

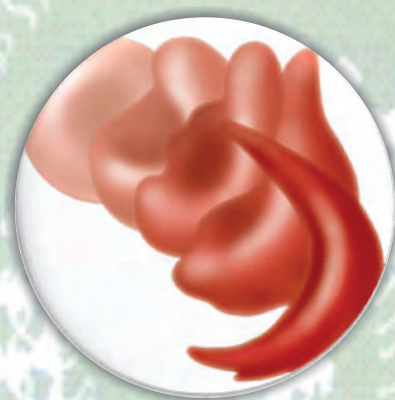
# IMMUNOHAEMATOLOGY BULLETIN



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**Farewell to Mr. S. T. Dukhande, Section Officer**



**3rd review meeting to monitor the development of RDB kit**

## Director's Message



National Institute of Immunohaematology (NIIH) was started originally as Blood Group Reference Centre (BGRC) by ICMR way back in 1957. As the name implied its original task was to study various blood group antigens

training and developing human resources in blood group serology and to become self sufficient with serology reagents. Naturally in its quest for distribution of blood group antigens different population groups were studied including various tribal populations of India. BGRC became Institute of Immunohaematology (IIH) in 1984. By that time the institute developed additional interest in studying red cell enzymopathies, hemoglobinopathies, autoimmunity, HLA, hepatitis to name a few. HbsAg was studied in various populations including large number of tribal population in different parts of the country. It was clearly shown that the tribal groups have higher prevalence of HbsAg seropositivity and this seropositivity did not always correlate with tattooing. Hence other mode of transmission was suspected. G6PD deficiency was studied in several tribal groups leading to detection of a couple of G6PD variants and its linkages to migration of population from Africa to Australia over Indian subcontinent were shown through the demonstration of G6PD Namoru in South Indian tribes. HLA studies in the tribes of Maharashtra showed HLA antigens linked to malaria resistance HLA B-53.

The institute did extensive work on sickle cell gene,

other hemoglobinopathies and their interaction in various tribal populations mainly in west, central and north-eastern parts of India. Iron deficiency and intestinal parasites were found to be increased the morbidity of sickle cell patients in this part of the country and the solutions are simple and effective. Genetic interaction of a Thalassemia and other polymorphisms in different parts of India were shown to strongly modulate the severity of sickle cell disease in various tribal groups. To help these tribal population prenatal diagnostic centres were established at Valsad in Gujarat and Nagpur in Maharashtra. Training programme on molecular diagnosis was conducted in Orissa, Jharkhand, Assam, Tripura, Mizoram and Sikkim to help developing molecular technology for detection of hemoglobinopathies, so that eventually prenatal diagnosis of serious hemoglobinopathies in tribal area will be possible. As in remote places where tribal population of the country generally lives, there was a need for simple and robust technique to detect sickle cell disease. Investigations including more than 3000 individuals in the tribal area of Dhule, Maharashtra conclusively proved that modified solubility test is cheaper and can readily be detected this condition with ease. We had some gap in knowledge about the morbidity of sickle cell disease in newborn in this country and a study was initiated 3 years back at Valsad and Nagpur. This study is continuing and is yielding interesting results with significant regional variation in mortality and morbidity of sickle cell disease. Feasibility of using hydroxyurea for management of sickle cell disease in tribal area was also demonstrated by us.

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Study on molecular pathology of hypertension was also undertaken among the tea garden workers from Assam who are largely tribals. Quite a few people from tribal areas of India migrate to nearby city/metropolis in search of livelihood. Coming to the city they face multiple challenges which spans across all the health issues. We have also studied some of those issues in Oraon population who migrated to Mumbai from Orissa.

We must understand that tribal population of India also suffer same diseases as we non tribal population. Since they live in the forest areas of India where in addition to malaria, other communicable diseases like leprosy, maternal and child health problems, hemoglobinopathies are also common. In addition to loss of earning and non conventional food/ fodders as obtained from the forest due to deforestation, family tension, alcoholism and mining in major tribal areas also produce environmental hazards. The solution of positive health not only for tribal health but everybody in this country should be based on quantum improvement in public health and general improvement of available health care facility in the affordable and equitable manner in this country. NIIH will always be available to provide solution to tribal health through research in its own area of expertise i.e hematological and immunological disorders.

August is an important month for the tribal welfare and 9th August is dedicated as World's Indigenous People day. I would like to thank the Editor of NIIH bulletin for bringing out a special issue where the work done by our Institute for India's Indigenous population has been highlighted. The crux of the problem seems to be empowering this population through education and other means to decide what they want for their well being. Over thousands of years our Indigenous population has acquired immense knowledge and wisdom to use nature and natural products without destroying the relationship of man with the nature. Finally we must not forget that Rishi Valmiki who

composed world's first poem and compared India's immortal classic "Ramayana" was one of the Indigenous people of this noble land.

Studies on tribal populations would not have been possible without the local help from various institutions. Our sincere thanks to Regional Medical Research Centre, Dibrugarh, Regional Medical Research Centre, Bhubhaneshwar, National Institute of Nutrition, Hyderabad, Govt. Medical College, Nagpur, Valsad Raktadan Kendra, Valsad, Govt. Medical College, Agartala, Nilgiri Adivasi Welfare Association, Nilgiri, Jiganshu Tribal Research Centre, New Delhi, Jawahar Medical Foundation, Dhule, Pt. J. N. Medical College, Raipur and other local government agencies in the respective state for their association and co-operation in these studies.



## Contribution of National Institute of Immunohaematology (NIIH) on Tribal Health Research

**Malay B Mukherjee**

The most remarkable feature of the Indian population structure is the clear division of its population into strictly defined endogamous castes, tribes and religious groups. India has the largest concentration of the tribal population in the world. It is generally believed that the tribal people, who constitute 8.2% of the total population (2001 census of India), are the original inhabitants of India and are generally called “Adivasis”. The tribals can be classified according to their ethnic origin, language, race, socio-economy and cultural pattern. It has been estimated that there are a total of 697 tribal communities including 75 primitive tribal groups in India. The tribals are found in all the states except in Punjab, Haryana, and Jammu & Kashmir. The primitive tribal communities have been identified by Govt. of India on the basis of i) Pre agricultural level of technology, ii) extremely low level of literacy and iii) small, stagnant and diminishing population.

Majority of the tribal people live below the poverty line. They generally reside in isolated hilly and forest areas and are not accessible at most of the times during the year. There is a consensus agreement that the health status of tribal populations is very poor and is even worse among the primitive tribes because of their isolation as a consequence of their residing in remote areas and thus being largely unaffected by the developmental processes going on in the country. Therefore, they are deprived from the basic amenities like health, education, proper sanitation etc.

The Institute over the last 50 years has concentrated its activities on tribal health research by undertaking various projects. A total of 46 tribal groups from 36 districts of Maharashtra, Rajasthan, Gujarat, Dadra and Nagar Haveli, Madhya Pradesh, Chhattisgarh, Orissa, Tamil

Nadu, Kerala, Assam, Tripura and Andaman and Nicobar islands were studied (Fig 1).

Anemia especially iron deficiency anemia (IDA) was found to be one of the commonest problems among the tribal groups and the prevalence rate varied from 5.30% to 57.70%. The highest prevalence was observed among the tribal groups of Orissa followed by Maharashtra, Gujarat and Tamil Nadu (Fig.2). Although IDA was found to be common in both children and adults, however, females of the child bearing age were more affected than the males. Among the children, the prevalence of IDA varied from 4.5 to 56.5% and 4.1 to 55.0% in the age group of 6 months to 5 years and 6 years to 18 years respectively whereas in adults it varied from 3.1 to 56.4% and 1.5 to 66.4% in males and females respectively. The high prevalence of anemia in some of the tribal groups from Orissa could be partially explained by the higher prevalence of helminthic infections like hook worm which is the commonest infection and varied from 10.9% to 17.9% followed by round worm infection (5.8 to 8.6%). It has been observed that by giving anti helminthic treatment the incidence of worm infection could have been reduced from 29.0% to 11.0% and their hemoglobin levels were also improved.

The hereditary disorders like hemoglobinopathies further added to the problems because of their high prevalence in some of the tribal groups which poses a major public health problem. Of these, sickle cell anemia is very important because the sickle cell gene was found to be present in almost all the tribal groups studied except the tribes of Assam, Tripura, Andaman and Nicobar Islands and the prevalence rate varied from 0.7% to 21.3% (Fig. 3). A very high frequency of sickle cell gene was observed among the tribal groups of Madhya Pradesh (21.3%), Tamilnadu (17.2%), Dadra and Nagar Haveli (15.2%),

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Gujarat (15.0%) and Maharashtra (11.5%). The clinical manifestations of sickle cell anemia were found to be mild to moderate as compared to African populations. Vasoocclusive crisis in the form of pain all over the body was observed commonly as one of the major clinical manifestations and some of the patients also required hospitalization for the painful episodes. Infections usually in the form of high grade fever and involving the upper respiratory or urinary tract were found to be common in these patients. Enlargement of the spleen and liver were also observed in these patients. Sickle cell anemia patients were advised to take ORS (electral powder) and plenty of fluids during vasoocclusive crisis. Hepatitis B, H influenza and pneumococcal vaccines were given to sickle cell anemia and sickle cell trait cases from Maharashtra and Gujarat. No evidence of proliferative retinopathy was seen. Visual acuity, peripheral field and color vision were found to be normal.

$\beta$ -thalassemia was not uncommon and was present in 0.7% to 7.8% of tribal individuals in different states (Fig.3). A higher prevalence of  $\beta$ -thalassemia trait was observed among some of the tribal groups of Rajasthan, Orissa, Dadra and Nagar Haveli, Gujarat and Maharashtra. Another striking observation was a very high prevalence of  $\beta$ -thalassemia trait among the Nicobarese (7.8%) and the presence of a very rare mutation, codon 47(+A) in this group. Sickle cell  $\beta$ -thalassemia which results from compound heterozygosity for sickle cell trait and  $\beta$ -thalassemia has also been observed among the tribal groups from Maharashtra and Gujarat. It is interesting to note that a higher prevalence of HbE trait was observed among the tribes from Assam, Tripura and Andaman and Nicobar Islands (Fig.3).  $\delta\beta$ -thalassemia/HPFH trait cases were also identified in some of the tribal groups from Maharashtra, Gujarat, Tamilnadu and Orissa with a prevalence of 0.6% to 4.1%. Sporadic cases of Hb D trait were also found among the tribals of Gujarat, Orissa and Tamilnadu. A higher prevalence (56% to 98%) of one or the other form of  $\alpha$ -thalassemia due to either one or two gene deletions was also found among some of the tribal groups of Maharashtra and Gujarat. The clinical importance of this is the interaction of  $\alpha$ -

thalassemia with other hemoglobinopathies like hemoglobin S or  $\beta$ -thalassemia. It has been observed that the clinical course of sickle cell anemia cases was milder whenever associated  $\alpha$ -thalassemia was present and splenomegaly was more common among these patients.

Iron deficiency anemia was found to be very common in sickle cell anemia patients (50.0%) followed by  $\beta$ -thalassemia trait (23.2%) and sickle cell trait (18.3%). Intervention and follow up was initiated in sickle cell anemia (SS) and sickle cell trait (AS) cases having IDA for a period of one year at an interval of three months. These patients were given 3mg/kg/day elemental iron supplementation in the form of ferrous sulphate for duration of 12 weeks and were reassessed clinically along with the measurement of hemoglobin (Hb) levels and zinc protoporphyrin/heme ratio (ZPP/H). Following iron therapy, a significant improvement in Hb level and a decrease in ZPP/H ratio were observed in both sickle cell anemia and sickle cell trait cases. An improvement in work efficiency was also observed in SS cases after intervention.

Laminated color coded report cards were distributed to all the tribal individuals whose blood was tested. Genetic counseling was given to the unmarried young individuals to avoid marriages between the carriers of hemoglobinopathies particularly HbS and the usefulness of blood testing before selecting a life partner was also explained. Awareness programme was also initiated in the tribal community as well as for the local doctors and health planners. The young carrier couples have been told about the option of prenatal diagnosis for having a healthy child.

The awareness programme seemed to be effective in the states of Maharashtra and Gujarat. It was evidenced by the fact that there was an increase in the number of individuals coming for voluntary blood testing for knowing the carrier status as well as the number of cases referred to NIIH for prenatal diagnosis has also been substantially increased. The medical and para medical staffs are now being trained by us regularly for dealing with cases of sickle cell disease in the tribal groups of Maharashtra and Gujarat.



The impact of genetic counseling is a long term process; however, in Maharashtra and Tamilnadu it has been observed that tribal people are getting their blood tested before marriage. In a study, 98 tribal individuals in the marriageable age could be followed up for five years after doing initial counseling. During this period, 12 marriages took place. Out of seven marriages in sickle cell trait cases, 6 marriages took place with normal subjects and one was with an unscreened person. The remaining 5 marriages were with unscreened persons.

Prenatal diagnosis for sickle cell anemia, sickle- $\beta$  thalassemia and  $\beta$  thalassemia major has been offered by us to several tribal couples from Maharashtra and Gujarat and a few from Madhya Pradesh and Rajasthan. We have also helped to establish two centres for prenatal diagnosis at Valsad and Nagpur to cater to tribal populations in South Gujarat and Maharashtra. The feasibility of undertaking newborn screening for sickle cell disorders and enrolling babies with sickle cell disease and sickle- $\beta$  thalassemia for comprehensive care has been demonstrated by us in these areas. In a pilot study in Gujarat, 13.3% of the new born babies were found to have sickle cell gene and sickle homozygous babies are now being followed up regularly to understand the natural history of sickle cell disease in this part of the country.

G6PD deficiency was also found in all the tribal groups and the prevalence rate varied from 0.4 % to 14.0% in different states (Fig. 3). In the males G6PD deficiency varied from 0.7% to 31.4% while in females it varied from 0.8% to 12.9%. G6PD Orissa (131 C $\rightarrow$ G) and G6PD Mediterranean were found to be the main mutational event causing G6PD deficiency among the tribal groups of Maharashtra and Gujarat respectively while G6PD Namoru (208 T $\rightarrow$ C) was exclusively found among the Dravidian speaking tribes of Nilgiri district, Tamilnadu which further supports the human migration from Africa to Australia along the coast of southern India.

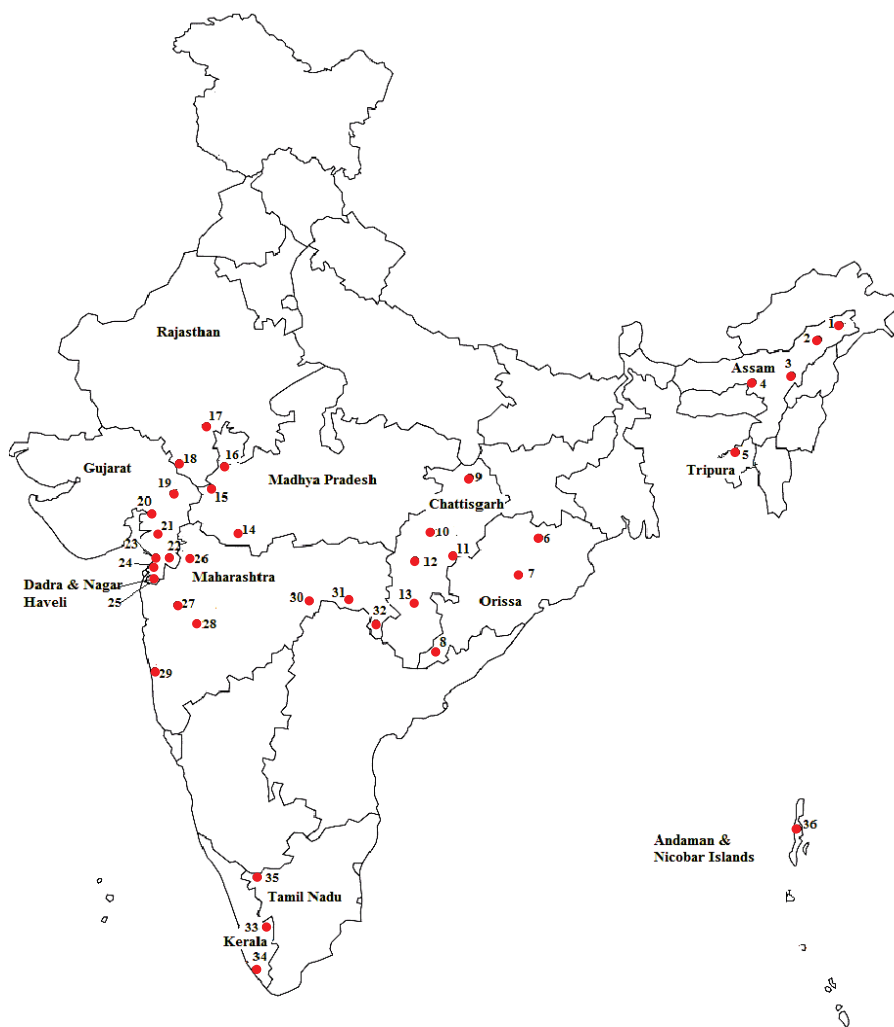
Hepatitis B virus infection, essentially a blood borne and sexually transmitted infection was found to be common among some of the tribal groups and the HBsAg carrier rate varied from 6.0% to 21.0%. A higher prevalence (10

to 21%) of HBsAg carriers were found among the tribals of Madhya Pradesh, Rajasthan and Maharashtra. A high incidence (12.28%) among the females from Yavatmal district of Maharashtra is a noteworthy observation.

To get an overview of other common health problems in these tribal groups, an elaborate history was taken and detailed clinical examination was done in all age groups and both sexes. Figure 4 shows the general health problems among the tribal groups studied in different states. Pallor and malaria were found to be very common among all the tribal groups except tribals of Tamilnadu. Parasitic infection is an important cause of poor nutritional deficiency and most of the tribal groups had a history of passing parasites in the stool with a high frequency. Diarrhoeal disorders were also found to be very common in all the tribal groups. Vitamin deficiency was found to be present in majority of the tribes with a prevalence rate of 14.7% to 36.8%. Some of these tribes also showed the signs of avitaminosis like Bittot's spot, angular stomatitis. Tuberculosis has also been encountered in some of the tribal groups. A substantial percentage of tribal individuals showed high blood pressure and this varied from 4.8% to 12.7% in different states suggestive of hypertension.

Hence, our study showed that tribal populations of India suffer from different types of hemoglobinopathies, G6PD deficiency, malaria, nutritional problems like iron, vitamin and other micronutrient deficiencies, anemia, gastrointestinal parasitosis and a host of common infections like diarrhea, respiratory tract infection, tuberculosis and sexually transmitted viral infections.

While NIIH can work in an advisory capacity for each state regarding management and control of genetic and acquired hematological disorders, however, a more comprehensive health care plan for each of the tribes needs to be drawn out by each state for their own geographical tribal back yards. Hence, the core plan needs to be varied and tailored for each of the tribal groups in their own geographical niche. Once this is done, only then we will be able to say that we have done something positive for the betterment of tribal health.



Sr. No.	Geographic Location	Name of the Tribes
1.	Tinsukia	Meistes, Mishing, Kachari, Bodo, Deori
2.	Dibrugarh	Meistes, Mishing, Kachari, Bodo, Deori
3.	Golaghat	Meistes, Mishing, Kachari, Bodo, Deori
4.	Kamrup	Meistes, Kachari, Bodo
5.	Agartala	Tripuri
6.	Kendujhar	Kondhas
7.	Phulbani	Juangas
8.	Malkangiri	Bondos, Didayis
9.	Ambikapur	Gond, Oraon, Kwar
10.	Raipur	Gond, Kwar, halba
11.	Mahasamund	Gond, Kwar
12.	Dhamtari	Gond
13.	Bastar	Gond
14.	Khargone	Barelas
15.	Jhabua	Bhil, Patelia, Bhilala
16.	Ratlam	Bhil
17.	Chittorgharh	Minas
18.	Dungarpur	Bhil
19.	Panchmahal	Bhil
20.	Bharuch	Dhanka
21.	Surat	Kathodi, Naik, Gamit, Dhodia, Koli
22.	Dang	Kokana
23.	Navsari	Kotwadia, Kolcha
24.	Valsad	Kotwadia, Kolcha, Dhodia Patel, Koli
25.	Dadra and Nagar Haveli	Warli, Dodiya, Kokana
26.	Dhule	Bhils, Pawara
27.	Nasik	Mahadeokoli, Bhil
28.	Raigad	Katkari
29.	Ahmednagar	Mahadeokoli
30.	Yavatmal	Madia Gond, Pardhan, Kolam
31.	Chandrapur	Raj Gond, Pardhan, Naiik Gond
32.	Gadchiroli	Madia Gond
33.	Idukki	Kadar
34.	Trivendrum	Malai Arayan
35.	Nilgiri	Irula, Kurumba, Paniyas, Mullukurumba, Toda
36.	Andaman & Nicobar Island	Great Andamanese, Nicobarese

**Fig 1: Map of India showing the geographical locations and name of the tribes studied at NIIH**



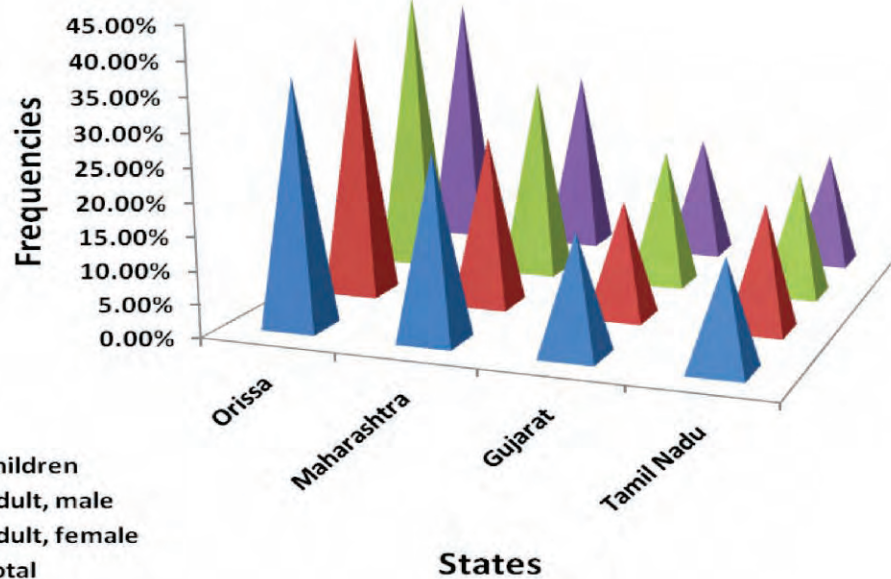


Figure 2: Iron deficiency anemia among the tribal groups studied in different states of India

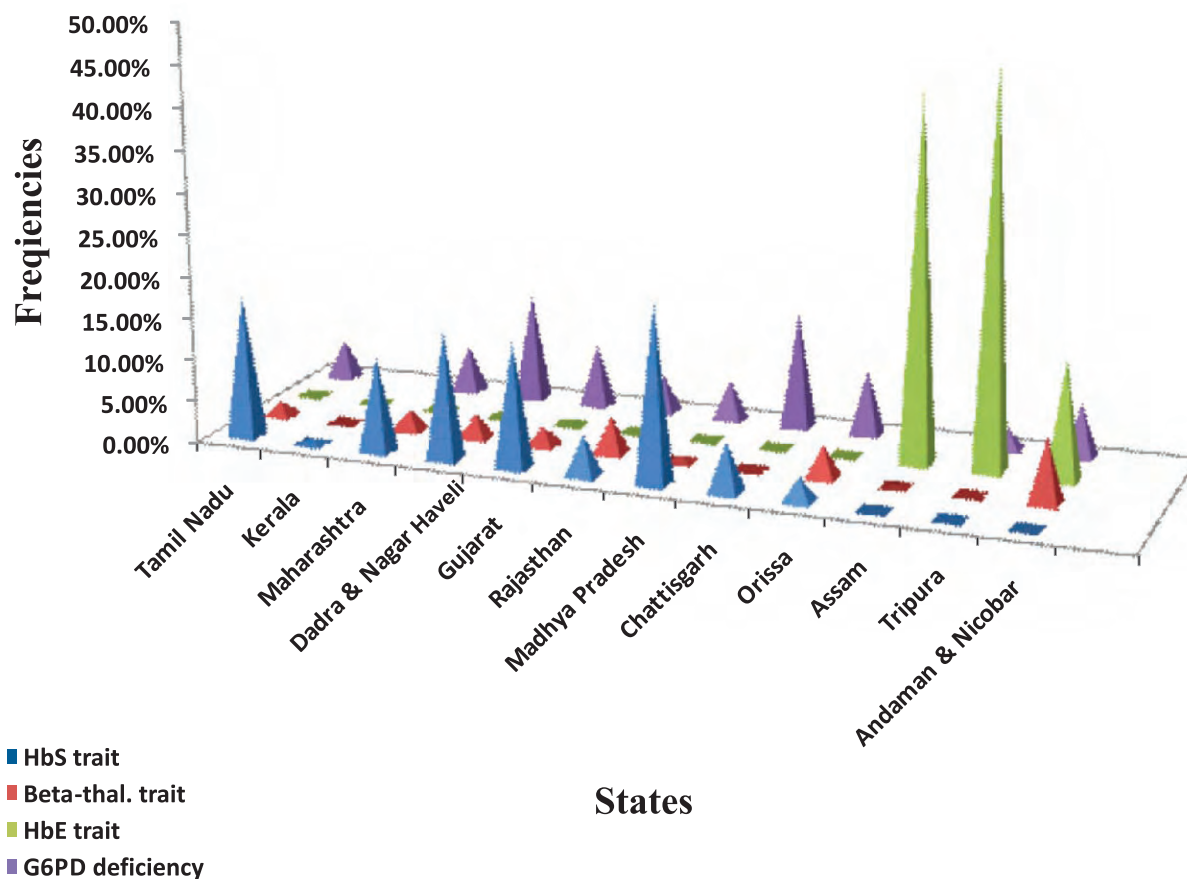
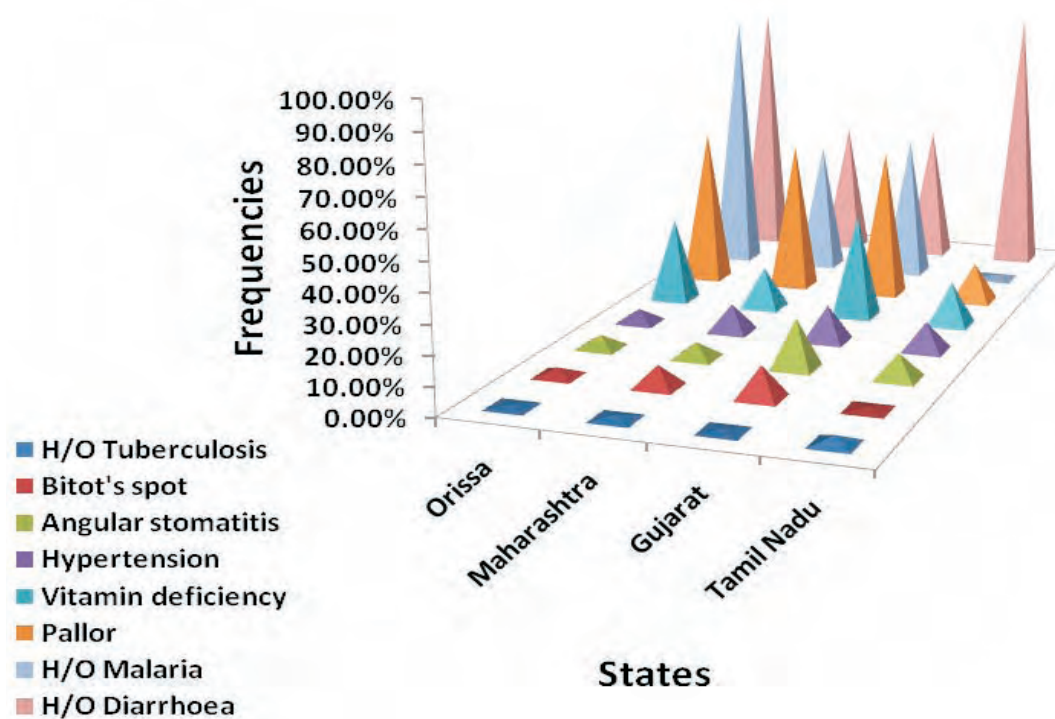


Figure 3: Red cell genetic abnormalities among the tribal groups studied in different states of India



**Figure 4: General health problem among the tribal groups studied in different states of India**

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## NIIH HAPPENINGS

### **Dr. K. Ghosh, Director**

1. Attended the Expert Group Meeting at ICMR Headquarters, New Delhi on 2nd May 2013.
2. Invited as an external examiner to conduct DM examination in Transfusion Medicine at PGIMER, Chandigarh from 3rd to 4th May 2013.
3. Invited to conduct the viva voce examination of Ph.D student at Pune University on 14th May 2013.
4. Attended the National Hemoglobinopathies Conference at St.John's Hospital, Bangalore from 8th to 9th June 2013.
5. Invited as an expert for the selection committee meeting at King George Medical College, Lucknow on 19th June 2013.
6. Attended the Brain Storming Meeting at ICMR, New Delhi on 20th June 2013.
7. Attended the FDA Expert committee meeting to examine the specifications and criteria for acceptance for tests performed in “Blood Glucose Test Strips” and “Analyser based Glucose Reagents” at Department of Science and Technology, New Delhi on 5th July 2013.
8. Attended the Tribal Health Meeting at Valsad from 11th to 13th July, 2013.
9. Attended the Scientific Advisory Committee Meeting of CDFD, Hyderabad from 26th to 27th July, 2013.
10. Invited as an expert committee member at Nicholas Piramal Health Care, Mumbai on 31st July 2013.
11. Attended the Tribal Health Forum Meeting at DMRC, Jodhpur from 9th to 10th August 2013.
12. Attended the Hemophilia AGM meeting at Bangalore from 17th to 19th August 2013.
13. Attended the Project Review Committee Meeting at ICMR Headquarters, New Delhi on 24th August 2013.

### **Hemato-Genetics**

#### **Dr Roshan Colah, Scientist F**

1. Invited to give a talk on “Genotype-Phenotype Diversity in the Thalassemias” at the National Conference on Thalassemia at St John's Medical College, Bangalore on 17th to 18th May 2013.
2. Invited to give a talk on “Current Status of Thalassemia Prevention and Management in India and Maharashtra and Possibilities of National / Regional Prevention Programmes” at the 1st Capacity Building Workshop for Patients / Parent's Organizations conducted by Thalassemia International Federation and Federation of Indian Thalassemics in Mumbai on 19th May, 2013.
3. Delivered two lectures on “Prenatal Diagnosis of Thalassemia” and “Hemolytic Anemias and Red Cell Enzymopathies” for students doing the Diploma in Transfusion Medicine at the College of Physicians and Surgeons, Mumbai on 5th July, 2013.
4. Visited Valsad Raktdan Kendra, Valsad for the Collaborative project on Newborn Screening for Sickle Cell Disorders under the ICMR's Tribal Health Research Forum from 11th to 13th July, 2013.
5. Attended the Tribal Health Research Forum meeting of ICMR at DMRC Jodhpur on 9th and 10th August, 2013.
6. Attended the Red Cross Blood Transfusion Sub-Committee meeting at the Red Cross Blood Bank, Mumbai on 13th August, 2013.

#### **Dr Malay Mukherjee, Scientist D**

1. Attended Combined Project Review Committee meeting on Anatomy, Hematology, Anthropology and Human Genetics held at ICMR Headquarters, New Delhi on 7th May 2013.

2. Visited Valsad Raktadan Kendra, Valsad to initiate a collaborative project on New Born Screening for sickle cell disorders among the tribal groups of South Gujarat under the ICMR's Tribal Health Research Forum from 11th to 13th July 2013.
3. Attended “Tribal Health Research Forum Meeting” held at DMRC, Jodhpur on 9th and 10th August 2013.

## Cytogenetics

### Dr Babu Rao, Scientist D

1. Attended as an external expert for scientific review committee meeting at National Institute of Research in Reproductive Health (NIRRH), Mumbai on 18th June 2013.
2. Attended advanced workshop on “Good clinical practices in clinical research for ethics committee members” at NIRRH, Mumbai on 27th August 2013.

## Pediatric Immunology and Leukocyte Biology

### Dr Manisha Madkaikar, Scientist E

1. Invited to deliver a lecture on 'Flowcytometry in hematology' during 3rd CME on “Clinical and Laboratory Hematology” held at Kozhikode, Kerala from 22nd to 23rd June 2013.
2. Invited to deliver a lecture on 'Flowcytometry: basics' at College of Physicians and Surgeons, Mumbai for DTM course on 10th June 2013.

## Hemostatis

1. Ms. Sharda Shanbhag, Technician C and Ms. Rucha Patil, SRF attended ISTH 2013 from 29th June to 4th July 2013 at Amsterdam, Netherlands and presented the papers “Molecular pathology of severe factor XIII deficiency from India” and “Elevated pro coagulant micro particles in women with recurrent pregnancy loss” respectively.

## Others

1. Mr S T Dukhande, Section Officer superannuated on 30th June 2013 after completion of 37 years of service.



**Scientists interacting with Dr Narla Mohandas, Vice President for Research & Laboratory Head, Red cell Physiology, New York Blood Centre, New York, USA**



**Dr Narla Mohandas delivering a lecture on Red Cell Membrane**





**Felicitation of the Staffs who have completed 25 years of service**

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