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NATIONAL GUIDELINES ON MANAGEMENT AND CONTROL OF SICKLE CELL DISEASE

INDIAN COLLEGE OF HEMATOLOGY (ICH)
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CHAPTER 1

Magnitude of Problem and Epidemiology

Sickle cell disease (SCD) is a monogenic disorder caused by a single nucleotide substitution at position 6 of the β-globin gene leading to polymerization of the resulting sickle hemoglobin (HbS) variant. The most severe form is the symptomatic homozygous SCD, which results from the inheritance of two copies of the sickle β-globin gene variant (SS). Individuals with mutation on one gene are called sickle cell traits (SCTs)/sickle cell carriers and are clinically asymptomatic; however, sickle-shaped red blood cells (RBCs) can be demonstrated in their blood film. Though clinically the sickle trait persons do not manifest disease they are important to recognize as the high prevalence of carriers is an important assessment and will give rise to higher burden of births of patients with homozygous SCD. Hence, identification of the sickle cell carriers has public health implications for awareness and prevention programs.

THE BURDEN OF SICKLE CELL DISEASE IN INDIA

Sickle variant of hemoglobin was first reported in India from Nilgiri hills among tribal population of South India in 1952. In the last 70 years, published literature has established clinical diversity among its various compound heterozygous phenotypes. SCD is now recognized as a major public health problem in the country with an increasing burden on its healthcare system. SCD was mainly believed to affect the tribal population of central India; however, nontribal persons are also affected in many states such as Odisha, Chhattisgarh, Gujarat, Maharashtra, and Madhya Pradesh show a burden of disease with a carrier frequency in the range of 1–44%.[1-4]

Globally, some of the highest βS allele frequencies have been reported in Indian populations[2-4] and India has been ranked the second worst affected country in terms of predicted sickle β-globin gene variant (trait and homozygous births, with 42,016 [interquartile range (IQR) 35,347–50,919] babies estimated to be born with sickle cell anemia (SCA) in 2010.[5]

The Ministry of Tribal health is undertaking screening and this initiative is an important beginning. The district-wide data from 16 states most impacted by the high prevalence of SCD is important for public health policy planning, some data has already been collected and further screening is being conducted. Once completed in all affected districts this will be an invaluable resource.

Limitation of the Present Available Data

The magnitude of the problem of SCD in the country is very large; the discussion on magnitude is impeded by the lack of a population-based registry. Though many publications about the prevalence of disease are available for some regions, complete district-wise national data is lacking. The studies reported in literature are mostly institution-based either retrospective or

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prospective compilation of consecutive cases, which are not representative of general population hence make it difficult to draw conclusion. The paucity of community-based surveys and variability in the methodology followed in the published prevalence studies make it difficult to draw comparison between the states. Also, the available community-based surveys are from different time periods, because of migration and intermarriages, the data may not reflect the picture as of today.

The target population and testing methods also vary between studies and hence the comparison of prevalence data between different states is not possible. The screening test used in earlier studies was only solubility test which does not differentiate between SCT and disease.

With the understanding that the published data is incomplete, we have still undertaken the task to compile and present some of the most recent published literature from various parts of the country and present the current situational analysis of SCD and trait in the country. We have also presented district-wise distribution of SCT as it is more relevant for the purpose of prevention. The legend scale of the figures is specific to each state and not comparable between states due to the earlier mentioned lacunae.

The SCD has varied spread from indigenous groups to other communities and now an overall reported prevalence of 4.3% in India. Heterogeneous distribution of HbS has been documented in diverse parts of India with a high prevalence in states Gujarat, Maharashtra, Madhya Pradesh, Chhattisgarh, Odisha, Jharkhand, and Telangana. In this chapter, we will describe the current data (published and few unpublished data shared) on epidemiology of sickle cell hemoglobin in various regions/states of India.

WESTERN INDIA

Gujarat

Gujarat state is known to have 12 tribal districts with 89.12 lakh (14.7%) tribal population. The estimated number of SCT cases is at least 9,00,000 (10%) and that of SCD is 70,000 (0.75%) in the state.[6] The *Dhodia, Dubla, Kukna, Gamit, Chaudhary, Halpati, Varli, Kokni, Kathodi, Kolcha, Kotwadia*, etc., are major tribes in Gujarat with documented prevalence of HbS.[7-11] The *Dhodia*, *Dubla*, *Gamit*, and *Naika* tribes are particularly reported to have a high prevalence of HbS in the range of 13–31%.[12] The reported prevalence of SCD ranged from 0.6 to 35%; however, it cannot be generalized as studies have adopted different methodologies with different approaches and different classification of castes and target population.[13] **Figure 1** presents the prevalence of SCT derived from district-wise premarital screening program of Gujarat conducted from 2004 to 2022 (unpublished data).

An extensive population survey has been done by the Indian Red Cross Society, Gujarat State Branch where 168,498 tribals from 22 districts were screened and the overall prevalence of sickle cell carriers was 11.37% among tribal areas and 1.1% among nontribal

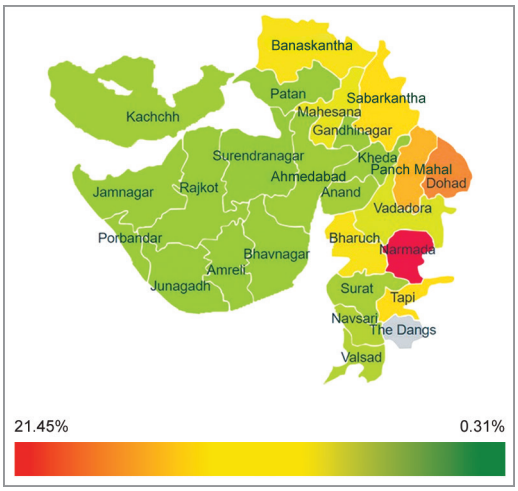

FIG. 1: *District-wise prevalence of sickle cell trait reported from premarital screening program* (conducted from 2004 to 2022). The range of prevalence is 21.45–0.31% from premarital screening program and legend is not comparable to other states.

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areas.[10,14] Some tribal groups in south Gujarat such as *Chaudry*, *Gamit*, *Rohit*, *Vasava,* and *Kukana* have shown both a high prevalence of HbS (6.3–22.7%) as well as β-thalassemia trait (BTT) (6.3–13.6%). These tribal groups would have the likelihood of coinheriting both these genes.[15,16]

In a voluntary community screening program, from rural south Gujarat, using a newer high-performance liquid chromatography (HPLC) methodology for confirmation of diagnosis, a prevalence of SCT (15.63%) in *Choudhary* labeled as general caste (nontribal) against 18.5% in *Rathva* (ST subpopulation) was cited, while the prevalence of 2.3% for SCD was documented using panel data methodology.[9]

Another larger community-based study based on camp approach screened 32,857 samples of students from different schools and colleges in South Gujarat, which found that the overall prevalence of BTT and SCT was 4.4% and 1.3%, respectively. The study also documented *Gamits, Vasavas, Mayavanshi,* and *Chaudhary* as the most commonly affected subcastes. The study documented prevalence of SCD among *Mayavanshi* subcaste (6.9%), which is not documented in any other published literature. Other prevalence studies among adolescents and medical undergraduates suggest the range of SCD from 12.7 to 37.5%. However, as these students were institutional-based, they do not reflect the community-level prevalence.[17]

A recent study analyzed the tribal maternal admissions, in the community-based hospital of SEWA Rural (Kasturba Maternity Hospital) in Jhagadia block, Gujarat from 2011 to 2015. The study reported 1.2% of tribal delivery admissions were homozygous for SCD and 15.6% of tribal delivery admissions had the SCT.[18]

Newborn screening program in South Gujarat reported results of 5,467 newborns, using HPLC, with diagnosis by molecular analysis, across four districts of South Gujarat over 2 years. There were (0.60%) babies identified as sickle homozygous, and (0.23%) had sickle-β-thalassemia; 12.5% were identified with SCT. 0.23% of sickle cell homozygous condition. The highest proportion of births with SCT was found in the *Warli* tribe (22.9%), followed by the *Bhils* (21.7%), *Chaudharys* (20.0%), and *Dhodia Patels* (18.5%). The proportion of births with SCA was highest among the *Dhodia Patels* (1.54%).[19] The same program adopted a targeted screening approach with HPLC test employed to test newborns of antenatal women found positive on solubility test. As a result of targeted screening, 3.5% of the newborns were diagnosed with HbS and started on the preventive penicillin treatment.[20]

Maharashtra

From initial studies, it was reported that sickle cell gene is widely spread in all districts of eastern Maharashtra (known as Vidarbha region), North Maharashtra (Satpura ranges), and some parts of Marathwada region.[21,22] The prevalence of sickle cell carriers in different tribes varies from 0 to 35%. The tribal groups with a high prevalence of HbS (20–35%) include the *Bhils*, *Madias*, *Pawaras*, *Pardhans,* and *Otkars*. It has also been estimated that Gadchiroli, Chandrapur, Nagpur, Bhandara, Yoetmal, and Nandurbar districts would have >5,000 cases of SCA.[23]

A study conducted to find out the prevalence of sickle cell genes in the tribal population in rural area of Palghar district from August 2015 to August 2017 screened almost 5,000 subjects. 1% sample was found to be affected by SCD (HbSS) and 4.08% were sickle cell heterozygous (HbAS). The subjects in the study belonged to schedule tribes (*Warli, Kakari, Malhar Koli, Dhor Koli Vanjari,* and *Wadwal*) and schedule caste (*Buddhist* and *Mahar*).[24]

Another study based on a *cross-sectional* sample, randomly collected and analyzed from 294 individuals (165 male and 129 female) in different rural areas of Chandrapur district of *Maharashtra*. The population

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was screened by solubility test followed by electrophoresis and prevalence of SCA was found to be 18.3%.[25]

A systematic mass screening was carried out in various schools and at the community level in four districts of Vidarbha region of eastern Maharashtra. A sample from premarital age group was screened for hemoglobin S and hemoglobin βT using solutions of qualitative solubility test and NESTROFT, respectively. It was observed that 6.4% individuals were positive for HbS and 2.1% for HbβT. The frequency for HbS and HbβT varied between 0–33% and 0–10%, respectively, among the studied populations. A very high frequency of HbS was encountered among the *Bais* (33.3%) the *Pardeshi* (25%), the *Pardhan* (23.8 %), and the *Marar* (20.4 %). A moderate HbS frequency was observed among *Dhiwar* (12.8%), *Gond* (12.4%), *Shimpi* (11.1%), *Mahar* (10.9%), *Madgi* (10.0%), *Khairekunbi* (9.3), *Bania* (9.1%) the *Zadekunbi* (7.7%), and the *Gowari* (7.3 %). Significant frequencies of HbS were also observed among the *Banjara* (5.9%), the *Dangekunbi* (5.6%), the *Kunbi* (4.9%), the *Telugu* (4.8%), the *Kalar* (4.7%), the *Bawanekunbi* (4.3%), the *Brahmin* (4.2%), the *Muslim* (3.7%), the *Tiralekunbi* (3.6%), and the *Teli* (3.2%). The range of *HbS* gene frequency of 1–3% was accounted for the *Chambhar*, the *Dhangar*, the *Dhobi*, the *Halba*, the *Kohali*, the *Lohar*, the *Maratha kunbi*, the *Mehetar*, the *Powar,* and the *Rajput* of eastern region of Maharashtra.[26]

The community-based descriptive cross-sectional survey was conducted in urban parts (cities and towns) of Amravati, Bhandara, Chandrapur, Nagpur and Yeotmal districts of East Maharashtra using screening camps arranged in schools, community halls. A total of 4.94% individuals were found to be positive for sickle cell disorder, of which 3.88% with heterozygous genotype and 1.06% with homozygous genotype. Bhandara district was found to be the area of maximum *SCD* gene frequency (9.02%), followed by Chandrapur (8.18%), Nagpur (4.0%), Amravati (3.73%), and Yeotmal (3.17%). The SCD was diagnosed from all tribal groups and 14 caste groups. Highest frequency of the disease was observed in *Gond* (14.28%) followed by *Pradhan* (11.49%), *Bhil* (11.42), *Teli* (10.48%), *Matang* (8.75%), and *Korku* (7.89%).[27]

A study assessed the prevalence of SCD among backward communities of Yavatmal district, Maharashtra using sickle cell solubility test to detect the presence of sickle hemoglobin and the positive samples were subjected to cellulose acetate membrane electrophoresis at pH 8.8 to confirm the diagnosis and classify HbSS and HbAS pattern. Out of 7,568 screened population prevalence of sickle cell affected person was 21.41%. Electrophoresis pattern revealed 60.33% as heterozygous state HbAS and 36.58% as homozygous state (HbSS), 3.08% cases were found with other Hb variants.[28]

Figure 2 represents district-wise prevalence of sickle cell trait in Maharashtra as reported in a state-wide study.[23] Although, there are reports from missing districts on prevalence of HbS, the data was not clubbed due to variance in methodology of conduct of the study.

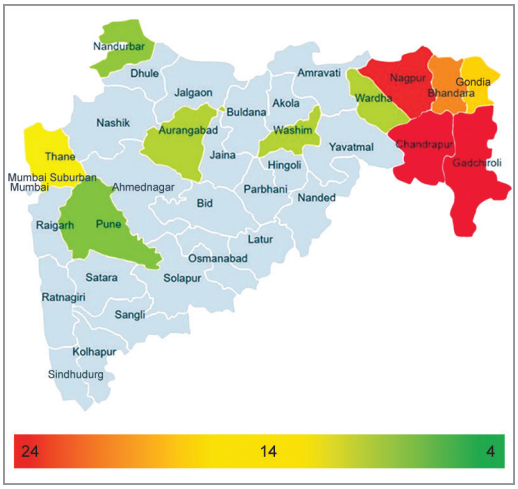

FIG. 2: District-wise prevalence of sickle cell trait in Maharashtra. The range of prevalence is 24–4% and legend is not comparable to other states. Data is not available for the districts in gray.

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Rajasthan

In Rajasthan, there are 228 communities that include 12 scheduled tribes which constitute 13.5% of the state's population. As per the census of the 2011, 5.73 million population are living in the scheduled area and 73.17% of them are tribal. *Bhil, Meena, Garasia,* and *Damors* are the principal tribes residing in the areas.

In scheduled area of Rajasthan, the maximum prevalence of *HbS* variant gene was found to be 14.6% and 31.14% in *Gameti* and *Garasiya* tribes, respectively.[29] Subsequently, 0.6–7.35% incidence of sickle cell gene in heterozygous (HbAS) was reported among different tribes of scheduled area of Udaipur division.[30-34] From the tribal area of Rajasthan, 1.47% incidence of sickle-cell gene in homozygous state, HbSS (sickle-cell anemia) in *Bhil* tribe has also been reported.[34] Besides the sickle cell genes, genes of other mutant Hb variants (HbD, E, C, J, and H) have also been found in people of scheduled area of Rajasthan. This indicates that the state of Rajasthan is pool of diverse Hb variants. Therefore, more hematological studies are required to screen the people of different caste groups residing in desert and arid environments of Rajasthan for current status and evidence of endemicity of any new Hb variants.[35] **Figure 3** represents the district-wise distribution of SCT in Rajasthan as reported in a review paper.[35]

A study was undertaken in the scheduled areas Pratapgarh, Banswara, Dungarpur, Udaipur (parts), and Abu Road block of Sirohi districts of Rajasthan to conduct sickle cell screening on the boarding students 6–12 years of age from the MaaBadi centers. The prevalence of sickle cell disorder was reported as 5.8% in the tribal subplan districts of Rajasthan. Among the sickle cell disorder cases, the prevalence of the heterozygous was 5.61% and homozygous prevalence was 0.17%. The prevalence of the sickle cell disorders was 10.5% in the Sirohi district, which was highest among all the districts.

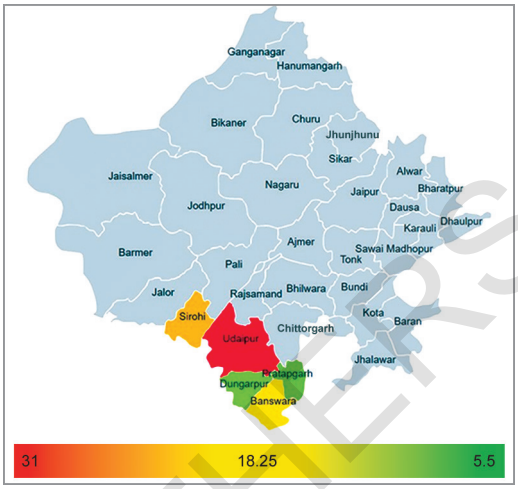

FIG. 3: *District-wise prevalence of sickle cell trait in Rajasthan*. The range of prevalence is 31–5.5% and legend is not comparable to other states. Data not available for the districts in gray.

This was followed by Banswara (7.42%) and Udaipur (6.53%). The prevalence of sickle cell disorder in Dungarpur and Pratapgarh districts were 1.89% and 5.51%, respectively. The highest prevalence of sickle cell disorder was reported in the Garasia tribe and the prevalence was 13.81%.[36]

During May 2014 to December 2015, health checkup camps for tribal children were organized in Sirohi and Udaipur districts of Rajasthan for tribal (*Garasia*) children under the age of 15 years. A total of 1,090 children were screened. The prevalence of SCD among tribal (*Garasia*) children of Sirohi and Udaipur districts was found to be 8.53% of which 0.77% were homozygous (HbSS), whereas 7.7% were heterozygous (Sickle Trait/HbAS).[37]

CENTRAL INDIA

Madhya Pradesh

Madhya Pradesh state contributes to about 15.0% of the total tribal populations of India, and tribal communities have been reported to suffer from various hemoglobinopathies. Madhya Pradesh has the highest load with an

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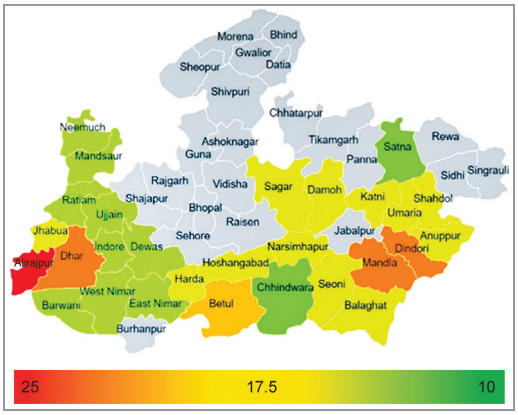

FIG. 4: *District-wise prevalence of sickle cell trait in Madhya Pradesh.* The range of prevalence is 25–10% and legend is not comparable to other states. Data not available for the districts in gray.

estimated number of 961,492 sickle heterozygotes and 67,861 sickle homozygotes. In addition, 27 of the 45 districts of Madhya Pradesh fall into the sickle cell zone, and the pervasiveness of HbS fluctuates between 10 and 33%. Four tribal districts of the state namely Alirajpur, Anuppur, Chhindwara, and Dindori constitute around 75% of the existing cases of sickle cell anemia according to the annual report 2020–2021.[38] **Figure 4** presents the prevalence and district-wise distribution of SCT in the state of Madhya Pradesh.[39]

A recent study screened a total of 3,992 tribal individuals comprising students of tribal schools, ashrams of Dindori, Mandla, and Chhindwara districts of Madhya Pradesh state. In this study, prevalence of homozygous SCD (0.7%), SCT (14.4%), BTT (1.4%) was observed. The prevalence of SCT varies from 5.9 to 34.7%. The allele frequency of sickle cell gene was highest in the *Pradhan* tribe followed by the *Panika* tribe. Dindori district had the highest prevalence of SCT. The *Gond* tribe is the major tribe of Madhya Pradesh with the prevalence of homozygous SCD in the range of 6.0–33.0%, whereas in the *Baiga* tribe, it varies from 6.0 to 20.0%.[40]

Similarly previous studies also reported the uneven distribution of prevalence of SCT among different tribes.[14,41-43]

Chhattisgarh

About 32% of population is of tribal origin in Chhattisgarh State and as public health measure they have started a screening program for sickle hemoglobin which focuses on children aged 3–15 years since 2007. This program had two objectives, the detection of patients with an SS phenotype who are referred for clinical care, and the education and counseling of subjects with the SCT in order to reduce the number of births affected by SCD. Target population selected for screening was aged 3–15 years and was approached in schools at village level. Screening was initially performed by solubility tests on finger prick samples in the field and those with positive tests have venipunctures for hemoglobin electrophoresis. In this program, 1,718,909 individuals from 11 districts and special camps in six districts were screened for presence of SCA. These 17 districts include Raipur, Baloda Bazar, Gariyaband, Dhamtari, Mahasamund, Durg, Balod, Kabeerdham, Bemetara, Kanker, Kondagaon, Mungeli, Raigarh, Dantewara, Korba, Bilaspur, Bastar, and Narayanpur. The average prevalence for sickle cell carrier/trait (HbAS) was 11.71%, whereas it was 0.46% for SCD. In this study, the highest occurrence of sickle gene was observed in *Gond* (20.63%) followed by *Halbi* (10.40%), *Khadiya* (5.03%), *Sanwra* (3.78%), and *Uranmi* (3.27%) tribes. In nontribals groups, the highest occurrence was depicted by *Teli* (13.1%) followed by *Panika* (5.48%), *Agharia* (5.08%) and *Rawat* (4.97%) in OBC while in the SC category, *Satnami* (6.21%), *Ganda* (5.70%), *Mahar* (4.97%) and *Gharsiya* (1.46%). SCA was also seen among the general social group with a highest prevalence in *Brahmin* (0.1%) and *Rajput* (0.08%) communities.[44-46]

A study assessed the prevalence of SCD among school-age children (3–15 years' age) in different regions and social categories of population of Chhattisgarh using the data generated through SCD screening program in Chhattisgarh. The calculated prevalence of

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carrier state (AS) in ST, SC, OBC, and general categories was found to be 9.56%, 8.33%, 10.82%, and 6.30%, respectively. Similarly, the calculated prevalence of SCD (SS) in ST, SC, OBC, and general categories was found to be 0.35%, 0.31%, 0.42%, and 0.26%, respectively by the researchers.[47]

A pilot study from Raipur in Chhattisgarh, was undertaken where 1,158 neonates were screened and 5.2% were sickle heterozygous, five babies had SCA, and one had sickle-β-thalassemia.[48]

A study was undertaken to assess the association between SCA and glucose-6-phosphate dehydrogenase (G6PD) deficiency from *Sahu* and *Kurmi* population of Durg and Rajnandgaon district of Chhattisgarh. Among 982 samples collected from Durg, 9.26% were found sickle positive and out of 767 samples from Rajnandgaon, 6.77% were found sickle positive and 106 individuals were found G6PD deficient among which 66 were sickle positive.[49,50]

NORTHERN INDIA

Uttarakhand

Tribes of Uttarakhand mainly comprise five major groups—the *Jaunsari* tribe, *Tharu* tribe, *Raji* tribe, *Buksa* tribe, and *Bhotiyas*. In terms of population, the *Jaunsari* tribe is the most significant tribal group of the state. A survey collected data from various Primary Health Centers, Certified Pathology laboratories, and district hospitals of Kumaon region and analyzed the status of anemia, thalassemia trait and variants, sickle cell β-thalassemia and thalassemia major in the state. It was reported that that most of the cases of hemoglobinopathies including HbS are present in Udham Singh Nagar, followed by Nainital, Pithoragarh, Almora, Champawat, and Bageshwar. Although, most of the cases were thalassemics but presence of SCD and trait was also noted. SCDs are very common in tribal communities, especially prevalent in *Tharu* communities in Sitarganj area.[51] Similar results were reported by a 3-year study conducted in healthcare facility of Uttarakhand.[52]

Uttar Pradesh

Uttar Pradesh is not known to be prevalent with HbS. However, an institution-based study conducted between 2009 and 2012 among premarital candidates, pregnant mother with known suspicious or unknown family history, clinically suspicious or hemoglobin fall patients referred by the physician and some self-participants assessed the prevalence of hemoglobinopathies in north UP. The study reported hemoglobinopathies among the participants 12.01%, with β-thalassemia heterozygous individuals (5.04%) was the most frequently encountered quantitative hemoglobinopathies, followed by HbAE (3.32%), β-thalassemia homozygous state (0.43%), HbE β-thalassemia trait (1.82%), HbAS (0.86%), and HbS β-thalassemia trait (0.54%).[53]

EAST INDIA

Odisha

The state of Orissa is inhabited by 36.7 million of population, comprising 22.4% scheduled tribes and 16.2% scheduled caste people. HbS variant hemoglobin is known to be prevalent in the tribal areas of Odisha; however, there is paucity of population-based screening studies in literature.[1] A cross-section of 15 major tribal communities from different parts of Odisha was randomly screened for hemoglobin variants and G6PD deficiency. High frequencies of sickle cell hemoglobinopathy (0–22.4%) and G6PD deficiency (4.3–17.4%) were found with 12 individuals inheriting both these abnormalities.[50] Unpublished data from Odisha sickle cell and thalassemia control Program involving 11 districts of the state covering 61,409 antenatal women suggests 9% prevalence of SCT while 0.3% and 4.3% for SCD and beta-thalassemia respectively.

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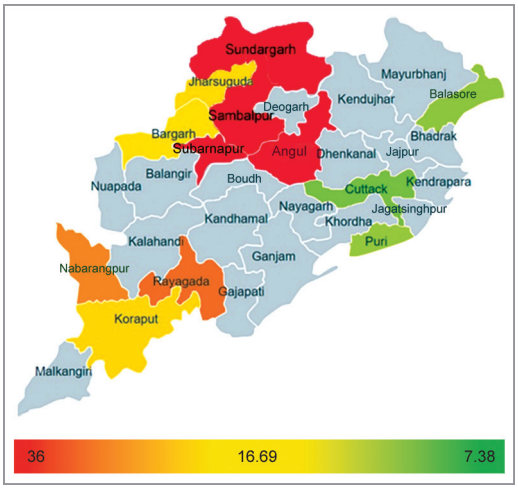

FIG. 5: *District-wise prevalence of sickle cell trait in Odisha.* The range of prevalence is 26–7.4% and legend is not comparable to other state. Data not available for the districts in gray.

Figure 5 presents the data on prevalence of SCT from the program.[54] In the Kalahandi district in Odisha, 1668 newborns were screened and 19.03% of tribals were sickle heterozygous and 2.1% with homozygous SCD were identified.[51]

A cross-sectional study for sickle cell carrier screening was conducted in Koraput district of Odisha. A total of 1,092 individuals from 22 villages were screened for SCT. Out of 1,092 individuals, 9.43% individuals were found to be sickle cell carriers. Also, the study found a significantly higher prevalence of sickle cell hemoglobins among SCs (9.98%) than STs (3.33%).[55]

An observational study was carried out for a period of 2 years at multiple institutes among the blood samples (cases) advised for diagnosis of different hemoglobin disorders. The most common abnormal hemoglobin disorder was found to be sickle hemoglobin variant (48.67%) which was diagnosed as SCT (22.1%), homozygous sickle cell anemia (20%), double heterozygous state of sickle cell-β-thalassemia (3.2%). The second prevalent variant was β-thalassemia states (11.32%) which was diagnosed as β-thalassemia trait, β-thalassemia major, and double heterozygous state with sickle cell, hemoglobin E and hemoglobin Lepore.[56]

A study from Medical College, Cuttack assessed the spectrum and magnitude of hereditary hemoglobin disorder from a large sample size comprising those referred for evaluation of anemia from 2008 to 2017. A total of 21,371 patients were enrolled during these 10 years of study period. Out of which 50.2% cases were diagnosed with different types of hemoglobinopathies. Beta-thalassemia was detected in 54.06%, HbS 52.48% and HbE in 9.19%. Other hemoglobinopathies such as α-thalassemia, HbD Punjab, Hb Lepore, hereditary persistence of fetal hemoglobin (HPFH) were present in <1% each.[57]

Jharkhand

The predominant population of the newly formed state of Jharkhand, is tribal. Incidence of SCD is 3.3% in tribal children of Chota Nagpur (Jharkhand) which is up to 10% in various parts of the state.[4] In a recent study on the prevalence of hemoglobinopathies in the eastern region of India (eastern Uttar Pradesh, western Bihar, Chhattisgarh, and Jharkhand); it was reported that the frequencies of thalassemia as well as HbS traits to be the same (3.6%), but while BTT was distributed uniformly through the region, HbS was confined to Chhattisgarh and Jharkhand, the regions abundant in tribal communities. However, in Jharkhand, which shares borders with Uttar Pradesh, Chhattisgarh, Odisha, Bihar, and Bengal, HbS was seen in the populations adjacent to Chhattisgarh and Odisha but not in those bordering UP and Bengal.[58]

A report assessing the genetic basis of the discriminatory distribution of HbS in different regions of Jharkhand recorded the number of HbS cases as 3.3%. The sub-categorization of the tribal samples from Sahibganj and Tatanagar districts included communities of *Santhals, Patars,* and *Oraon*. Though tribals constitute major part of the population, only 3% of the examined samples showed HbS as

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against 13% in Chhattisgarh, with a rather uneven region-wise distribution, it being highest in Tatanagar (10%), nil in Sahibganj, and only a minor presence in Garhwa and Ranchi. However, this distribution follows a regional bias: Tatanagar is contiguous with the Odisha border whereas Sahibganj is adjacent to West Bengal. The other two regions, Garhwa, borders with UP and Chhattisgarh, while Ranchi, being the state capital, is nearly at the center of Jharkhand state.[59]

West Bengal

A community-based screening was conducted from June 2010 to August 2013 to evaluate the prevalence of β-thalassemia, HbS, HbD, and HbE in the state. A total of 50,487 cases were subjected to study from different districts of rural areas of West Bengal by arranging camps in schools, colleges, and university also for screening of individuals for detection of different hemoglobinopathies using HPLC. The prevalence of β-thalassemia trait was 6.61% making this the major hemoglobinopathy in West Bengal, followed by HbE trait at a prevalence of 2.78% in the study population. A total of (0.56%) of SCT were detected in the study.[60]

Earlier studies by Mohanty et al. have shown a prevalence of 0.14% and 0.13% from Kolkata and Dibrugarh respectively.[61] A study from Kolkata done on retrospective data of a diagnostic center showed only 0.276% of SCT among 14,145 cases included in the study.[62] Another institution-based study from North Bengal included cases of pallor and weakness from camps and diagnosed HbS variant with HPLC reported sickle cell hemoglobin variant in 2.16% of the study subjects.[63] Unpublished data from state screening revealed a prevalence of HbS as 0.1% while that of thalassemia trait as nearly 10%.

SOUTHERN INDIA

Tamil Nadu

The HbS hemoglobin was first described in the Nilgiri Hills of northern Tamil Nadu in 1952. The scheduled tribal population of Tamil Nadu was found to be 6.51 lakhs widely distributed in 30 districts constituting 36 tribes. The Nilgiri district includes six primitive tribal communities, viz., *Todas, Kothas, Kurumbas, Irulas, Paniyas,* and *Kattunaikkans* unevenly distributed in forest and hilly areas of six *talukas* of this district. The distribution of SCD in various tribal populations in Nilgiri district of Tamil Nadu has been studied to identify the high risk areas. Among these population 11.7% were found to be sickling homozygous (HbSS), whereas 28% population examined had heterozygous state (HbAS). The highest incidence of SCD cases were reported in six village *panchayats* namely Cherangode, Nellakota, Jakkanarai, Konakkarai, Kengarai, and Arakkode. A maximum of cases were recorded in Jackanarai of Kotagiri taluka.[64]

The sickle cell gene is known to be wide spread among people of the Deccan plateau of central India with a smaller focus in the north of Kerala and Tamil Nadu. Extensive studies performed by the Anthropological Survey of India have documented the distribution and frequency of the SCT which reaches levels as high as 35% in some communities.[61]

Kerala

In Kerala, SCA is prevalent in Wayanad district and the Attappady block of Palakkad district. Prevalence of homozygous SCD among tribals in Wayanad is about 0.31% and that of SCT is about 4.33%.[65]

A population-based study of gene frequencies and disease characteristics using hemoglobin electrophoresis was done

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in 1,016 subjects belonging to the tribal and Chetti communities in Wayanad district. The study was conducted in schools by evaluating everyone present at the time of the visit. The gene frequency of HbS ranged from 0.019 in Kattunayakan to 0.196 in Wayanadan Chettis.[66]

Andhra Pradesh and Telangana

Andhra Pradesh and Telangana are the Indian states with a total population of 76.2 million and harbor 5 million tribal population that constitutes 6.6% of the total population. These two states are rich reservoirs of *HbS* gene. The prevalence of carriers (HbAS) is ranged up to 24.5% in Andhra Pradesh and 30% in Telangana. In an analysis of 13,922 people from 27 tribal communities conducted to estimate SCD from different studies among the states, it was found that *HbS* gene was present in almost all tribal groups and the gene frequency ranged from 0.0014 (in *Chenchu* tribe) to 0.1545 (in *Pardhan* tribe). Based on *HbS* gene frequencies, birth rate, and inbreeding coefficient of these tribes, the expected births with SCD are calculated. The expected number of children born with SCD is 1.8 and 1.7 per 1,000 births in Andhra Pradesh and Telangana states, respectively.[67]

In Andhra Pradesh, the highest frequency of sickle cell carriers are recorded among tribes, such as *Pardhan, Konda Kammara, Bod Mali, Manzai Mali, Valmiki, and Parangi Poraja*, which inhabit hilly terrains with dense forest cover. Interestingly members of the *Yanadi* and *Yerukula* tribes residing in the plain areas show total absence and very low incidence of SCT, respectively. Among early surveys, very low frequencies of homozygous sickle cell anemic individuals were recorded in the state. Most of these studies were carried out as part of population variation investigations with anthropological perspective and hence all these studies are based on the screening of only adults. The sickle cell anemic children with severe phenotype may have might have expired. The frequencies of SCA patients in the dense forests of Andhra Pradesh, varies between tribes such as Pardhan (31.78%), Konda Kammara (22.3%), Bod Mali (15%), Valmiki (14.8%), and Manzai Mali (13.7%).[68]

A study assessing prevalence of SCA among the *Thotis*, of Andhra Pradesh reported 12.84% individuals who had positive screen test for sickle cell hemoglobin, 9.32% were heterozygous (AS) for SCT while 2.52% were homozygous (SS).[69]

NORTH EAST INDIA

Assam

Hemoglobinopathy, particularly HbE and HbS and thalassemia are considered to be contributing factor in occurrence of anemia in Assam and HbS was reported to be mostly restricted to the tea garden community of Assam. A community-based study conducted at 16 tea estates of Assam assessed the determinants of anemia among adolescent girls. They reported that 12% of the anemic girls had HbS.[70] Another study carried out to determine the frequency and types of hemoglobinopathies in the tea garden community near Dibrugarh town assessed 250 cases from two different tea gardens, irrespective of age and sex. The study reported abnormal hemoglobins as HbE trait (1.6%), HbS trait (12.0%), and HbS disease (2.0%) among the study population.[71]

The study was carried out to determine the prevalence of hemoglobinopathies and β-thalassemia among the tea garden workers of Assam, where 1,204 samples were assessed with HPLC. The study results indicated a higher prevalence of β-thalassemia (3.07%) among the *Munda* ethnic group and higher prevalence of SCA (4.73%) among the *Lohar* ethnic group. 1.66% of the participants were compound heterozygotes of β-thalassemia which coinherited with HbE and HbS.[72] A community-based cross-sectional study conducted among 770 numbers of adult females belonging to the tea garden

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community reported momozygous HbSS in 2.4% and heterozygous HbAS among 14.2% of study population.[73]

Tripura

Nineteen tribes are represented in the population of Tripura, the two largest being the *Tripuri* and *Reang*, which together accounted for 71% of the tribal population in 2001. Newborn screening for hemoglobinopathies was also undertaken in the malaria endemic region in Agartala in Tripura where HbE is widely prevalent but HbS is also seen among the tea garden workers who are migrant laborers from other states.[74]

In summary, the data is useful as it sheds light on the magnitude of the problem, but the varied target populations, different test methodology used and other lacuna, limit the use of this data for good policy implementation. Registry data and well-planned screening from the 16 states, particularly from the districts with high sickle cell burden have been initiated and this complete dataset will be invaluable for improving the care that the patients receive.

Summary

- Exact prevalence of SCD in most parts of India based on population-based survey is not available.
- SCD (HbAS, HbSS, and sickle beta-thalassemia) have variable frequency of 1–44%, constitute one major public health problem. It varies from place to place.
- SCD is considered a major socioeconomic burden of India by considering its magnitude and multiple impacts.

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