Scenario of haemoglobin variants in Central-East coast of India

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Haemoglobinopathies are the most common monogenic inherited disorders of erythrocytes. Carriers of haemoglobinopathies are partially protected against morbidity and mortality of *falciparum* malaria, resulting in their higher prevalence in tropical countries. Estimates in India show 3–17% prevalence of β-thalassaemia, but its magnitude in the Central-East coast of India, especially in Orissa is not known. One thousand fifteen cohort cases of anaemia were analysed, referred from different peripheral hospitals and medical colleges and hospitals in the Central-East coast of India during 1994 to 2003. Background data of each individual were recorded like age, sex, caste, place of origin, consanguinity, etc. Standardized laboratory procedures and techniques were followed. Most common haemoglobinopathies observed out of 1015 cases were: sickle cell trait (29.8%), sickle cell disease (7.5%), sickle cell-β-thalassaemia (1.7%), β-thalassaemia trait (18.2%), β-thalassaemia major (5.3%), thalassaemia intermedia (0.9%), Hb E trait (0.9%), Hb E disease (0.3%), Hb E-β-thalassaemia (0.7%), Hb D trait (0.2%) and SD disease (0.2%). Sickle cell disorders with high level of foetal Hb were common in general castes (0.3–20.7%), scheduled castes (0–8.9%) and scheduled tribals (0–5.5%). Transfusion-dependent β-thalassaemia syndrome was prevalent among Brahmins, Karans, Khandayats, Telis, etc. Most of the cases belong to Anugul district, followed by Khurda, Nayagarh, Kandhamal, Cuttack, Jajpur, Dhenkanal, Ganjam, Keonjhar, Mayurbhanj, etc. The heterogeneous population harbours almost all major haemoglobinopathies in general castes, scheduled castes and tribes, belonging to coastal and southwestern regions of Orissa. This study provides a comprehensive database on the pattern of spectrum of haemoglobinopathies in the Central-East coast of India.

Keywords: Central East coast of India, ethnic diversity, structural haemoglobin variants, population health, β-thalassaemia syndrome.

THE inherited disorders of haemoglobin are quite prevalent in tropical countries of the world, including India. While the general incidence of β-thalassaemia trait and sickle cell haemoglobinopathy varies between 3–17% and 1–44% respectively, because of high consanguinity, and caste and area endogamy, some communities show high incidence, making the disease a major public and genetic health problem in India[1,2]. Inherited disorders of haemoglobin synthesis are an important cause of high morbidity and mortality worldwide. They place a huge burden on the patients, their families and the communities. They are generally not curable, but can be prevented by population screening, prenatal diagnosis, genetic counselling and avoiding marriage between the carriers[2].

Orissa presents a kaleidoscopic mosaic of various communities and inhabits 36.7 million people comprising 22.4% scheduled tribes and 16.2% scheduled castes. Widespread poverty, illiteracy, malnutrition, absence of safe drinking water and sanitary conditions, poor maternal and child health services, ineffective coverage of national health and nutritional services, etc. are the major contributing factors for dismal health in Orissa. People have their unique socio-cultural customs, traditions, breeding practices and lifestyles quite distinct from each other, which affect the breeding structures and vulnerability towards silent-killer hereditary diseases in Central-East India[3].

There is a dearth of community-based genetic research in the Central-East coast of India[4]. The Regional Medical Research Centre at Bhubaneswar, under the Indian Council of Medical Research, New Delhi, caters to research facilities for population screening, provides diagnostic and genetic counselling services to referred cases from Central-East India to the affected persons and their families. Since the suspected cases of anaemia are referred from the entire Central-East India, representing vulnerable communities, ethnic groups, etc. they could well represent the local population and pattern of haemoglobinopathies in the region. This article presents the pattern of haemoglobinopathies in a cohort of referral cases of anaemia for the period from 1994 to 2003 in the Central-East part of India. The present analysis was carried out with the following aims and objectives in mind: (i) to determine the pattern of spectrum of haemoglobinopathies in a cohort in Orissa; (ii) to identify high risk communities/ethnic groups with frequencies of haemoglobinopathies, (iii) geographic clustering or distribution of haemoglobinopathies, (iv) attempts to trace emigrational pattern/gene flow of population, and (v) to delineate the genetic heterogeneity and related epidemiological aspects of cases of haemoglobinopathies in the region.

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Materials and methods

The subjects included in this study were natives of Orissa having permanent resident status. A total of 1015 people were referred to the Division of Human Genetics, Regional Medical Research Centre (ICMR), Bhubaneswar as suspected cases of hemolytic anaemia from different peripheral hospitals and medical colleges and hospitals in Central-East India during the period from 1994 to 2003.

About 2–3 ml intravenous blood samples were collected after obtaining the informed consent, using disposable syringes and needles with disodium salt of ethylene diamine tetra acetic acid (EDTA) as anticoagulant from each individual free of at least one month's blood transfusion. Hematological indices were measured using MS4 Blood Cell Counter (Melet and Schloesing Laboratories, France), which was calibrated with commercially available controls (Bio Rad Laboratories, Hercules, CA, USA). Laboratory investigations were carried out following standard procedures after cross-checking for quality control from time to time. Data of each individual pertaining to age, sex, caste, place of origin, consanguinity, etc. were recorded.

Using freshly prepared sodium metabisulphite solution as reducing agent, the sickling test was performed[5]. The routine haemoglobin electrophoresis was carried out on cellulose acetate membrane (CAM) in Tris–EDTA–borate buffer at pH 8.9 and quantification of A_2 fraction of adult haemoglobin by elution method[5,6]. A value more than 3.5% of A_2 fraction of haemoglobin was taken as the cut-off point for determining the β-thalassaemia trait and more than 10% was assumed[7] to be haemoglobin E. Electrophoresis in acidic medium (pH 6.2) was also carried out to identify and confirm the presence of haemoglobin D or E band[6]. Foetal haemoglobin was estimated by the method of Betke *et al.*[8], as described by Weatherall[6]. Family studies were carried out to confirm the diagnosis, wherever it was necessary; results of relatives were also included in analysis of the present study.

Results

A total of one thousand fifteen suspected cases of anaemia were referred to the Regional Medical Research Centre, Bhubaneswar during the period of ten years (1994–2003) for further diagnostic investigations and counselling and 354 families were screened. Out of 1015 cases, 348 (34.3%) were found normal and 667 (65.7%) had some form of haemoglobinopathies. Out of 667 abnormal cases, 349 (52.3%) were males and 318 (47.7%) females, thus giving preponderance of males over females. Due to socio-cultural factors, more importance is given to males than females regarding healthcare in India, which is reflected in this cohort study of referral cases.

The spectrum of haemoglobinopathies encountered during the cohort period, i.e. 1994 to 2003 is given in Table 1. It is interesting to note that the sickle cell trait is the most common haemoglobinopathy (29.8%), followed by β-thalassaemia trait (18.2%), sickle cell disease (7.6%), β-thalassaemia major (5.3%), sickle cell-β-thalassaemia (1.7%), δβ-thalassaemia (0.9%), haemoglobin E trait (0.9%), Hb E-β-thalassaemia (0.7%), etc. in decreasing order. Two cases each of haemoglobin D trait and SD disease were encountered. Haemoglobin abnormalities were detected in both male and female populations. Since these cases represent the local population, they reflect the vulnerability, incidence and morbidity of functional and abnormal haemoglobins in the population. Moreover, all major haemoglobinopathies prevalent all over India were encountered thereby showing the population admixture in this Central-East part of India[9].

Patients with anaemia falling in normal range of hematological parameters and without any haemoglobin abnormality after electrophoresis were considered as the control group. Patients homozygous for β-thalassaemia or sickle cell gene, or compound heterozygosity for both alleles, showed significantly lower haemoglobin levels and increased levels of foetal haemoglobin, Hb A_2 and reticulocyte counts compared to sickle cell trait and control group (Table 2).

Table 3 gives the age and sex-wise distribution of cases of different haemoglobinopathies. As expected, it is apparent from Table 3 that a majority of the cases of haemoglobinopathy belongs to the reproductive age group, i.e. 16 to 45 years, followed by neonatal to childhood period (0–15 years), and only a few cases of old age (46 + years) are being detected when they face clinical complications. Most of the cases of haemoglobinopathy in India, in general, are detected accidentally when the couple is advised by the physician to go in for laboratory investigations to find the cause of anaemia. The results of the present study are consistent to this notion explicitly.

The attending referral cases were classified according to their caste affiliation. It is apparent from Table 4 that a

Table 1. Spectrum of haemoglobinopathies in Central-East coast of India

Type of haemoglobinopathies	No. of males	No. of females	Total no.	Percentage
Normal	184	164	348	34.3
Sickle cell trait	171	131	302	29.8
Sickle cell disease	41	36	77	7.5
Sickle cell-β-thalassaemia	4	13	17	1.7
β-Thalassaemia trait	91	94	185	18.2
Thalassaemia major	29	25	54	5.3
δβ-Thalassaemia	4	5	9	0.9
Haemoglobin E trait	2	7	9	0.9
Haemoglobin E disease	2	1	3	0.3
E-β-Thalassaemia	5	2	7	0.7
Haemoglobin D trait	1	1	2	0.2
SD disease	1	1	2	0.2
Total	535	480	1015	100.0

Table 2. Mean haematological values of parameters studied for different patients of haemoglobinopathies

Diagnostic category	Hb (g/dl) mean ± SD	RBC (10^6/µl) mean ± SD	WBC (10^3/µl) mean ± SD	Hb F (%) mean ± SD	Hb A_2 (%) mean ± SD	Retics. count (%) mean ± SD
Normal (N = 348)	11.6 ± 2.0	4.3 ± 0.8	7.5 ± 1.8	0.9 ± 0.5	2.8 ± 0.6	1.1 ± 0.4
Sickle cell trait (N = 302)	11.5 ± 1.7	4.2 ± 0.7	7.4 ± 1.7	1.5 ± 0.9*	3.0 ± 0.5	1.2 ± 0.6
Sickle cell disease (N = 77)	8.2 ± 1.8	3.1 ± 0.9*	8.9 ± 1.9*	10.4 ± 4.5*	3.0 ± 0.4	4.8 ± 0.8*
Sickle cell-β-thalassaemia (N = 17)	8.7 ± 1.7	3.6 ± 0.8*	8.8 ± 1.5*	11.8 ± 5.3*	4.5 ± 1.2*	5.3 ± 1.1*
Thalassemia major (N = 54)	5.6 ± 1.9	2.8 ± 0.7	13.5 ± 4.5	44.6 ± 20.0*[a]	4.8 ± 1.6*	3.4 ± 1.3
β-Thalassaemia trait (N = 185)	11.2 ± 2.3	4.2 ± 1.0	7.3 ± 1.8	1.2 ± 0.8	5.7 ± 1.1*[b]	1.2 ± 0.7
δβ-Thalassaemia (N = 9)	7.6 ± 1.2*	4.7 ± 0.9	5.8 ± 0.7*	51.0 ± 5.2*	6.7 ± 2.1*	4.2 ± 0.3*
Hb E disease (N = 3)	9.1 ± 1.7*	5.2 ± 1.2	6.4 ± 1.3	1.8 ± 0.9	98.2 ± 0.2*	3.6 ± 0.5
Hb E-β-thalassaemia (N = 7)	7.3 ± 1.3*	3.0 ± 0.8*	11.7 ± 3.5*	16.2 ± 8.0*	58.4 ± 7.2	3.5 ± 2.2*
Hb E trait (N = 9)	11.8 ± 2.0	4.3 ± 1.0	8.3 ± 3.4	1.4 ± 0.9*	28.6 ± 4.1**	1.2 ± 0.6
Hb D trait (N = 2)	11.5 ± 0.3	3.7 ± 0.6	7.1 ± 2.3	1.2 ± 0.7	2.4 ± 1.0	2.0 ± 0.5
Hb SD disease (N = 2)	6.1 ± 1.3*	3.6 ± 0.7	7.2 ± 2.4	2.6 ± 0.4*	1.3 ± 0.2	4.5 ± 0.6*

*All values are statistically significant in comparison to normal, $P < 0.05$.
**Hb E and Hb A_2 were measured together.
[a]Comparison with Hb SS, Hb S-β-Thal and Hb E-β-Thal shows statistical significant difference, $P < 0.05$.
[b]Comparison with Hb AA, Hb AS and Hb SS shows statistical significant difference, $P < 0.05$.

Table 3. Age and sex-wise distribution of cases of different haemoglobinopathies

Age group	No. of males	Percentage	No. of females	Percentage	Total no.	Percentage
0–15	140	40.1	116	36.5	256	38.4
16–45	194	55.6	191	60.1	385	57.7
46+	15	4.3	11	3.4	26	4.9
Total	349	100.0	318	100.0	667	100.0

majority of the patients of haemoglobinopathy belong to general castes for sickle cell disorders (64.6%), β-thalassaemia syndrome (79.6%) and other haemoglobinopathies (91.3%) respectively, in Central-East India. These results are contrary to the findings reported elsewhere in India where the problem of haemoglobinopathy is stated to be confined only to scheduled tribes or scheduled castes, and that the general castes are not affected[10]. However, a considerable number of people belonging to scheduled castes in the region also suffer from haemoglobinopathies (Table 4), but their frequency is comparatively low (8.7–27.4%). Hereditary disorders of haemoglobin among the tribal population (0–8%) are uncommon in the region. This may be due to the breeding isolation from the general stream and strictly following tribal endogamy at the respective niches.

The distribution of sickle cell disorders and β-thalassaemia syndrome cases in different ethnic groups of the region is provided in Table 5. The Khandayat community is at the highest risk of haemoglobinopathies (there is high prevalence of sickle cell disorders, 20.7% and β-thalassaemia syndrome, 30.3% amongst them), followed by Brahmins (β-thalassaemia syndrome, 21.1%), Chasa and Kshatriya (sickle cell disorders, 19.8 and 6.8% respectively), Karan, Teli and Gauda (β-thalassaemia syndrome, 9.2, 8.5 and 5.6% respectively), among the general castes; Pana, Haddi, Gonda, Ghasi and Dhoba (sickle cell disorders, 8.9, 6.8, 2.5, 2.5 and 2.1% respectively) among the scheduled castes, and Kondh and Kutia Kondh (sickle cell disorders, 5.5 and 1.7% respectively), Saora and Santal (β-thalassaemia syndrome, 2.1 and 1.4% respectively), among the scheduled tribes. These results further testify that the hereditary hemolytic disorders of haemoglobin are more common in the general castes and scheduled castes than among the tribals of Central-East India.

It is apparent from the geographical distribution of sickle cell disorders and β-thalassaemia syndrome cases in Central-East India (Figure 1) that there are certain pockets or regions that are more vulnerable to haemoglobinopathies than others (Table 6). For example, Anugul, Kandhamal, Khurda, Cuttack, Dhenkanal, Keonjhar, Nayagarh, Ganjam, Sundargarh and Kalahandi districts in Orissa have the highest number of cases of sickle cell disorders. β-Thalassaemia syndrome is common in Khurda, Puri, Jajpur, Nayagarh, Cuttack, Keonjhar, Mayurbhanj, Jagatsinghpur, Kendrapara and Bolangir districts of Orissa. These results clearly indicate that the sickle cell disorders are generally confined to central, western and southern Orissa and β-thalassaemia syndrome is generally limited to coastal regions or districts of Orissa[11]. Further, these results can be interpreted in the light of migration or gene flow of sickle cell abnormality from Central India (Gondwanaland) towards western and southern Orissa and that of β-thalassaemia syndrome from northern and eastern India towards eastern coastal and southern regions of Orissa.

Distribution of other abnormal haemoglobins in communities belonging to different districts/regions of Orissa is given in Table 7. Haemoglobin E and E-β-thalassaemia syndrome are generally confined to those communities residing in the coastal regions of Orissa due to gene flow from the northern and eastern regions of India.

Table 4. Caste-wise distribution of cases of sickle cell disorders, β-thalassaemia syndrome and other haemoglobinopathies in Orissa

Caste	Sickle cell disorders* $N = 396$ (%)	β-Thalassaemia syndrome** $N = 248$ (%)	Other haemoglobinopathies*** $N = 23$ (%)
General castes	64.6	79.6	91.3
Scheduled castes	27.4	16.2	8.7
Scheduled tribes	8.0	4.2	0.0
Total	100.0	100.0	100.0

*Includes sickle cell trait, sickle cell disease and sickle cell-β-thalassaemia cases.
**Includes β-thalassaemia trait, thalassaemia major and δβ-thalassaemia cases.
***Includes Hb AE, Hb EE, E-β-thalassaemia, Hb AD and SD disease cases.

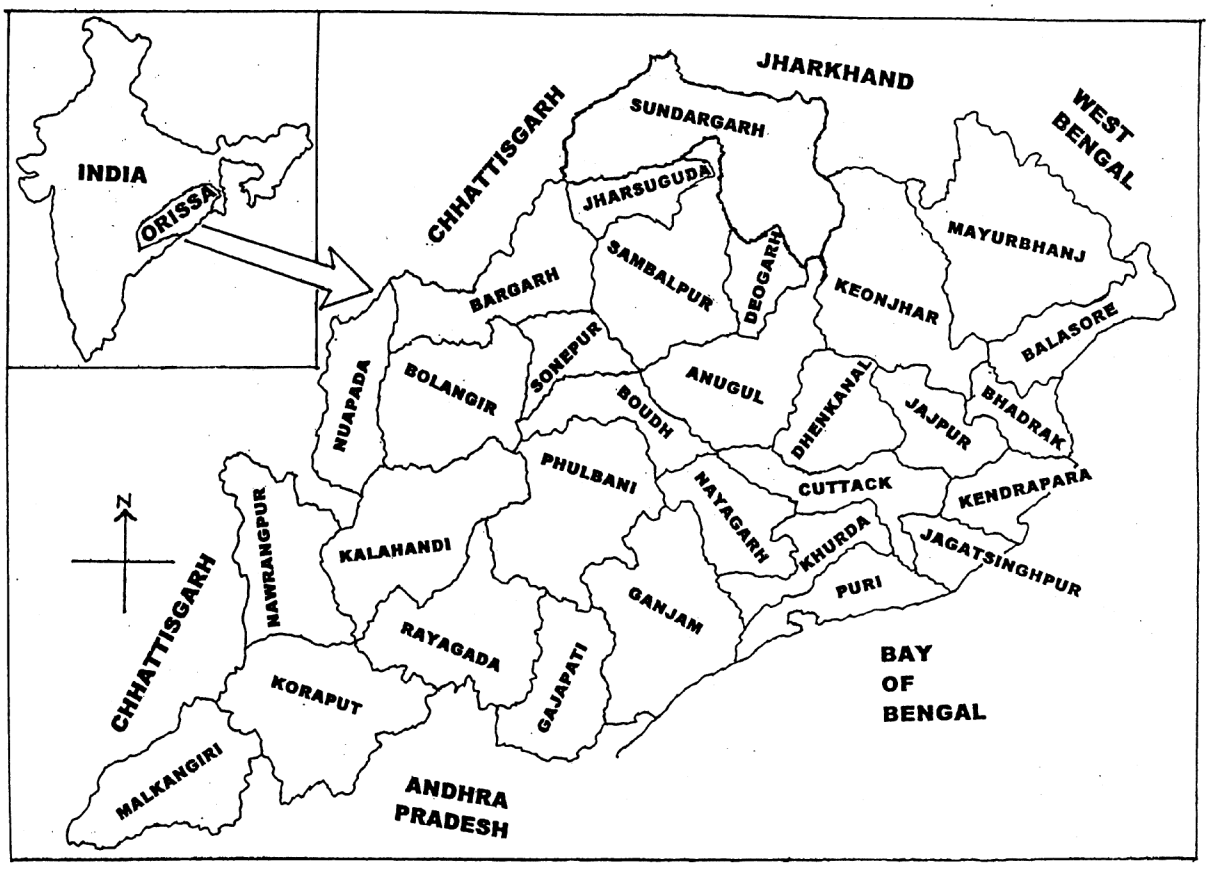

Figure 1. Map of Orissa showing thirty districts.

Discussion

The thalassaemias and related haemoglobinopathies are responsible for the largest number of genetic disorders and hence are of great public health importance in India. A large number of haemoglobin variants prevalent among the populations of Central-East India indicates that haemoglobinopathies and also their related clinical complications are not uncommon at birth. The inherited disorders of haemoglobin synthesis are one of the important public health problems in the region. The present scenario of haemoglobinopathies reflects the genetic heterogeneity of the population of the region. Historical accounts[3] reveal that several ethnic elements with varied genetic heritages have been absorbed into the mainstream, resulting in population diversity with the passage of time[12]. The findings of prevalence of different haemoglobinopathies in the region are in agreement with the population admixture in Central-East India.

All the β-thalassaemia major patients were transfusion-dependent, whereas only 10% of the sickle cell disease cases needed blood transfusion. High levels of foetal haemoglobin ranging from 2 to 30% were observed among the sickle cell disease patients as well as in sickle cell trait cases. It is interesting to note that splenomegaly was consistently observed in haemoglobin-β-thalassaemia, β-tha-

lassaemia major and in sickle cell disease cases in this population. *Plasmodium falciparum* malaria is rampant in this region, which may also be responsible for splenomegaly in subjects with either a normal haemoglobin profile or with sickle cell or β-thalassaemia trait.

Due to the intriguing nature of the people, historical accounts[3] regarding the gene flow or migrations of different waves of people from different corners of Central-East India are obscure. However, scanty accounts available point out that there were at least three waves of people who entered through the northern, eastern and western corridors of Central-East India. The northern waves (for example, the Brahmin community of Orissa brought in as priests by the King of Puri are said to have emigrated from Uttar Pradesh and shows their resemblance with the names of clans), have also brought the abnormal β-thalassaemia gene with them; the eastern migrants from West Bengal and Assam came with haemoglobin E gene, and the western counterparts bestowed with sickle cell gene in Orissa were from Gondwanaland (presently part of Chhattisgarh, Madhya Pradesh, Andhra Pradesh and Maharashtra) in Central India. Subsequently, the admixture and merger of these three waves of people occurred with the passage of time. These haemoglobin defects are in abundance in endemic form in the parent populations from where they had spread to other parts of the country[13,14]. The erythrocytic prevalence of genetic abnormalities of haemoglobin is quite high in general castes like Khandayat, Chasa, Kshatriya, Brahmin, Karan, Gauda, Teli, etc. and scheduled castes, namely Pana, Haddi, Gonda, Ghasi and Dhoba of Central-East India (Table 5). Kar[15], and Garewal and Das[16] found almost similar results for the Indian population. It is interesting that among the isolated tribal populations of Orissa (Oraon, Saora and Santal), these defective genes have not penetrated vigorously, as evident from the present study. However, in some tribal populations of Orissa such as Dhelki Kharia, the abnormal haemoglobin E gene has already penetrated and been absorbed into the population[7].

Table 5. Distribution of sickle cell disorders and β-thalassaemia syndrome cases in different ethnic groups of Orissa

Caste/ethnic group	Sickle cell disorders* $N = 396$ (%)	β-Thalassaemia syndrome** $N = 248$ (%)
General caste		
Khandayat	20.7	30.3
Brahmin	1.3	21.1
Karan	4.2	9.2
Teli	2.1	8.5
Gauda	2.1	5.6
Muslim	1.3	2.1
Chasa	19.8	0.2
Kshatriya	6.8	0.3
Agharia	3.0	0.2
Rajput	1.7	0.0
Dumal	0.3	0.0
Kumbhar	0.3	0.0
Scheduled caste		
Pana	8.9	0.2
Haddi	6.8	0.2
Gonda	2.5	0.2
Ghasi	2.5	0.0
Dhoba	2.1	0.2
Bhulia/Tanti (weaver)	1.3	0.2
Domb	0.3	0.3
Bauri	0.3	0.0
Keuta	0.3	0.0
Madari	0.3	0.0
Kuanwar	0.2	0.0
Kurma	0.2	0.0
Kurmi	0.0	2.1
Lohar	0.2	0.0
Badhei (carpenter)	0.0	0.3
Barber	0.0	3.5
Gokha	0.0	2.1
Gudia	0.0	2.1
Scheduled tribe		
Kondh	5.5	0.2
Kutia Kondh	1.7	0.0
Oraon	0.2	0.0
Saora	0.2	2.1
Santal	0.0	1.4

*Sickle cell disorders include sickle cell trait, sickle cell disease and sickle cell-β-thalassaemia.
**β-Thalassaemia syndrome includes thalassaemia major, thalassaemia trait and δβ-thalassaemia cases.

Table 6. Geographical distribution of sickle cell disorders and β-thalassaemia syndrome cases in Orissa

District	Sickle cell disorders* $N = 396$ (%)	β-Thalassaemia syndrome** $N = 248$ (%)
Anugul	33.2	0.2
Kandhamal	11.5	0.3
Khurda	9.7	27.1
Cuttack	7.5	4.9
Dhenkanal	6.6	0.5
Keonjhar	5.3	4.9
Nayagarh	4.9	4.9
Ganjam	4.9	0.7
Sundargarh	4.0	0.2
Kalahandi	3.5	0.0
Mayurbhanj	1.0	4.2
Boudh	1.0	0.0
Deogarh	0.7	0.5
Jagatsinghpur	0.2	4.2
Bolangir	0.2	3.5
Jharsuguda	0.2	0.0
Sonepur	0.2	0.0
Jajpur	0.0	9.0
Puri	0.0	17.4
Kendrapara	0.0	4.2
Balassore	0.0	0.5
Gajapati	0.0	0.5
Sambalpur	0.0	0.2
Rayagada	0.0	0.3

*Sickle cell disorders include sickle cell trait, sickle cell disease and sickle cell-β-thalassaemia.
**β-Thalassaemia syndrome includes thalassemia major, thalassaemia trait and δβ-thalassaemia cases.

Table 7. Distribution of other abnormal haemoglobins in Orissa

District	Community	Abnormal haemoglobins
Puri	Brahmin, Khandayat	Hb AE = 7; Hb EE = 1; Hb E-β-thalassaemia = 4
Khurda	Brahmin	Hb AE = 1; Hb EE = 1; Hb E-β-thalassaemia = 1
Nayagarh	Gauda, Brahmin	Hb AE = 1; Hb EE = 1; Hb E-β-thalassaemia = 2
Anugul	Barber, Chasa	Hb AD = 2; Hb SD = 1
Sundargarh	Khandayat	Hb SD = 1

There is geographic clustering of genetic variants of haemoglobin in Orissa. The geographical scatter of sickle cell disorders, β-thalassaemia syndrome, and other haemoglobinopathies in Central-East India shows the differential emigrational pattern of the people. Populations near the place of parent-origin have higher frequency of sickle cell disease, β-thalassaemia syndrome or abnormal haemoglobin E gene than those far away. For example, Hb E is often encountered in cases referred from eastern coastal part of the state (Puri, Khurda, Balassore and Bhadrak districts), a region exposed to South East Asia through West Bengal, Assam, Manipur, Meghalaya, Nagaland and Tripura, where this abnormal haemoglobin E gene is highly prevalent[13,14,17]. Hence it is reasonable to postulate that its occurrence in Orissa is essentially through gene flow from these areas. Similarly, the gradual inflow of sickle cell gene from Gondwanaland in Central India towards western and southern Orissa is clearly evident in the populations of that region[18]. Gradual movements of such people are evident from the distribution of haemoglobin E and sickle cell disorders in the present study (Table 6).

It has been observed that rapid proliferations of haemolytic genetic disorders in a given geographical pocket or region due to comparatively small population size, caste and area endogamy, consanguinity, lack of medical facilities, and natural barriers like geographical landscape, forests and ecological niches, river, etc. have further compounded the complexity of sickle cell disorders and β-thalassaemia syndrome in the Central-eastern part of India. The bioenvironmental and socio-cultural factors further put constraints on the viability, proliferation and growth of the population under threat from malaria[19]. The harbouring of a spectrum of haemoglobinopathies perhaps provides the heterozygote advantage for protection against malaria in the agricultural and wet environmental conditions of Central-East India.

Unlike many other genetic disorders where couples at risk cannot be easily diagnosed, thalassaemia syndrome and abnormal haemoglobin give tremendous opportunity for effective control of birth of an affected child. The prevention and control of a spectrum of haemoglobinopathies in Central-East India is an uphill task for the planners, policy makers and medical and healthcare machinery of the state, with political will of the people[20]. The results of the present study would provide a cost-effective method to combat the hereditary disorders of haemoglobin in different high-risk communities of Central-East India. How far this genetic disease burden is being eliminated from the society for the betterment of future generations is a matter of concern for all of us.

Conclusion

Haemoglobinopathies are the most common monogenic disorders of erythrocytes in humans. India is home to several haemoglobin variants, causing much suffering to afflicted individuals and impose considerable financial, genetic and psycho-social burden on family, society and the nation at large. The most common haemoglobinopathies observed out of 1015 cases were: sickle cell trait (29.8%), sickle cell disease (7.5%), sickle cell-β-thalassaemia (1.7%), β-thalassaemia trait (18.2%), thalassaemia major (5.3%), thalassaemia intermedia (0.9%), Hb E trait (0.9%), Hb E disease (0.3%), Hb E-β-thalassaemia (0.7%), Hb D trait (0.2%) and SD disease (0.2%). Male preponderance was seen with age of presentation varying from early childhood to adult in sickle cell disorders, followed by β-thalassaemia trait, and thalassaemia major in Central-East India. Sickle cell disorders with high level of foetal haemoglobin are common in general castes (0.3–20.7%), scheduled castes (0–8.9%) and scheduled tribes (0–5.5%). Transfusion-dependent β-thalassaemia syndrome is prevalent among Brahmins, Karans, Khandayats, Telis, etc. Haemoglobin E was detected among Brahmins and Khandayats and haemoglobin D among Chasas and Khandayats. Most of the cases were from Anugul district, followed by Khurda, Nayagarh, Kandhamal, Cuttack, Jajpur, Dhenkanal, Ganjam, Keonjhar and Mayurbhanj. The heterogeneous population of Central-East India harbours almost all major haemoglobinopathies in general castes, scheduled castes and tribes belonging to coastal and southwestern regions. This study provides a comprehensive database on the spectrum of haemoglobinopathies in Central-East India. These data will be useful and facilitate identification and prevention of prevalent molecular mutations in vulnerable communities and for extending prenatal diagnostic facilities in future and also for genetic counselling to affected families in the region.

What is the importance of this wealth of data to the clinicians or physicians is that amongst the widely prevalent nutritional anaemia cases, the silent-killer genetic problem

of thalassaemia syndrome and abnormal haemoglobins is of major concern. This dimension of heavy genetic load needs prevention of further spread of the disorders among vulnerable communities in the region. At present, poor infrastructure of medical laboratory facilities in the country and the hindrance of cost involved interfere with their diagnosis. Lack of knowledge regarding their prevalence, poor diagnostic facilities, inability to provide genetic counselling to needy people and presence of limited centres for prenatal diagnosis have resulted in the failure of preventing such dreadful genetic disorders. Funds and facilities do not permit effective treatment of thalassaemia syndrome and sickle cell diseases in the affected regions. Cure by bone marrow/stem cell transplantation is available, but only to a handful of those who can afford it. Still a lot remains to be done. There is need of a political will to implement and achieve the above targets.

1. Balgir, R. S., The burden of haemoglobinopathies in India and the challenges ahead. *Curr. Sci.*, 2000, **79**, 1536–1547.
2. Balgir, R. S., The genetic burden of haemoglobinopathies with special reference to community health in India and the challenges ahead. *Indian J. Hemat. Blood Transfus.*, 2002, **20**, 2–7.
3. Russel, R. V. and Lal, H., *Tribes and Castes of the Central Provinces of India.* Four volumes, Macmillan Company, London, 1916, pp. 215–218.
4. Balgir, R. S., The spectrum of haemoglobin variants in two scheduled tribes of Sundargarh district in northwestern Orissa, India. *Ann. Hum. Biol.*, 2005, **32**, 560–573.
5. Dacie, J. V. and Lewis, S. M., *Practical Hematology*, Churchill Livingstone, Edinburgh, 1991, 7th edn, pp. 227–258.
6. Weatherall, D. J., Hematologic methods. In *Methods in Hematology: The Thalassemias* (ed. Weatherall, D. J.), Churchill Livingstone, New York, 1983, vol. 6, pp. 1–53.
7. Balgir, R. S., Prevalence of abnormal haemoglobin E gene in the Dhelki Kharia tribal population. *Curr. Sci.*, 2003, **85**, 1604–1608.
8. Betke, K., Marti, H. R. and Schlict, L., Estimation of small percentages of fetal haemoglobin. *Nature*, 1959, **184**, 1877–1878.
9. Balgir, R. S., Pattern of haemoglobinopathies in pediatric age group of Orissa. *Indian Pract.*, 1994, **47**, 189–193.
10. Bhasin, M. K., Walter, H. and Danker-Hopfe, H., Glucose-6-phosphate dehydrogenase deficiency and abnormal haemoglobins (S and E) in people of India. *J. Hum. Ecol.*, 1994, **3**, 131–159.
11. Balgir, R. S., Population, ecology and epidemiology of the sickle cell disease in Orissa. *J. Hum. Ecol.*, 1995, **6**, 273–276.
12. Balgir, R. S., Dash, B. P. and Murmu, B., Blood groups, haemoglobinopathy and G-6-PD deficiency investigations among fifteen major scheduled tribes of Orissa, India. *Anthropologist*, 2004, **6**, 69–75.
13. Balgir, R. S., Blood groups, G-6-PD enzyme and haemoglobin studies among the three endogamous populations of Assam. *Indian J. Hemat. Blood Transfus.*, 1993, **11**, 237–243.
14. Balgir, R. S., Genetic epidemiology of the three predominant abnormal haemoglobins in India. *J. Assoc. Physicians India*, 1996, **44**, 25–28.
15. Kar, B. C., Sickle cell disease in India. *J. Assoc. Physicians India*, 1991, **39**, 954–960.
16. Garewal, G. and Das, R., Spectrum of β-thalassaemia mutations in Punjabis. *Int. J. Hum. Genet.*, 2003, **3**, 217–219.
17. Balgir, R. S., Emerging trends in genetic epidemiology of haemoglobinopathy in the seven sister states of north eastern India. In *North East India in Perspectives: Biology, Social Formation and Contemporary Problems* (eds Das, R. K. and Basu, D.), Akansha Publishing House, New Delhi, 2005, pp. 17–37.
18. Balgir, R. S., Indigenous and independent origin of the β^S-mutation in ancient India: Is it a myth or reality? *Mankind Q.*, 2001, **42**, 99–116.
19. Balgir, R. S., Genetic dimension of sickle cell haemoglobinopathy among five scheduled caste populations of Orissa, India. *Indian Pract.*, 2002, **55**, 503–514.
20. Balgir, R. S., Mishra, R. K. and Murmu, B., Clinical and hematological profile of haemoglobinopathies in two tribal communities of Sundargarh district in Orissa, India. *Int. J. Hum. Genet.*, 2003, **3**, 209–216.

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