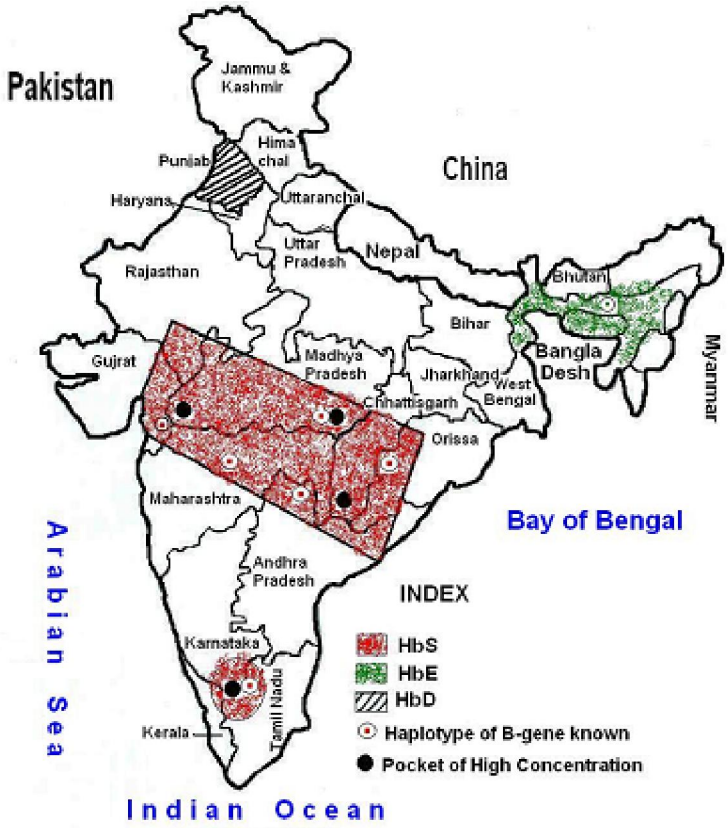
In India, haemoglobinopathies, especially sickle haemoglobin are the commonest genetic disorders in the tribal belt of Central and Southern India (Fig. 2). Undivided Madhya Pradesh (Madhya Pradesh and Chhattisgarh) harbours the largest tribal population in India, which is about one fourth of the total tribal population of the country. These tribal groups are characterized by their unique socio-cultural and religious practices and follow strict endogamous practice. These tribal populations are stated to be aboriginal population of India. Sickle haemoglobin was first discovered from a tribal population of Nilgiri Hills of South India in 1952 (Lahman and Cutbush, 1952). Later, it was reported from the tribal population of Central India i.e. Madhya Pradesh and Chhattisgarh and its surrounding areas falling in the states of Rajasthan, Gujarat, Maharashtra, Andhra Pradesh and Orissa. This led to an impression/ belief that sickle haemoglobin is confined to tribal populations/ belt. Later, in some tribal groups like Bhils of Jhabua district, tribal groups of Bastar and Pradhans of district Mandla, Halbas of districts of Rajnandgoan and Durg (unpublished observations), the prevalence rate of sickle haemoglobin have been very high i.e. over 30 percent (Bhatia and Rao, 1986; RMRCT unpublished reports). The prevalence of sickle haemoglobin from various parts of Madhya Pradesh and Chhattisgarh varied from 15 to 30 percent. It was found that the non-tribal people of HbS belt especially Scheduled Castes and other Backward class communities have sickle haemoglobin in similar proportion as that of tribals of the area. We have also found prevalence of β- thalassaemia in various proportions, average 2-4 percent, among the various tribal populations. In some pockets, Scheduled Castes populations e.g. Jharia, Mehra, Dahariya etc. have very high prevalence of sickle haemoglobin i.e. over 30 percent. Co-inheritance of β -thalassaemia gene alongwith gene for sickle haemoglobin also causes sickle cell disease.

There are large variations in prevalence of sickle haemoglobin in various tribal/ Scheduled Caste populations of a geographical area/ district and within a tribe/ caste population scattered over a large area (Fig. 1). Gond and Bhil group of tribals constitute a large proportion of tribal population of the state. Among Gond group of tribals the prevalence rate of sickle haemoglobin generally varies from 10 to 25 percent whereas in the Bhil group of tribals the prevalence rate varies from 15 to 33 percent. Earlier studies carried out by various workers show that in Madhya Pradesh the Scheduled Caste and Backward Class communities of the tribal predominant area also have sickle cell gene in almost similar proportion (Unpublished reports). As this disorder is recessive in nature the heterozygotes are absolutely asymtomatic but the homozygous suffer from serous complications leading short life span. The transmission of the disorder depends on the marriage patterns / customs of the population or the affected person. The tribal populations as well as other non-tribal populations of Central India are strictly endogamous and generally the marital distances are small. Hence it requires to map the prevalence of sickle cell gene and β-thalassaemia gene in various population (STs and SCs) groups at district level in Central India (states of Madhya Pradesh and Chhattisgarh).

Sickle cell disease load can be computed if we know the heterozygote prevalence rates and the population size. But we do not have tribe and caste wise population for various district of Madhya Pradesh and Chhattisgarh. As per census 2001, the total Scheduled tribe and Scheduled Caste population of Madhya Pradesh is over 120 lacs and 91 lacs respectively which is about 20% and 15% of the total population of the

Fig. 1: Normal and sickle haemoglobin

Fig. 2: Distribution of Common Abnormal Haemoglobins in India



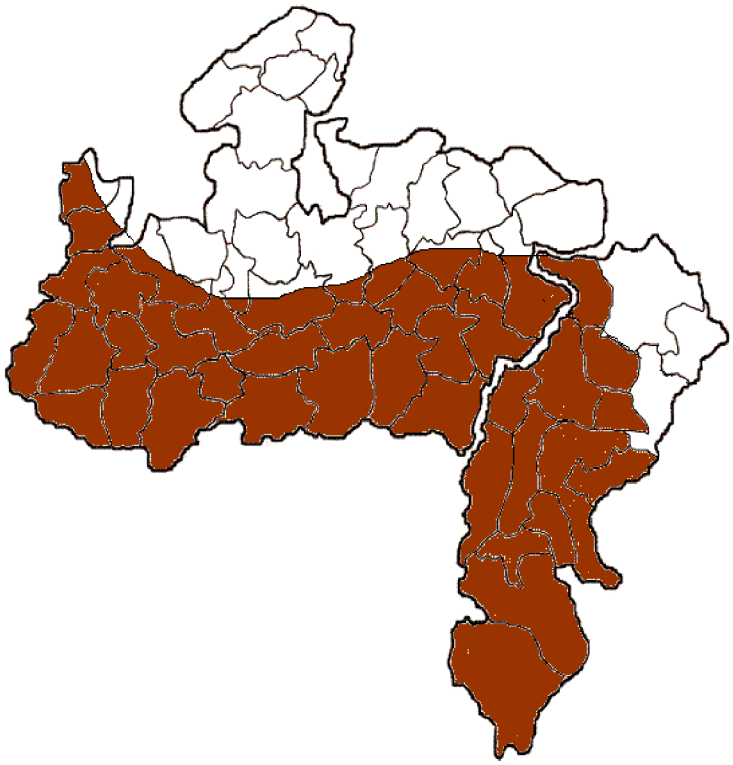
state. Out of 45 districts of the state, 27 districts fall under the sickle cell gene belt. These districts (arranged in descending order according to percentage of ST and SC population) are Jhabua, Barwani, Dindori, Mandla, Dhar, Shahdol, Umaria, Betul, Seoni, West Nimar, Chhindwara, Harda, East Nimar, Jabalpur, Ratlam, Dewas, Katni, Damoh, Hoshangabad, Sagar, Satna, Balaghat, Ujjain, Indore, Mandsaur, Neemuch and Narsimhpur. Similarly in Chhattisgarh, the sickle haemoglobin is common in Central and Southern parts i.e. barring few districts like Raigarh, Jashpur, Surguja, and Koriya. In these non-sickle haemoglobin districts main tribal populations are: Oraon, Kanwar, Hill Korba, Korba and Bhiror. In rest of Chhattisgarh most of the tribes belong to Gond and its sub-tribes. These tribes are Gond, RajGond, Muria, Maria, Hill Maria, Bhatara, Dhurva, Halba etc. The tribes of Chhattisgarh which have shown high prevalence rates of sickle haemoglobin are: Halba of Rajnandgaon and Durg districts, Muria and Hillmaria of Bastar districts. The studies also suggest that the Scheduled Castes and some of the OBC groups like Sahu, Chandrakar, Kurmi and Yadav of Southern and Central Western Chhattisgarh also have sickle haemoglobin which is almost in the same proportion as that of tribals of the area. Prevalence of sickle haemoglobin in the Gond group of tribes in Chhattsgarh generally varies from 15-25 percent. There are 12 districts in Chhattisgarh which fall in main sickle cell belt of the state. These districts are: Dantewada, Bastar, Kanker, Korba, Mahasumund, Rajnandgaon, Dhamtari, Kawardha, Bilaspur, Durg, Raipur and Jangjir-Champa. The total SC and ST population of these districts of both the states is about 2.14 crores as per census 2001. The prevalence rates of β -thalassamia are not well known for many tribes and Scheduled castes populations. However, some studies conducted by us show that a few tribal groups have high prevalence rate i.e 6 to 10% as carrier state. But in most of tribals and Scheduled Caste communities its prevalence generally varies from 0 to 4 percent. The population groups which have high prevalence of sickle haemoglonin (over 25%), generally have low prevalence of β - thalassaemia e.g. Pardhan of Dindori district and Mehra (SC group) of Betul district; whereas, the populations which have low prevalence of sickle haemoglobin, have high prevalence of β -thalassaemia e.g. Kol of Satna. On the whole, it can be safely presumed that the average prevalence for β -thalassaemia in SC and ST communities is about 2 percent.

Information regarding the prevalence of sickle cell haemoglobin is known for most tribal populations of sickle cell belt of both the states. Prevalence of sickle haemoglobin is variable among the Scheduled Caste and tribal populations of the state. Even there are variations within the same tribe scattered over a large area. Census data for each tribe/caste wise population are not available for the state. Hence average prevalence of sickle haemoglobin for each district was presumed based on the prevalence of the gene in different population groups of the district. The average prevalence of sickle haemoglobin in Gond group of tribes is 15 percent except in Chhindwara, but generally it varies from 15 to 25 percent. In Chhindwara district, Gond tribe has a low prevalence rate i.e. 4 %, whereas in Bharia and Korku tribes, which reside in the same district, its prevalence is 20% and 15 % respectively. Hence a average prevalence of 10% was taken for computing the disease load. The Scheduled Caste population of Central and Eastern M.P. has HbS ranging from 15 to 33 percent. Hence, an average prevalence of 15% was taken for computing the figures. In Satna district, the prevalence of HbS among Kol tribe is low i.e. about 5%. But Gond, Bhumia and Baiga tribes, living in the district in a large proportion, has a prevalence of HbS as 15 to 20 percent. Hence, on average prevalence of 10% was taken for computation.

Likewise, the prevalence of HbS in tribes of Western M.P. i.e. Bhil group of tribes,

varies from 18 to 33 percent but it varies from 10 to 15 percent in Scheduled castes. The least prevalence rate of β-thalassaemia was taken as 2 percent for all these 39 districts for computations of disease load. These rates ware taken to compute the expected disease load due sickle cell disease in among the Scheduled tribes and Scheduled castes for these 39 districts. Other assumptions, which were considered in the present study were as follow: Birth rate – 30/1000, Number of eligible couple - 170/1000.

Fig. 3: Sickle cell belt in Madhya Pradesh and Chhattisgarh



B/W

Disease load due to sickle cell disease in Central India

As per Census 2001 population, the situation of sickle cell disease is very alarming in Madhya Pradesh and Chhattisgarh. It is estimated that about 150 thousand patients (112 thousand from MP and 39 thousand from CG) belonging to Scheduled castes and Scheduled tribes would have sickle cell disease in both these state. A large proportion of these patients might have died, as the life expectancy of these patients are low. Most of these patients remain undiagnosed, as the facilities for its diagnosis are either absent or inadequate at most of the hospitals in both the states. As per present estimates, since 2001, about 4500 newborn babies with sickle cell disease are expected to be added every year and about 18,000 pregnancies are at risk annually. These expecting mothers needs to be identified and monitored for prenatal diagnosis in order to avoid birth of a sickle cell diseased child. About 110 thousand high-risk couples of

eligible age group need be counselled for management and prevention of sickle cell disease. The figures (estimates) are based on the Census 2001 and at present the actual load is expected to rise further due to following reasons; a) The computation is based on census 2001, since than population of both the states has increased considerably (about 10%). b) the backward class communities have not been taken into account as the prevalence rate and population size for OBC groups are not known. c) These estimates are based on average prevalence rate. In some population, the prevalence rate of sickle haemoglonin, β- thalassaemia are more than presently taken for computation.

Prevention and management

With advances of molecular genetics, it is possible to detect this defect at early stage (10 to 15 weeks) of pregnancy. The management cost of these patients shall be exorbitant. However the resources with Government are limited. Hence, the prevention appears to be only solution in present circumstances. With a comprehensive medical care of management approach, grievances of these patients can be reduced to a great extent and the life expectancy as well as quality of life of these patients can be improved considerably (El-Hazmi 1994, Schnog et. al. 2004).

1. Infra-structutural facilitites: The infra-structural facilities and technical know-how for diagnosis of the disorder and its clinical management should be generated at PHC/ district hospital level depending upon the disease load. At PHC or sub-centre level in the high risk districts screening facilities should be established. The medical officers and the paramedical staff should be trained to diagnose/ identify the sickle cell disease patients so that treatment and management of the patient can be initiated at an early stage.

i. Genetic counseling and Prenatal Diagnosis: There should be at least two to three centres in each state for prenatal diagnosis and genetic counselling. The State Governments should have comprehensive plan for prevention and management of the sickle cell disease.

2. Identification of High risk Couple: The high-risk couples for these disorders should be identified at the time of ante-natal care and each pregnancy should be monitored for sickle cell disease. Hence the state Government should strengthen ante-natal services in high risk areas, incorporate the screening of antenatal women at the time of registration in both the states so that either the birth of sickle cell diseased children can prevented or can be diagnosed at the time of birth. For this, the women and general public at large should be educated regarding the transmission, clinical complication, management and prevention expects of the disease. The couple should be given appropriate counselling after prenatal diagnosis.

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