Thalassemia among the tribal communities of India

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Abstract

Though the tribal communities constitute a major part of India, unfortunately they are highly vulnerable to many hereditary disorders causing high degree of morbidity and mortality. To map out thalassemia among the Indian tribes, an extensive review study was conducted from the literature published since last 20 years.

Literature review shows that thalassemia and other haemoglobinopathies are highly prevalent (0.028-18%) among the tribal communities. Some types of deleterious mutation are restricted to some particular tribes. Such as tribes of Maharastrya and Gujrat have shown prevalence of 619bp deletion mutations in 49.2% and 45.5% carriers, respectively. HbS (codon 6A□T) mutant allele is widespread among many Indian tribes. HbE mutation among the Bodo Kachari of Assam is found to be the highest observed frequency in the world followed by the tribes of adjoining Tripura. The evidence of the hereditary persistence of rare HbF is also prevalent among the Indian tribes. In case of Gond in Central India, HbF levels varied as much as 42.55% with high G-gamma values.

Since last 20 years the high frequencies of these mutant alleles is maintained by the tribal populations probably due to consanguinity and endogamous mating for a long period of time, along with ignorance, lack of awareness and conveyance, low-income status and high cost of treatment make them vulnerable.

Thus, action like community awareness, screening of carriers, establishment of prenatal diagnosis facilities, optimum treatment of thalassemia babies etc. should be taken immediately.

INTRODUCTION

Thalassemia and other haemoglobinopathies (production of structurally defective genes) are the most common monogenic disorders in the world. Thalassemia has an autosomal recessive pattern of inheritance ([1]). It arises from a mutation or deletion in one or more globin gene(s), which leads to a reduction or absence in the production of hemoglobin [Hb]([2]) and an abnormal Hb ratio (□: non-□). Ultimately it causes varying degrees of microcytic anemia that can range from insignificant to life threatening.

Thalassemia is classified according to the affected globin, i.e. Alpha thalassemia and Beta thalassemia. Alpha thalassemia is characterized by deletion or mutation of one or more □-globin genes located in the short arm of chromosome 16 ([3]). Whereas beta thalassemia is caused by mutation of □-globin gene ([4]) on chromosome 11 ([5]) affecting all aspects of transcription, translation and the stability of □-globin gene product.

Severity of the syndrome depends on the nature of mutation. Carriers of thalassemia, are apparently healthy and normal, but may have slight anemia. In alpha thalassemia, severe anemia begins even before birth and survival past the first few hours of life is rare ([6]). In children with beta thalassemia, symptoms appear in the first two years of life and include paleness, headache, fatigue ([7]), irritability, failure to grow ([8]), shortness of breath ([9]) etc. Besides these, unexpectedly slow development along with jaundice ([10]), enlarged spleen or liver ([11]), or deformed bones ([12]) can be the common signs of thalassemia.

Various evolutionary forces are found to regulate the frequency of a deleterious mutation in human populations. People of Mediterranean, Middle Eastern, African and Asian descent are at higher risk of carrying the genes for thalassemia, for which it is also called Mediterranean Anemia. This is a special importance in developing countries like India, where it increases the burden of health care delivery system ([13]). Every year 10,000 children with thalassemia major are born in India, which constitutes 10% of the total number in the world ([14]), and one out of every 8 carriers of thalassemia worldwide lives in India ([15]). But the action programmes like intensive counselling may be instituted to the groups, which show high prevalence rate rather than general population to make the programme not

only cost-effective but cost-efficient as well ([16]).

The large Indian population is multi-ethnic and divided into subgroups. As per the 2001 census, there are about 635 biological isolates (tribes and sub tribes) that constituted 8.08% (about 84.3 million) of the total population of India. Tribal communities in India constitute the largest tribal population in the world. Most of them have been practicing endogamy for a long period of time, for which tribal communities are highly vulnerable to various hereditary diseases.

As the frequency of thalassemia is increased by the consanguinity and endogamous mating, it may be assumed that the tribal communities in India are facing the problem at large scale. But the frequency and distribution of thalassemia among tribal India is less well-documented. Though some studies have reported the incidence of haemoglobinopathies among the tribes of India, the results are scattered and limited to specific region. Thus, the aim of the present study is to 1) have a vivid picture regarding the distribution and present situation of thalassemia among various tribal communities inhabited in the different parts of India 2) to analyze critically whether the strategies, adopted for the control of thalassemia in India, are feasible for tribal population also.

STUDY DESIGN

A search of earlier studies on thalassemia and other haemoglobinopathies published since last 20 years (between 1987 and 2006) was conducted using different journals (both national and international), as well as Medline, Pubmed and Embase databases through Internet.

At the onset of the review study, about 100 literatures were retrieved, of which 38 literatures were examined in details. The detail review was restricted to English language studies. To satisfy the inclusion criteria, studies had to contain articles that were specific to: a) Frequency and distribution of thalassemia and other hemoglobinopathies among different tribal communities of India, b) any related problem that they are facing and c) any proposed solution by the authors that may be implemented for the tribes.

RESULTS FROM PUBLISHED REPORTS

The previous reports have shown that thalassemia along with other hemoglobinopathies are distributed all over India. But the distribution of the gene is not uniform in the Indian subcontinent. The map of India showing their distribution has been presented in Figure 1.

In this respect, it should be mentioned that extensive studies were done among the tribes of Orissa ([17,18,19,20,21,22,23,24,25,26]). Apart from this, other previous reports are scanty, scattered and limited to few specific tribes only. Bur as far as the tribes are studied, it is at least clear from these reports that thalassemia and other haemoglobinopathies are prevalent among the tribal communities of India and make a public health problem among them. However, from these scattered reports, we tried to categorize them systematically according to their types of mutation. The result is summarized in table 1. Three main types of abnormal haemoglobin syntheses are described under the following sub-heads:

I) NUMERICALLY ABNORMAL GLOBIN CHAIN:

a) Alpha-thalassemia: Studies on alpha-thalassemia among the tribal groups of India are scare, patchy and incomplete. Especially field based systematic studies are rare. But these rare studies have found remarkably high prevalence of alpha-thalassemia among the tribal population e.g. Kachari population of Assam ([27]), Koya Dora and Konda Reddi of Andhra Pradesh ([28,29]), Gond tribes of Madhya Pradesh ([30]) etc.

On the basis of 1,647 blood samples from Rajasthan ([31]), Choubisa et al. have shown that alpha-thalassemia (Hb-Barti's) is more prevalent among the tribal communities (3.07%) than scheduled castes (1.43%) and general castes (0.77%). Sen et al. ([32]), with larger sample (5013 individuals) also supported the high prevalence of alpha-globin deletion allele among the tribesmen of three eastern Indian states-West Bengal (18%), Arunachal Pradesh (3.9%) and Assam (3.85%). Even coexistence of alpha- and beta-globin gene abnormalities was also observed in upto 18% of some tribal groups ([32]).

b) Beta-Thalassemia: Previous studies revealed that the tribal groups of India have high risk of beta-thalassemia, the prevalence of carrier status in some being as high as 17% ([33]). Agarwal et al. ([34]) stated that the majority of the beta-thalassemia carriers were of Uttar Pradesh origin. But according to Verma et al. ([35]), the majority of β-thalassemia carriers in India were migrants from Pakistan and their pattern of mutations differed from the rest.

The geographical distribution of Sickle cell disorder, β-thalassaemia and other haemoglobinopathies in Central Eastern part of India shows the differential migration pattern of the population ([20]). The highest frequency of beta thalassemia trait is reported in Gujarat, followed by Sindh,

Punjab, Tamil Nadu, South India and Maharashtra (1.9%) as shown in Ambekar et al. ([36]).

Rao and Gorakshar ([37]) have shown that (Figure 2a) the Gond of Maharastrya is a high risk group for beta-thalassemia gene (2.83%). The result was supported by Gond and Gond related tribes of Madhya Pradesh [30](Gupta et al., 1991). In Rajasthan beta-thalassemia syndrome were encountered in 3.79% ([38]). The author have shown the higher incidence of mutant gene (Hb S, Hb D, Hb E) among scheduled tribes (6.85%) like Bhil, Damor, Garasila and Mina as compared to scheduled castes (3.08%) and general calstes (2.32%).

In a study by Balgir et al. ([24]), high prevalence (Santal 8.0%; Kolha 2.0%; Bhumiz 1.7%; other 3.8%) of beta-thalassemia trait was detected among the tribal students of Orissa. Among the tribal students (Bhil and Power) of Maharastrya, the trait was detected as 1.6% and 2.4% for male and female respectively ([39]). In Orissa, the trait was found to be present in Kharia (6.3%) and Bhuyan (6.5%) tribes, with the variation among their sub-tribes ([20]) (Balgir, 2005a). But when 15 major tribal communities of Orissa were randomly screened, the frequencies have found to vary from 0-8.5% ([22]) (Balgir, 2006a).

II) STRUCTURALLY ABNORMAL HAEMOGLOBIN CHAIN:

c) HbE: Apart from some sporadic appearances, HbE (Codon 26 G→A) is confined exclusively (frequency 0.4-64.5%) to persons originating from Eastern India, especially the North East. The highest prevalence of HbE is found in the periphery of the area of distribution (Bodo-Kachari, a Tibeto Burman language group of upper Assam) and tribal population of adjoining Tripura ([40,41,42]). Surprisingly the Bodo Kachari population has been reported to be 64.5%, the highest observed frequency of this mutation in the world ([43]). The phenotype genotype interaction of Hb E is also variable in the population ([44,45]). According to Murhekar et al. ([46]), the frequency of HbE heterozygotes is not low (14.3%) among the primitive Negrito tribe of Andaman and Nicobor Islands.

d) HbS: The presence of Hb S was first reported by Lehmann and Cutbush ([47]) in the tribal populations of the Nilgiris in the southern state of Tamil Nadu. Since then, the high incidence of Hb S has also been reported in about 50 tribal populations in other areas of India ([48,49,50]). HbS (Codon 6 A→T) mutant allele is widespread among many of the tribal populations of India (frequency 0.1-22.2%). Five distinct haplotypes of HbS gene have been described with prevalence in different geographical areas. The prevalence of Hb S traits (Figure 2b) is 31.58% for Gond related traits ([51]); 1.0% for Santal and Bathudi each, and 0.9% for Bhumiz of Orissa ([24]); and 0-22.4% for 15 major tribes of Orissa ([23]). For the case of Sickle-cell syndrome, the frequencies are among the tribes as follows: 1.74% for all of the tribes of Bardoli ([52]); 2.4% for Bhuyan and 5.6% for Kharia in Orissa ([20]); 0-5.5% for different scheduled tribes of Orissa ([21]); 5.5% for Khond, 1.7% for Kutia Kondh, 0.2% for Oraon and 0.2% for Saora ([23]).

III) FAILURE TO SWITCH GLOBIN CHAIN SYNTHESIS:

e) HbF: Hb F or Fetal hemoglobin, a kind of beta thalassemia, is an autosomal co-dominant rare condition. But unfortunately the hereditary persistence of Hb F is also found to be prevalent among the Paraja Bhuyan tribal population of Orissa ([19]). Gupta et al ([30]) have also found that while in normal adult the amount of HbF should be 1% or less, but for the tribes (Irulas, Kurumbes, Paniyas and Bagada) of Nilgiri regions this level ranges from 6-25.3% ([53]). Among the Gond tribal groups of Madhya Pradesh it varies between 7.5 and 42.5% with high G gamma values.

Figure 1

Figure 1: Map of India (not to scale) showing distribution of major forms of haemoglobinopathies (Hbs D, E, J, K, L, M, Q and S) in the different states. (Source: Balgir, 2000)

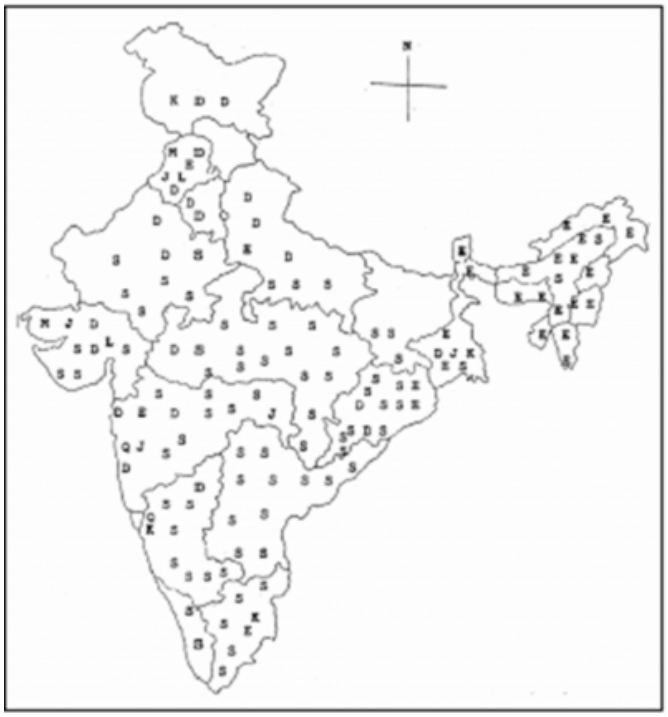

Figure 2

Figure 2a: The prevalence of Beta-thalassemia syndrome among different tribes of India

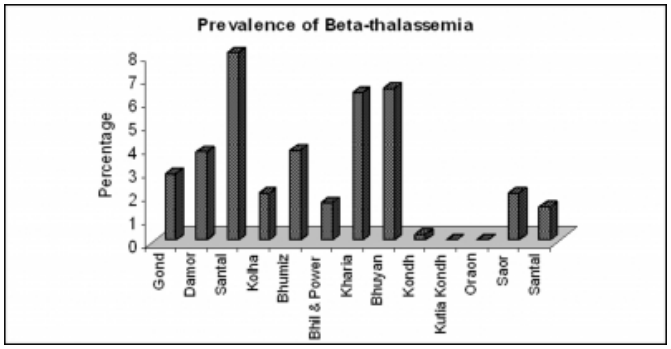

Figure 3

Figure 2b: The prevalence of HbS Syndrome among different tribes of India

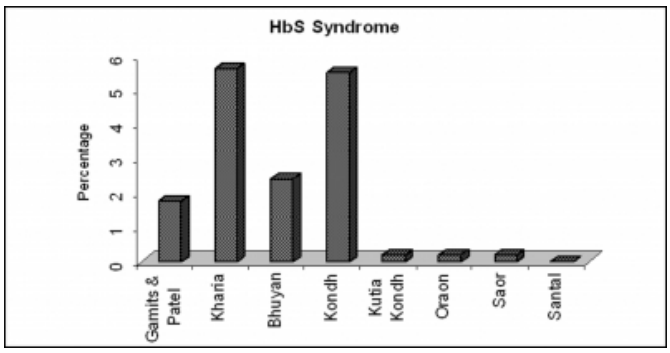

Figure 4

Figure 3: Float chart showing the strategies for prevention and control of thalassemia in India

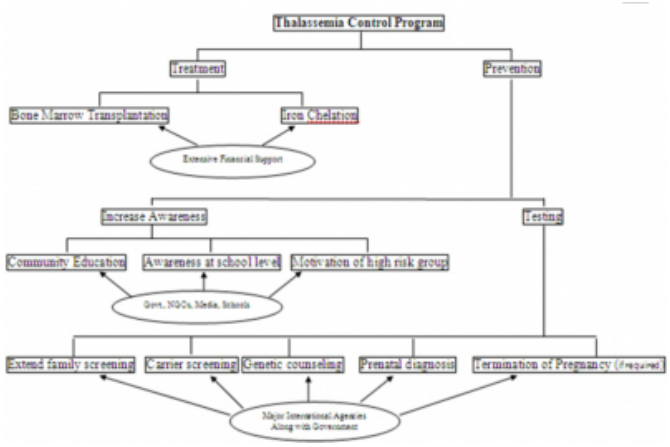

Figure 5

Table 1: Frequency & Distribution of Thalassemia & related haemoglobinopathies among different Tribal population in India

State	Tribes	Types	n	Percentage of thalassemia (%)	Source
Alpha-thalassemia					
Rajasthan	Scheduled tribes	Syndrome	618	3.07	31
West Bengal, Arunachal Pradesh & Assam	Various tribes	Syndrome	5013	1.8 (West Bengal), 3.9 (Arunachal Pradesh), 3.84 (Assam)	32
Beta-thalassemia					
Maharastra	Gond	Syndrome	--	0-2.83	37
Rajasthan	Bhil, Damor, Garasia & Mina	Syndrome	1124	3.79	38
Orissa	Santal, Kolha, Bhumiz & other	Syndrome	465	8.0 (Santal), 2.0 (Kolha), 1.7 (Bhumiz), 3.8 (other)	24
Maharastra	Bhil & Pawar	Syndrome	314	1.6 (Male) 2.4 (female)	39
Orissa	Kharia (Dudh Kharia, Delki Kharia)	Syndrome	767	6.2 (avg.), 8.1 (Dudh Kharia), 4.1 (Delki Kharia)	20
Orissa	Bhuyan (Paudi, Paik, Paraja)	Syndrome	836	6.5 (avg.), 2.1 (Paudi),7.8 (Paik),12.7 (Paraja)	20
Orissa	15 tribes	Syndrome	--	0-8.5	22
Orissa	Kondh, Kutia Kondh, Oraon, Saora, Santal	Syndrome	248	0. 2 (Kondh), 0.0 (Kutia Kondh), 0.0 (Oraon), 2.1 (Saora), 1.4 (Santal)	23
Hb E					
Andaman & Nicobor Island	Negrito	Syndrome	29	14.3	60
Orissa	Kharia & Bhuyan	Syndrome + Trait	767	1.4	20
Hb S					
Maharashtya	Gond related tribes	Trait	--	31.58	61
Orissa	Santal, Bathudi & Bhumiz	Trait	465	(1.6) Santal, (1.0) Bathudi, (0.9) Bhumiz	24
Chhattisgarh	Choudhary, Gamits, Patel, Koknis	Syndrome	13, 4, 5, 2 respectively	1.74	62
Orissa	Kharia	Syndrome	767	5.6	20
Orissa	Bhuyan	Syndrome	836	2.4	20
Orissa	Kondh, Kutia, Kondh, Oraon, Saor, Santal	Syndrome	Total 396 (including castes)	(5.6) Kondh, (1.7) Kutia Kondh, (0.2) Oraon, (0.2) Saor, (0.0) Santal	23

DISCUSSION

On the basis of earlier reports published since last 20 years, it is clear that several tribal groups of India have been identified as high-risk groups for thalassemia and other haemoglobinopathies. It causes high degree of morbidly and mortality among them ([25]). In India, with about 4635 ethnic communities five common and 12 rare mutations have already been reported ([14], [54]).

Previous studies have given some probable causes of such high frequency of the disease among the tribal people. Migration of tribal groups from higher risk zone may be one of the causes of having high prevalence of haemoglobinopathies ([22],[42], [55]). Similar haplotype for tribal groups from different parts of India may be consistent with the hypothesis of the Unicentric origin of the mutation in the globin chain ([53]) as well as Unicentric origin of the tribal population ([56]). But due to the practice of non-random mating pattern for a long time, some particular mutations are restricted to some specific groups ([57]). High inbreeding rate due to consanguineous practices of marriage make this situation more complex, because consanguinity is an important issue to spread the disease ([58]). In addition to this, lack of proper medical facilities, natural barriers like forest, ecological niches etc., poverty, illiteracy, poor sanitation, lack of safe drinking water, faith in traditional beliefs and taboos ([26]) have further compounded the complexity ([23]).

Despite of considerable advancement in management strategies of thalassemia in India, the problem still remains for tribal and isolated populations. Because implementation of technological advances to the realities of health care in developing countries is a challenge. The strategy that has been taken in India is sometimes problematic to implement. Thus the problems related to the tribal groups claim a special intervention strategy for prevention and control of thalassemia, which may be more feasible for the Indian tribes.

A strategy model for controlling thalassemia among the tribes of India (Figure 3) may include treatment and prevention. The only curative treatment available is bone-marrow transplantation and iron chelation, which is highly expensive and not easily affordable by a tribal family. Prevention and control of new thalassemic baby is, therefore, more important to reduce the prevalence of these diseases. Prevention can be done through increasing the awareness and testing at a mass level. But lack of awareness and indifferent attitude towards thalassemia is very common among the tribal people. They are ignorant about the medical, social and financial burden of the disease. Thus in this prevention program priorities should be given on the public awareness, which can be done through community education, awareness camp, awareness at school level and motivation of high risk group. For these, schools, colleges and different government sectors may play major role with active involvement of media. In remote areas where even the media is not accessible, NGOs can take the responsibilities.

The next step of the strategy may include testing at four levels. The first strategy that can be implemented for the tribal population is extended family screening (i.e. the testing of the relatives of thalassemia patients), as the first-degree relatives of a thalassemic patient have “14% higher risk of having an affected child compared to the general population” ([58]). Second level of testing is the carrier screening of unmarried girls and boys of the tribal communities. Next strategy that can be adopted is the

genetic counseling of married couple before pregnancy. Another strategy for screening the target population may be the testing of pregnant women attending hospital/healthcare unit, after which the husband is asked to be tested if the wife is found to be a carrier. The later one is a cost effective strategy as it reduces the screening cost by 50%. This test should be mandate for each and every pregnant woman and should be free of cost for them. And if the result of the test is positive, then the only way is the selective termination of affected fetuses.

But some tribal populations of India live in virtually inaccessible forests and hills and isolated from the main stream of the society. Naturally, regional level prenatal diagnosis centers and facility for medical termination of pregnancy in these areas are not available. Even for the tribal groups inhabited in the rural areas, these facilities are not always accessible. Thus, before implementation all of these strategies, ready availability of the regional diagnostic center or screening center is essential. In this respect, financial support can be sought from major international agencies with the corporation of government to implement the strategies and to achieve the target at urgent basis.

There are still certain tribal groups on which no study is available regarding their thalassemic characters. There is, therefore, a need to study such groups to identify the tribes with high risk for thalassemia so that the target population can be enlisted for rapid action. Apart from this, it may be noted that only awareness is not enough for tribal communities. Constant monitoring is essential through community participation. After the rapport establishment with the community members, people may be sensitized for bringing a positive change in attitude towards the community participation so that they will come forward by themselves for screening test and contribute to the reduction of the prevalence of thalassemia.

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