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REVIEW ARTICLE

A Brief Review of Sickle-Cell Haemoglobin, β-Thalassaemia and G-6-PD Deficiency Genes among Tribals of Scheduled Area of Rajasthan, India: Focus on Tribal Health

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ABSTRACT

Rajasthan, situated at the north-western part of India is the biggest state in the country of India and has total of 33 districts. By merging eight tribal dominating districts namely, Banswara, Chittourgarh, Dungarpur, Pali, Pratapgarh, Rajasamand, Sirohi, and Udaipur of these, the government has created a special area called the 'schedule area" in which >70% of the people are tribal. This area is mostly backward and underdeveloped where malaria is also hyperendemic. In this area, Bhil, Damor, Meena, Garasiya, Kathudia and Sahariya are the most dominating and major endogamous tribes. Besides the several communicable and non-communicable diseases in this area, certain erythrocyte genetic disorders, sickle-cell haemoglobin (Hb-S), β-thalassaemia and G-6-PD deficiency (G^d) are also deteriorating the tribal health and causing morbidity and mortality in them. Genes of these red cell genetic disorders are more prevalent and widely distributed among tribal people. The maximum prevalence of these blood genetic disorders in tribes was found as 31.14%, 9.00% and 22.00%, respectively. Since the groundwater of this tribal area contains a high amount of Fluoride (F), drinking it poses a high risk of premature death of tribal people who already have homozygous state of sickle-cell and β-thalassaemic genes. In present communication, besides the focus on tribal health, the status of genes of sickle-cell haemoglobin, β-thalassaemia and G-6-PD deficiency in different tribal ethnic groups of scheduled area, the correlation of these blood genetic disorders with malaria, impact of F intoxication in tribal subjects possessing red cell genetic disorders and the prevention and control of these erythrocyte genetic disorders in tribal people have been critically reviewed. The results of this review are significant and advantageous in making and execution of prevention and control programme of these blood genetic disorders in tribals of scheduled area of Rajasthan, India. Moreover, in this review, research gaps are also highlighted for further research work.

INTRODUCTION

Rajasthan, situated at the north-western part of India is the biggest state in the country of India and lies between 23˚ 30' and 30˚11' North latitude and 69˚ 29' and 78˚ 17' East longitude. Eco-geographically, this state is separated in to two different regions, desert and humid due to presence of Aravali Mountains and these are located towards western and eastern part of the state, respectively. In the humid region, malaria disease is hyperendemic. The state has a total population of human is 73.53 million who live in its total number of 33 districts. The state of Rajasthan in India is in more discussion because the amount of fluoride (F) in the drinking groundwater here is more than in other states, due to which most of the villagers and their domesticated animals are suffering from dreaded fluorosis disease [1-8].

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During the human evolution, under pressure of certain environmental and biological factors, numbers of erythrocyte or red cell genetic disorders developed due to genetic mutation. In human population, the most common red cell genetic disorders are abnormal or mutant haemoglobins, thalassaemia and G-6-PD deficiency (G^d). These blood genetic disorders may confine or extensively disseminated in specific human populations inhabiting special environmental regions. Generally, genes of these genetic disorders are found in heterozygous and homozygous states in diverse human populations. However, they may also exist in double heterozygous state but these are rare in occurrence. When genes of some genetic disorders, such as sickle-cell Hb and β-thalassaemia found in homozygous state then these are serious to human health and causing morbidity and mortality. These genetic disorders are also known as 'killer' and genes of these disorders are generally referred as 'lethal genes'.

In India, erythrocyte genetic disorders have been extensively investigated in diverse populations or ethnic caste groups of different states and union territories and reported their evidence and prevalence by several researchers [9-35]. In the state of Rajasthan, these blood genetic disorders have also been well studied in subjects belonging to different populations, such as Schedule Tribe (ST), Schedule Caste (SC), Other Backward Caste (OBC), General Caste (GC) populations and minor communities as well [36-47]. Especially, in the malaria endemic scheduled area, Hb-S, β-thalassaemia and G^d disorders have been extensively investigated in various endogamous tribal ethnic groups. The district wise prevalence of these genetic disorders in different tribes of scheduled area has been depicted in table 1 [48-60].

In present review, besides the focus on tribal health, the status of mutant genes of sickle-cell haemoglobin (Hb-S), β-thalassaemia and G-6-PD deficiency among different endogamous tribal ethnic groups of scheduled area, the correlation of these genetic disorders with malaria, impact of F intoxication in tribal subjects possessing red cell genetic disorders and the prevention and control of these erythrocyte genetic disorders in tribal people have been briefly and critically discussed. Findings of this review are significant and advantageous in making and execution of prevention and control programme of these genetic disorders in tribal people residing in the most backward and underdeveloped scheduled area of Rajasthan, India. Moreover, in this review, research gaps are also highlighted for further research work.

Scheduled area and endemic tribes

In India, Rajasthan is the biggest state and has total of 33 districts. By merging eight tribal dominating districts namely, Banswara, Chittourgarh, Dungarpur, Pali, Pratapgarh, Rajasamand, Sirohi, and Udaipur of these, the government has created a special area called the 'schedule area" (Figure 1), located in south eastern part of Rajasthan. This area is the most backward and underdeveloped and characterised with preponderance of diverse tribal communities.

As per Census of 2011, total population of scheduled area is 64, 63,353, out of which scheduled tribe population is 45, 57, 917 which is 70.43% of the total population of the scheduled area. Three districts of this tribal dominating area, namely, Banswara, Dungarpur and Pratapgarh are known as full tribal districts and remaining are partial tribal districts. In the scheduled area, the most dominating and major endogamous tribes are Bhil, Damor, Meena, Garasiya, Kathudia and Sahariya. Later three tribes are the most primitive tribes.

Health status of tribal people

The socio-economic status of the tribal people of scheduled area is very poor. In this area, the literacy rate is considerably very low and the status of health education is almost negligible. These people are not even health conscious. In general, tribal people prefer to live in the forest and remote areas of Arawali hills in isolated form. Financially, the tribal people are depending on traditional agriculture (crop yields), animal husbandry and forest yields. However, for daily income for their family, they prefer daily wages and farming work. Their nutritional status is also very poor. In their staple diet, the main food stuffs are maize, barley, rice, onion, garlic and with or without pulses and vegetables. Occasionally, they consume meat, milk, curd, cooking oil, ghee, seasonal fruits and vegetables. Most of the tribal people have several bad habits, such as consuming of local made wine, tea, smoking and tobacco. Young tribal subjects of both sexes, frequently consume Supari (betel nut) and tobacco containing flavoured Pan Masala and Gutkha. Though, these harmful food items are carcinogenic and responsible for deteriorating the teeth and oral health, tribal boys and girls are frequently consuming both food items.

In General, tribal people are shy, conservative, highly orthodox and superstitious, and have deep faith in their local deities and they believe that they will keep them healthy and away from various diseases. Mostly, tribal people generally used their own traditional methods for the treatment of various diseases including sickle- cell anaemia and β-thalassaemia. One of the methods, which is cruel, terrible and very painful method, they stained with hot iron rods on the patient's forehead, hands, feet, back and abdomen for the treatment of these inheritable diseases. Many times patients die by this method due to secondary infection. This practise is still prevalent in the scheduled area of Rajasthan. In over all, most of the tribal people are not healthy. They are physically weak and many of them are suffering with various kinds of diseases. Most of the tribal children and women are anaemic [11].

Table 1: District wise distribution and incidence (%) of sickle-cell Hb (Hb-AS/SS), β-thalassaemia trait (β-thal trait) and G-6-PD deficiency (G^d) genes among diverse tribes of scheduled area of Rajasthan, India [11,47].

District	Tribes	Hb- AS	Hb-SS	β-thal trait	G^d	References
Bansawara	Bhil	18.0	-	-	-	[43]
	Dumaria	1.45	-	-	-	
	Koli	7.14	-	-	-	
Dungarpur	Damor	4.29	-	-	-	[44]
	Bhil	6.37	1.47	4.90	14.70	[45]
	Mina	6.45	-	5.91	19.35	
	Damor	5.00	0.58	8.52	19.75	
	Garasiya	4.73	0.52	5.78	21.05	
Sirohi	Garasia	20.0	-	-	-	[43]
	Gamit	3.45	-	-	-	
	Garasiya	5.97	-	7.60	15.21	[46]
	Garasia	8.4	-	-	-	[47]
Udaipur	Garasia	31.14	-	-	-	[43]
	Meena	-	-	-	-	
	Bhil	4.28	-	-	-	
	Gamit	14.67	-	-	-	
	Bhil	4.2	-	2.9	16.3	[48]
	Bhil	-	-	-	16.8	[49]
	Mina	4.29	-	-	-	[50]
	Bhil	5.7	-	3.0	13.5	[51]
	Mina	4.4	-	4.8	21.2	[52]
	Garasia	1.1	-	5.0	17.2	
	Damor	-	-	7.9	17.3	
	Gameti	0.6	-	7.4	-	
	Sahariya	3.5	-	5.7	22.0	
	Adivasia	-	-	-	17.5	
	Bhil	7.35	-	4.08	8.16	[53]
	Mina	5.88	-	6.47	15.29	
	Roat	7.27		9.00	10.00	
	ST	-	-	-	16.35	[54]
Humid areas*	Bhil	5.67	0.88	6.73	16.48	[55]
	Damor	4.63	0.51	4.63	14.63	
	Garasiya	4.15	0.34	6.41	13.86	
	Kathudia	5.28	0.96	7.69	15.38	
	Mina	3.03	0.23	4.62	11.00	
	Sahariya	5.46	0.54	6.55	16.19	

*Blood sample collected from various districts of scheduled area of Rajasthan.

In the scheduled area, numerous communicable and non-communicable diseases are still prevalent and hyperendemic [61-78]. In fact, these endemic diseases are the main reason for deteriorating the health of tribal people. The most common and serious diseases which are highly prevalent or hyperendemic in the scheduled area are tuberculosis, malnutrition, sexually transmitted diseases, fluorosis and erythrocyte genetic disorders. These endemic diseases are causing mild to severe morbidity and high rate of mortality in tribal individuals of both sexes of all age groups. Interesting, except few endemic diseases, no enough scientific data are available on these diseases in this tribal region of Rajasthan. Therefore, more epidemiological studies on diverse endemic diseases as well as health surveys in tribal people of this backward tribal area are highly suggested. Outcome of these studies and surveys are important and useful in making of health policy for the saving and improvement of tribal health.

Sickle-cell haemoglobin (Hb-S)

Mammalian Haemoglobin (Hb) molecule (Figure 2) is a conjugated protein with a molecular weight of 64,458 and found in erythrocytes. Normally, it comprises four subunits, each having one polypeptide chain and one haem group. All haemoglobins carry the same prosthetic haem group iron protoporphyrin IX associated with a polypeptide chain of 141 (alpha) and 146 (beta) amino acid residues. These chains are synthesised under the control of genes located

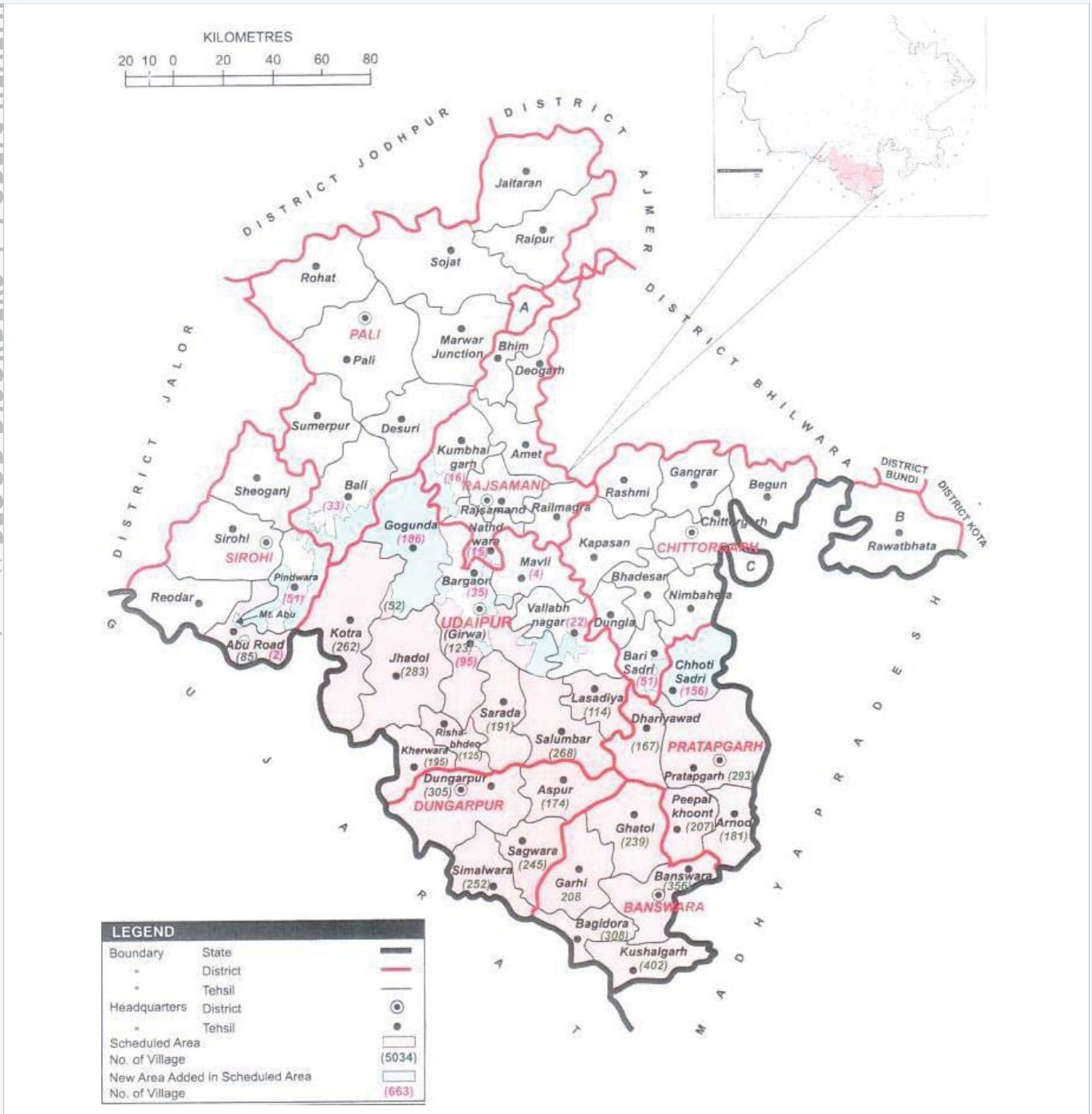

Figure 1 Map showing scheduled area of Rajasthan as per notification of Government of India, 2018.

on chromosomes, 16 and 11, respectively. The polypeptide chains of adult Hb themselves are of two kinds, known as alpha and beta chains, similar in length but differing in amino acid sequence. The alpha chain of all human haemoglobins, embryonic and adult, is the same. The non-alpha chains include the beta chain of normal adult haemoglobin, Hb-A ($\alpha_2^A\beta_2^A$), the gamma chain of foetal haemoglobin, Hb-F ($\alpha_2^A\gamma_2^F$) synthesised prenatally in the foetus, and the delta chain of HbA_2. In some variants, the gamma genes are duplicated, giving rise to two kinds of gamma chains. Before the birth, in foetus, Hb-F initiates to decrease and reach to at zero level at the age of six month. Nevertheless, Hb-F and Hb-A_2 are found in adult person up to 2.5% and 2-3%, respectively [47].

Several abnormal Hbs are synthesised due to structural defects either in alpha or beta polypeptide chains of globins by the mechanism of substitution or deletion of amino acid residues. This is also known as 'point mutation' which is generally taking place under the control of genes that

are responsible for synthesis of Hb molecule. In human population, >1100 abnormal or mutant haemoglobins are identified [79]. However, medical and health and anthropological point of view, abnormal Hb, Sickle-Cell Haemoglobin (Hb-S) is more important as compared to other Hb variants.

Sickle-cell haemoglobin (Hb-S) has existed in humans for thousands of years. This abnormal Hb variant was first described in the peripheral blood of an anaemic patient from the West Indies by Robert Herrick [80]. While homozygous sickle-cell anaemia is the most common and severe form of sickle-cell disease, other sickling disorders combining Hb-S with α and β thalassaemia and other mutant Hb variants share a similar pathophysiology. This abnormal Haemoglobin (Hb-S) results from a single base-pair mutation in the gene for the beta-globin chain of adult haemoglobin. An adenine-to-thymine substitution in the sixth codon replaces glutamic acid with valine in the sixth amino acid position of the beta-globin chain. This mutant Hb can be identified by electrophoresis (Figure 3) and High-Performance Liquid Chromatography (HPLC) techniques. In the deoxygenated form of Hb-S, the beta-6 valine becomes buried in a hydrophobic pocket on an adjacent beta-globin chain, joining the molecules together to form insoluble polymers which give rise to sickle- shape morphology of erythrocytes.

In India, among diverse erythrocyte genetic disorders or abnormal haemoglobin variants, sickle-cell haemoglobin (Hb-S) is the commonest genetic disorder and more prevalent in various human populations as compared to other abnormal Hb variants (Hb-D, E, J, etc.). However, the maximum incidence of sickle-cell gene has been encountered and reported in tribal subjects of both sexes residing in different geographical regions [9,19,20]. In India, the origin of sickle-cell gene is still not known. However, this gene has been reported and detected for first time in India by Lehman and Cutbush [81]. These researchers have reported relatively a high incidence (3.3% to 30.0%) of Hb-S genes in different endogamous tribes. In scheduled area of Rajasthan, the maximum prevalence of this mutant gene

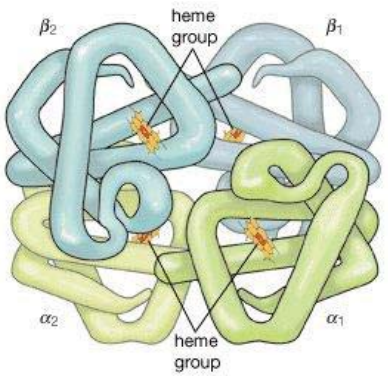

Figure 2 Molecular and basic structure of normal adult Haemoglobin (Hb-AA).

was found 14.6% and 31.14 % in Gameti and Garasiya tribes, respectively [48]. Subsequently, 0.6% to 7.35% incidence of sickle-cell gene in heterozygous (trait) form (Hb-AS) in subjects of different tribes of Udaipur division of scheduled area has also been reported [53,55-58]. From this tribal area of Rajasthan, 1.47% incidence of sickle-cell gene in homozygous state, Hb-SS (sickle-cell anaemia) in Bhil tribe has also been reported [50]. Interesting, this gene was also found in subjects of non-tribal communities, SC and OBC of scheduled area (Table 2 and figure 3). Besides the sickle-cell genes, genes of other mutant Hb variants (Hb-D, E, C, J and H) have also been found in people of scheduled area of Rajasthan [41,42,60,82-84]. This indicates that the state of Rajasthan is pool of diverse Hb variants. Therefore, more haematological studies are required to screen the people of different caste groups residing in desert and humid environments of Rajasthan for current status and evidence of endemic of any new Hb variants.

The present review indicates that sickle-cell genes are not confined to tribal people but are also endemic in non-tribal subjects with an average frequency of 4.3% (range: 0-44%) [85]. It is not surprising and it could be possible by sexual contacts and marriages between subjects of tribes and non-tribes. Nevertheless, based on survey reports, the prevalence of sickle-cell gene in tribal communities found to be 0-18% in north eastern India, 0-33.5% in western India, 1-40% in southern India and 22.5-44.4% in central India and its frequency varies between 0.31- 0.41 [86]. The highest prevalence of sickle-cell gene in the tribal subjects of scheduled area is 31.14% which is relatively higher than the prevalence reported in subjects of SC (10.88%) and OBC (5.98%) populations and other minor communities (1.56%) [46,50,60]. Interestingly, this mutant gene has not been detected in subjects of General Castes (GC). Why it so, reason is not yet clear. To know the reason, more blood screening in subjects of GC population of different geographical provinces in India is highly needed. The co-inheritance of the Hb-S gene with abnormal Hb-C (Hb-SC) was also reported in tribals of scheduled area [60,82] which is the rarest combination being reported from India.

β-thalassaemia

Thalassaemia is also one of the haemoglobinopathies and found more common in diverse human populations. Abnormal haemoglobins are the resultant of changes in structure of polypeptide α and β-globin chains while thalassaemia is due to delay or unbalanced production of these chains. During their production, both are structurally normal. Based on delay in synthesis of α and β-globin chains, two forms of thalassaemia, α-thalassaemia and β-thalassaemia are recognised which are widely distributed globally. Though, genes α-thalassaemia have been detected and reported in different populations of scheduled area [87,88] but medical and health point of view, these genes are least important and significant as compared to

Table 2: The highest incidence (%) of Hb-S, β-thalassaemia and G^d genes in diverse populations of scheduled area of Rajasthan, India [11,47].

Population	Hb-S	β-thalassaemia	G^d
ST	31.14	9.00	22.00
SC	10.88	3.96	16.66
OBC & GC	5.98	7.05	17.60

ST: Scheduled Tribe; SC: Scheduled Caste; OBC & GC: Other Backward and General Caste Populations.

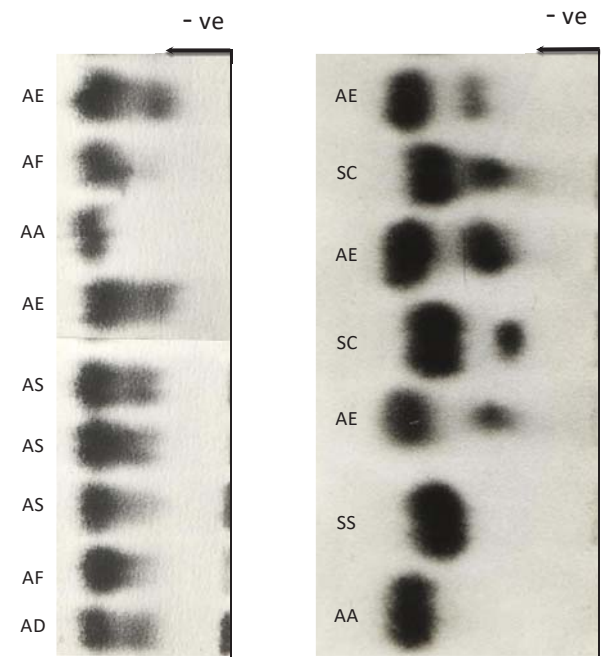

Figure 3 Paper-electrophorosis at pH 8.6 showing migration pattern of homozygous and heterozygous form of various Hb variants, Hb-AA, AF, AD, AE, AS, SS and SC [11].

β-thalassaemic genes. Hence, at global level, the maximum research works have been carried out on β-thalassaemia genetic disorder.

In India, basically two forms of β-thalassaemia, β-thalassaemia minor or trait and β-thalassaemia major or disease are endemic. However, genes of β-thalassaemia trait are rampant in Indian population and prevalent in almost all the endogamous caste gropes with varying incidence. Subjects having these genes are the carriers of β-thalassaemia major. Generally, these people (carriers) are normal in appearance and live life-long as healthy person. The frequency of β-thalassaemia carriers in India varies from 1% to 17% with an average of 3.2% [89]. β-thalassaemia major is lethal and appeared always in disease form in children. In India, first case of β-thalassaemia major was detected in a Bengali boy [90]. Subsequently, genes of β-thalassaemia were reported in diverse populations from all over the country. This indicates that India is a rich reservoir for β-thalassaemic genes [15,17,18,26,89].

In the scheduled area of Rajasthan, the incidence of β-thalassaemic genes varied greatly in population to population. The maximum prevalence (9.0%) of β-thalassaemia trait was reporoted in the Bhil tribe. However, 0.35% prevalence of β-thalassaemia trait in GC, 3.96% in SC and 7.05% in OBC population has also been reported (Table 2) [11]. In few unrelated tribal children, genes β-thalassaemia major have also been detected. However, interaction β-thalassaemic genes with genes of abnormal Hb-S, D and E has also been detected in tribal and non-tribal subjects of scheduled area but the prevalence of such association of mutant genes are rare [11,91].

G-6-PD deficiency (G^d)

It is well known, the mature erythrocytes are lacking of mitochondria, and therefore, the production of energy much more depends entirely on anaerobic glycolysis in Embden-Meyerhop Pathway (EMP). Under steady state conditions, 95% of the glucose is metabolised to lactate, generating energy in the form Adenosine Triphosphate (ATP). Remaining 5% of the glucose enters the Pentose Phosphate Shunt (PPS) or oxidative Hexose Monophosphate Shunt (HMS), which serves as the source of reduced Nicotinamide Adenine Dinucleotide Phosphate (NADPH). The reducing potential of NADPH has great importance for the integrity of the erythrocytes and protects them from drug induced haemolysis or oxidative destruction [92]. In PPS, G-6-PD is first and fate-limiting enzyme and plays a key role in detoxification of H_2O_2 in the erythrocyte and thus prevents lysis of erythrocyte itself. G-6-PD enzyme deficiency (G^d) is a sex-linked defect located on X-chromosome. This defect, generally transmit from mother to son.

G^d is also most common defect in human population of all over the world and more than 400 million people have this red cell genetic defect. In India, this defect has been extensively investigated in diverse populations. However, the maximum surveys on this defect have been conducted, especially in tribal populations residing in diverse malaria endemic provinces. The incidence of G^d is highly variable in different tribes of Western, Central, Southern, Eastern, North, and North-East India and was found as 1.4-31.4%, 13.0.21.5%, 0.10.6%, 1.3-17.4%, 1.2-4.4% and 15.6-27.0%, respectively [27]. In the scheduled area of Rajasthan, G-6-PD deficiency has also been extensively investigated in people of various ethnic groups. Its prevalence varies from 8.03-22-0% among various tribes (Table 1) followed by 1.31-16.66% in SC and 0.64-17.60% in OBC and GC populations (Table 2). The highest incidence (22.0%) of G^d gene was reported in the Sahariya primitive tribe [57]. The co-inheritance of G^d gene with abnormal Hb and β-thalassaemic genes has yet not been detected from scheduled area of Rajasthan. However, to know the status of this defect in primitive tribes residing in other areas of Rajasthan, more studies are highly suggestive.

Correlation of Hb-S, β-thalassaemic and G-6-PD deficiency with malaria

In the state of Rajasthan, relatively a high prevalence

of sickle-cell haemoglobin, β-thalassaemia and G-6-PD deficiency genes has been detected and reported in tribal people residing in humid environment where scheduled area is also located as compared to people inhabiting desert environment (Figure 4). In the scheduled area, malaria is also hyper endemic. Evolution or natural-selection point of view, the occurrence of high incidence of these mutant genes in tribal people of malaria endemic provinces has great significance. The human evolutionary point of view, this deference in the prevalence of these blood genetic defects in malaria endemic and non- malaria endemic geographical regions has a much more significance in understanding of natural-selection. This difference is the resultant of natural-selection in tribal people who are living in malaria endemic area. In fact, in these people, mutation was taking place in genes of erythrocyte located on the chromosomes under the pressure or influence of malaria parasites, *Plasmodium* spp. Tribal people having Hb-S, thalassaemia and G^d genes are protected from *Plasmodium* infection or people having such types of genetic disorders malaria parasites are unable to survive or thrive in their red blood cells [48,93-98].

In evolution, such selection has playing an important role the one hand, in the evolution of living organisms in achieving change in gene frequency by differential survival and reproduction of genotype, and on the other hand, playing a conservative role by producing equilibrium between mutation and selection. Hb-S is one of the best examples for balance polymorphism or natural-selection which is more prevalent in tribals living in the malaria endemic geographical regions. Subjects having Hb-AS (trait) are well protected from malaria parasite infection and do not suffer from sickle-cell disease (Hb-SS) which is a lethal [47]. The relationship between malaria and these mutant genes has been investigated and it is now generally accepted that malaria exerts a selective pressure for the maintenance of higher frequencies of Hb-S, β-thalassaemia and G^d genes in tribals inhabiting malaria endemic areas. However, scientific studies are still requiring confirming the correlation between the incidence of these abnormal blood genes and varying degree of malaria endemicity.

Impact of excess F ingestion

In the scheduled area of Rajasthan, potable groundwater is fluoridated [1,99-102] and contains Fluoride (F) higher than the maximum scheduled limit 1.0-1.5 ppm [103]. Thousands of tribal individuals of both sexes and all age groups of this area are suffering with chronic F intoxication in the form of fluorosis disease and other toxic health hazards due to excess ingestion of such fluoridated groundwater [3]. Chronic F exposure for prolonged period destructs both hard (teeth and bones) and soft tissues including blood cells. Recently, in the study it has been claimed that excess ingestion of F for long-time or chronic F exposure from industrial F pollution causes various haematological degenerative changes leading to death of erythrocytes and causing mild to severe anaemia [104-106]. In the present tribal scheduled area, certain lethal erythrocyte genetic disorders such as sickle-cell anaemia and β-thalassaemia major are also prevalent

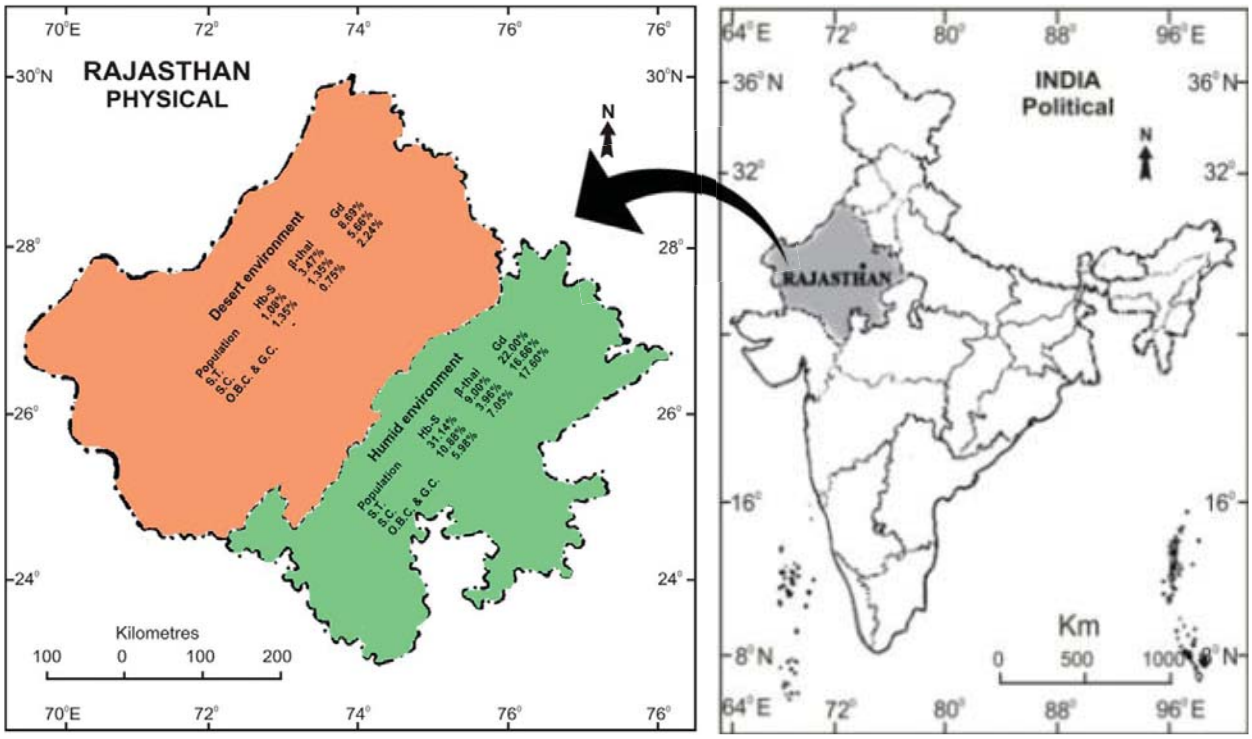

Figure 4 Map showing distribution of genes of Hb-S, β-thalassaemia and Gd in different populations of malaria endemic (humid environment) and non-malaria endemic (desert environment) region of Rajasthan, India [47].

and causing mild to severe anaemia in adults and children, respectively [11]. That's why those who have this type of genetic disorder are more likely to die early due to chronic F intoxication. However, for its confirmation, well designed research studies are highly recommended.

Prevention and control

Among the tribal individuals of scheduled area of Rajasthan, blood diseases, such as sickle-cell anaemia and β-thalassaemia major are more prevalent and considerably responsible for morbidity and high rate of mortality in them. In fact both diseases are fatal. For survival, sicklers and thalassaemic children needed frequent blood transfusions. Though, these diseases could be treated by stem cell and gene therapy and bone marrow transplantation, but the patient is not guaranteed to survive much longer, on the other hand, these techniques are so expensive that they may not be accessible to tribal people. Without effective national planning, curbing these genetic disease and their commodities may seem difficult at the moment but it is not impossible at all.

For good health of tribals of this region, it is necessary to prevent these blood borne genetic diseases from being passed on to the generations to come. Those who are carriers of these diseases, as far as possible, they should neither be married nor have physical relations with them. It is necessary to take these steps so that children are not born with genetic diseases. This is possible through genetic counselling. That is why it is important to have a genetic counsellor at primary health centres in rural areas. Moreover, to identify the carriers, more and more people should have the facility of blood testing by modern techniques at the primary health canters as well as at the district hospital without any charges.

The health of most of the tribals of this area is generally very poor, because many types of diseases, such as fluorosis, malaria, malnutrition, tuberculosis, sexually transmitted diseases, trematodiases, etc. are still endemic in this area. Therefore, in order to maintain good health of the tribal people of this backward and underdeveloped region, it is necessary to provide them with fluoride-free clean drinking water, nutritious food and adequate health facilities. Creating general awareness about health and providing health education among the tribal people also helps in improving their health and control of various endemic diseases.

CONCLUSION

In scheduled area of Rajasthan, genes of sickle-cell haemoglobin (Hb-S), β-thalassaemia and G-6-PD enzyme deficiency (G^d) disorders are endemic and widely distributed among the tribal people of different ethnic groups. The highest incidence of these genes, 31.14%, 9.0% and 22.0% has been reported from this tribal region, respectively. Though, these genes in heterozygous states are beneficial and provide protection against malaria but their homozygous states are more serious to tribal health and causing considerable morbidity and mortality among the tribal people. Inheritable sickle-cell anaemia and β-thalassaemia major disease are fatal, irreversible and untreatable. Therefore, it is more important to run a health project to prevent and control these diseases. It is also suggestive that "neonatal screening" is also better way for early diagnosis of these lethal diseases and their carriers. To know the status of inheritable these red cell genetic disorders in diverse primitive tribes surviving in different districts of Rajasthan, an epidemiological health survey studies are also needed. The results of these studies prove to be helpful not only in formulating health policies but also in improving the health of tribals.

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