International Journal of Public Health and Epidemiology ISSN: 2326-7291 Vol. 2 (5), pp. 101-107, December, 2013. Available online at www.internationalscholarsjournals.org © International Scholars Journals

Full Length Research Paper

Epidemiology of sickle cell disorder: The urban scenario in Maharashtra, India

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Accepted 13 September, 2013

The present study was designed to determine the current status of sickle cell disease (SCD) in urban population of eastern part (Vidarbha) of Maharashtra State in India. A total of 3479 subjects belonging to 40 ethnic groups, including 29 non tribal, 8 tribal and three migratory groups were sampled. Blood samples were collected aseptically from all individuals and positive samples were further subjected to cellulose acetate hemoglobin electrophoresis for discriminatory confirmation. The overall prevalence of sickle cell trait was found to be 4.94%, of which genotype HbS and HbSS were found to be represented by 3.88% and 1.06% respectively. All tribal populations were found to be SCD positive with moderate frequency (0-14%). Among non tribes, out of 32 ethnic groups, SCD was diagnosed from 14 groups with frequency ranging between 0and 10%. The age group 0-30 years was found to be more prone to the disorder and the rate declined progressively with increasing age especially in people above 30 years of age.

Key words: Sickle cell disease, urban population, Maharashtra, tribal population, caste population, ethnic groups.

INTRODUCTION

Sickle cell anemia (SCA) is a recessive genetic disorder that affects the proper functioning of red blood cells. The cause of the disease is genetic mutation in the gene responsible for the β-subunit of hemoglobin tetramer (Mehanna, 2001). The abnormal hemoglobin is less soluble than normal hemoglobin HbA and therefore tends to crystallize out, resulting in deformation of cell which instead of being round become sickle shaped. The sickle shape red blood cells are oxygen deficient. (Hahn and Gillespie, 1927) confirmed the intimate relationship between the sickling of red blood cell and a reduced supply of oxygen. The transmission of the SCD follows the simple Mendalian principle (Neel, 1949) and thus, expression of disease requires both aberrant copies of defective hemoglobin gene (Koch et al., 2002). Heterozygote's denoted as carriers of the disease and sustains normal life with much milder symptoms. SCA causes chronic destruction of red blood cells, episodes of intense pain, susceptibility to infections and in some cases premature deaths.

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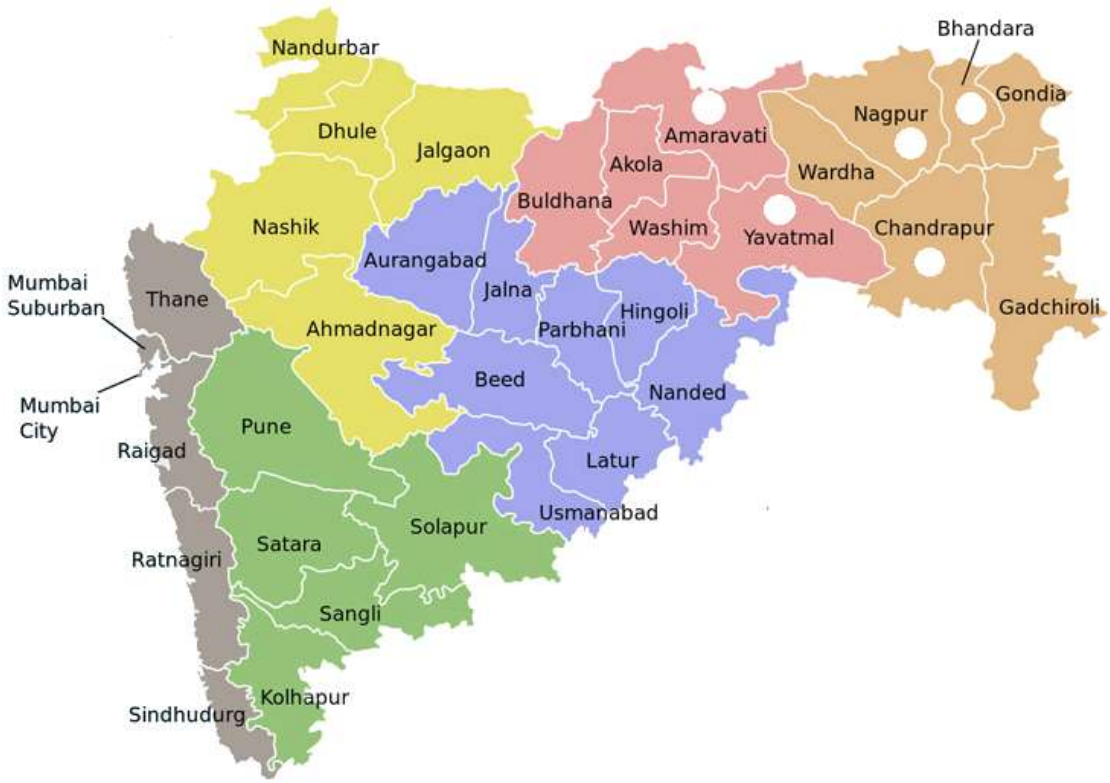
SCD affects mainly the African descendents and spread all over the world as a result of migration (Technical Report SCA, 2009). The Central-West Africa, East Asia and India are the most SCD prone regions of the world (WHO report, 2006). Even in developed countries like USA, it is the most common hereditary blood disease with carriers 1 in 500 North American African descendents and 1 in 1000-1400 North American Hispanic descendents (ASCAA Annual Report, 2011).

In India, (Lehman and Kutbush, 1952) detected sickle cell anemia in tribes of Nilgiri Hills in Southern India after 42 years of its discovery by James Herrick. Later subsequent studies conducted by various workers confirmed high distribution of HbS gene in Central, Southern and North Eastern India (Dunlop and Mujumdar, 1952; Buchi, 1955; Sukumaran et al., 1956; Rao et al., 1986; Kar et al., 1998; Feroz and Arvindan, 2001; Kate and Lingojwar, 2002; Sahu et al., 2003; Balgir, 2008; Patra et al., 2011; Urade b, 2012). In certain states such as, Madhya Pradesh, Chhattisgarh, Maharashtra, Orissa, Jharkhand and Gujarat it forms the major public health problem and many more states would be listed in future. Although, it is really sad and unfortunate thing that SCA is neglected field of research in India.

In India, the spectrum of epidemiological studies in urban area is very limited because it poses many difficulties. The urban peoples are working in either organi-



Map-1. Map of Maharashtra (India) showing study area.

zed or unorganized sector. They are available only on holidays but most of them want to spend their spare time with their families and friends at home or elsewhere. Thus, it was quite difficult to get adequate samples from them. Despite that fact in order to maintain good urban health, it is a prime need to ascertain current updates on SCD from the urban population. Understanding the actual rate of prevalence should facilitate the planning of public policies and other actions that can contribute towards the reducing homozygote's from the population and improving the quality of life of people with SCD.

The east Maharashtra was taken into consideration for this study since limited researchers have contributed to SCD research in this area earlier (Deshmukh et al., 2006; Kamble and Chaturvedi, 2000; Ankushe, 1993; Shukla and Solanki, 1958).

MATERIAL AND METHODS

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 between April 2009 and March 2011 (See Map-1). For this investigation five cities (one from each district) and ten towns (two from each district) selected randomly.

Screening camps were arranged in schools, community halls or in big multistoried apartments in randomly selected wards with the help of local leaders and social workers. People of all age groups were enrolled for sampling. In order to exclude any bias, the data was strictly adhered to indigenous populations of unrelated and healthy individuals free from any alignment. An informed consent was obtained from the participants prior to the commencement of screening either from the individuals in case of mature participants or from their parents in case of children. The prepared questionnaires were provided to all the participants containing information related with age, sex, resident, nationality, educational qualification, occupation and financial status. Immediate after filling of questionnaire, a volume of 20 µl blood sample was collected by finger prick from each individual in EDTA containing aseptic tubes and screened by solubility test. Screening was followed by taking 2 ml of blood sample from each positive subject by using BD vacutainer (USA), stored in cool until it is brought to the Zoology Departmental Laboratory at RTM Nagpur University, Nagpur, for further investigation. Standard procedures were employed for hematological investigations (Dacie and Lewis, 1995). All the samples along with known controls were subjected to hemoglobin electrophoresis on cellulose acetate membrane in TEB buffer at pH 8.6 for confirmation of their patterns. The

Table 1. Prevalence of Sickle Cell Disease in Selected Districts in Urban Maharashtra.

District	Screened population	HbAS	HbSS	Total (AS+SS)	Percentage
Amravati	696	19	07	26	3.73
Bhandara	388	29	06	35	9.02
Chandrapur	513	34	08	42	8.18
Nagpur	1125	33	12	45	4.00
Yeotmal	757	20	04	24	3.17
Total	**3479**	**135**	**37**	**172**	**4.94**

majority of samples were investigated at aforementioned center and the rest were performed by other reputed laboratories.

The collected data was checked and entered on Microsoft Excel Worksheet. Frequencies and percentages were used to describe categorical variables. Gene frequency was assessed by using Hardy-Weinberg law. The frequencies of nominal variables were compared by using the chi-square test. A p-value of ≤ 0.05 was considered statistically significant.

Social Stratification

Indian society fragmented into thousands of caste groups and more than 500 tribal groups including 75 primitive communities (Indian STs, govt. doc, 2011). Indian constitution classified them into Scheduled Caste (SC), Scheduled Tribe (ST), Other Backward Class (OBC) and General caste (GC) on the basis of their financial and social status.

RESULTS

During the period studied, a total of 3479 subjects were screened for assessing SCD gene frequency from the urban parts of east Maharashtra. Maximum (n = 1125) number of subjects were screened from Nagpur district and minimum (n = 388) from Bhandara district. Although, Bhandara district had minimum share in total screening was diagnosed to be the area of maximum SCD gene frequency (0.09 or 9.02%), followed by Chandrapur (0.0818 or 8.18%), Nagpur (0.04 or 4.0%), Amravati (0.0373 or 3.73%) and Yeotmal (0.0317 or 3.17%). A total of 172 (4.94%) individuals were found to be positive for sickle cell disorder, of which 135/172 (3.88%) with heterozygous genotype AS (Carrier) and 37/172(1.06%) with homozygous genotype SS (Disease). The overall frequency of HbS gene in east Maharashtra was found to be statistically significant (p = 0.05). The frequency was found insignificant in Bhandara and Chandrapur district (p > 0.25). (Refer Table-1).

Table-2 reveals that, highest prevalence of SCD was diagnosed among the people belonging to age group bracket between 10 to 20 years (26.74%) whereas lowest prevalence was recorded in individuals who exceeded their 50s (2.32%). The decreasing frequency of HbS gene with increasing age was noticed especially in the people above 30 years of age. Out of total positive cases, 2.47% (89/3479) were males and 2.38% (83/3479) were females

The prevalence of SCD gene among various ethnic groups is shown in Table-3. The SCD has been diagnosed from all tribal groups and 14 caste groups. However, no positive cases were identified from 16 caste and two migratory populations. 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%) whereas lowest frequency was recorded from Muslim Gawali, Bhangi and Koli Mahadeo. Banjara, only migratory group has recorded to be positive for HbS with moderate frequency. Prevalence of sickle cell gene in tribes was found somewhat higher than non-tribes except Koli Mahadeo (2.63%). Majority of SCD positive cases (87.20% or 150/172) were noticed from Hindu and very little prevalence was noticed from other religious people.

With relation to the social and economic background retrieved from the questionnaire illustrates that, 66.27% (n = 114) of positive individuals were belonging to the families having monthly per capita income of less than Rs. 4000 and 18% of them this figure was less than Rs. 2000. The lowest reported per capita income of their families was zero and the highest was more than Rs. 1, 00,000. At the time of study the national monthly per capita income was Rs. 4379 (INR $56 = US 1.00). Literacy point of view, 82.46% (127/154) positive individuals above 6 years of age were literate. 29.92% (n = 38) of them had not completed primary education, 25.98% (n = 33) had reached secondary school and only 4.27% (n = 6) had completed their education up to post graduation.

All ethnic groups that were investigated are well distributed throughout east Maharashtra except Korku and Kolam. Korku population is exclusively found in Amra-

Table 2. Prevalence of Sickle Cell Disease Among Different Age Groups in Selected Districts in Rural Indian Urban Mahrashtra.

Age	Screened population	Frequency	Percentage	Male	Female
0 ≤ 10	788	38	22.09	18	20
10 ≤ 20	909	46	26.74	23	23
20 ≤ 30	601	40	23.25	21	19
30 ≤ 40	712	26	15.11	15	13
40 ≤ 50	314	18	10.46	09	07
50 ≥	155	04	2.32	03	01
Total	**3479**	**172**	**100**	**89**	**83**

vati district and Kolams are restricted to Yeotmal and Chandrapur district.

DISCUSSION

In this investigation the frequency of HbS gene was observed in between 0 and 14% which was in accordance with the frequency (0-20%) reported by (Urade, 2012) although, it is quite lower than those reported in earlier studies (Shukla and Solanki, 1958; Deshmukh, 1968; Negi, 1976; Jain et al., 2003; Balgir B, 2008). The disparity may be attributed to the differences in the study design, study area or even in sample size selected. For instance, this study designed to determine the SCD status from the cities and towns whereas earlier studies documented SCD prevalence without any such limitations. With respect to land area, India is a seventh largest country in the world and it is divided into number of geographical areas. Thus, different results could be obtained in different geographical areas are concerned (Urade B, 2012). One of the important factors that influence the results is sample size selected. For instance, (Shukla and Solanki, 1958) have sampled five patients in their clinic base study. The small sample size obviously underestimates the true probability of prevalence of the disease.

The average prevalence of SCD in Eastern Maharashtra was found to be 4.94%. (Ankushe, 1993; Kamble et al., 2000; Deshmukh et al., 2006) have reported a prevalence of 5.7% and 2.9% respectively of the same from rural Wardha. It demonstrates that there is no statistical difference in prevalence of SCD in urban and rural parts of eastern Maharashtra ($p< 0.001$). Comparative high HbS gene distribution was estimated from Bhandara and Chandrapur districts (9.02% and 8.18% respectively). This observation was often expected from Chandrapur district as it is situated in close proximity of tribal belt. In fact, it was surprised to observe such result from Bhandara district. The probable reasons for high HbS distribution in Bhandara may be assigned in limited sample size, secondly the area may have been kept high prevalent by the laws of natural selection in the absence of effective intervention programs. Interestingly, Yeotmal district is also occupied by good numbers of tribesmen, but minimum prevalence of SCD was estimated from its urban parts.

Although, the available data of Eastern Maharashtra revealed that most of the tribal population live in rural areas (Indian census report, 2001), however, in the last couple of decades many have migrated in search of employment and settled in urban areas. The previous investigations have suggested that, SCD is more common in tribes (Bhatia and Rao, 1986; Mohanti and Das, 2001; Babu et al., 2002). The reason for that may be traced back in early migrations from Africa to Asia, about 50 to 100 thousand years ago, between the Paleolithic and Mesolithic periods (Technical report, SCA, 2009). Few studies were in favor of independent origin of sickle cell gene in India and West Africa by separate mutation (Kan and Dozy, 1980).

The mean reported prevalence among tribes was found to be 8.37% which was more or less in confirmation with the findings of (Kate et al., 2002) in Central India (10%) and (Patel, 2012) in Western India (11.37%). However, it is quite lower than earlier reported prevalence (29%) from North East India (Balgir, 2005). We have noticed moderate frequency of SCD in Pradhan(11.49%) which is in confirmation with (Deshmukh et al; 2006) although, very high frequency was reported in the same group by

Table-3: Distribution of SCD gene in different ethnic groups of E. Maharashtra.

Sr. No.	Community	Category	Population screened	AS	SS	Total (AS+SS)	%
1	Bari	OBC	92	-	-	-	-
2	Banjara	NT	99	05	02	07	7.07
3	Bhangi	SC	117	03	-	3	2.56
4	Bharadi	OBC	13	-	-	-	-
5	Bhavsar	OBC	08	-	-	-	-
6	Bhil	ST	105	10	02	12	11.42
7	Bhoi	OBC	66	-	-	-	-
8	Boudha	SC	262	15	03	18	6.87
9	Charmkar	SC	114	-	-	-	-
10	Christian	-	59	02	-	02	3.39
11	Daudi Bohra	-	19	-	-	-	-
12	Dhangar	NT	53	-	-	-	-
13	Dhanwar	NT	21	-	-	-	-
14	Gond	ST	126	14	04	18	14.28
15	Gowari	ST	102	04	02	06	5.88
16	Halba	OBC	132	-	-	-	-
17	Jain	-	61	-	-	-	-
18	Kalar	OBC	141	4	-	04	3.83
19	Kolam	ST	29	-	02	02	6.89
20	Koli Mahadeo	ST	38	01	-	01	2.63
21	Komati	OBC	77	-	-	-	-
22	Korku	ST	42	03	01	04	7.89
23	Kosti	OBC	80	-	-	-	-
24	Kumbhar	OBC	12	-	-	-	-
25	Kunbi	OBC	275	11	02	13	4.72
26	Mali	OBC	133	07	01	08	6.01
27	Maratha	GC	89	02	01	03	3.37
28	Marwadi	GC	92	-	-	-	-
29	Matang	SC	217	15	04	19	8.75
30	Muslim	-	69	01		01	1.44
31	Muslim Gawali	-	40	-	01	01	2.5
32	Nhavi	OBC	45	-	-	-	-
33	Parit	OBC	22	-	-	-	-
34	Pinjari	OBC	08	-	-	-	-
35	Powar	OBC	123	05	01	06	4.87
36	Pradhan	ST	87	08	02	10	11.49
37	Sonar	OBC	84	04	-	04	4.76
38	Teli	OBC	248	18	08	26	10.48
39	Wadhai	OBC	28	-	-	-	-
40	Warli	ST	61	03	01	04	6.55

other investigators (Babu et al., 2002; Blake et al., 1981; Bankar et al., 1984). We have diagnosed relatively low but alarming frequency of HbS gene in Korku (0.068 or 6.89%) and Kolam (0.078 or 7.89%) which is in agreement with the findings of (Kate and Lingojwar, 2002) although (Urade, 2012) has reported negligible prevalence from the same groups.

Among caste population studied, the highest prevalence has been recorded in Teli (10.48%) followed by Matang (8.75%), and Boudha (6.87%). Almost all previous studies observed alarming rate of prevalence of sickle cell disorder in Boudha of this area. Interestingly, more than 95% of them are belongs to scheduled caste as they have adopted Buddhism from Hindu caste Mahar in 1956 under the leadership of Dr. B. R. Ambedkar and are no longer willing to revert to Hindu. The same may be true about Muslims as large portion of their current population is drawn from local communities. However, compared to scheduled caste, Muslims have shown lower prevalence. The reason could be attributed to the small sample size obtained from them. In east Maharashtra most of the workers reported either nil or very low frequency of HbS gene in Charmkar but in Western India the frequency was quite high as recorded by (Patel et al., 2012).

Although, it was treated as a tribal disease for few decades after its discovery in India, later epidemiological studies confirmed that, sickle cell anemia is rampant not only in tribal population but is also prevalent among non tribal counterpart (ASHWINI) and still hundreds of caste groups remain uninvestigated from sickle cell screening (Ramesh et al., 2006). ASHWINI has reported 30% prevalence from Southern India in non tribal group such as Chetties. In the same group (Feroz, 2001) has reported 19.6% from Waynad, Kerala. Among other authors who have reported high SCD prevalence from non tribal's were (Balgir, 2005) and (Patel et al., 2012), they have reported higher frequency of Hbs gene among non tribal group Chasa (19.8%) in Orissa state and Choudhary (15.63%) in Gujarat state respectively. (Bhasin et al., 2006) demonstrated that the sickle cell trait has been transmitted to non tribe population due to social interactions between tribes and non tribes, living in close proximity with one another. It is not surprising that SCD has changed its dynamics because of changes in the prevalence and distribution of the same depending on the prevailing biological (malaria interventions) and social factors (marriage pattern) (Andrew et al., 2010). In Asia, no relation between HbS allele frequency and malarial endemicity was found thus, the malaria-sickle cell hypothesis does not hold well in India so far as the occurrences of HbS in different indigenous tribes as well as non tribes in varied ecological zones are concerned (Urade B, 2012). Nevertheless, Eastern Maharashtra had moderate number of sickle cell carriers; it is free from hyper endemic malaria. Marriage pattern might have some role in changing dynamism of SCD. However, most of Indian ethnic groups trying to maintain their endogamy, the sickle cell trait is most serious problem which acts as a carrier for propagation of anemia among the society through consanguineous marriages.

More than 70% of HbS persons were belonging to financially weaker sections of the society and only few of them were well educated. These results illustrate that in SCD social factors are strongly associated with the biological determinants. Therefore, government organizations such as planning ministry, Health ministry and social welfare ministry have need to be taken collective efforts to improve financial status of the society that can contribute towards delimiting further spread of SCD.

Wintrobe (1961) found that SCD is more frequent in females than males whereas Sahu et al., (2003) has recorded the opposite result. We did not notice any such correlation and reported the same frequency in both male and female. High prevalence was observed between the age 0 and 30 years and its severity declined with increasing age. The reason for the low prevalence in higher age groups may be attributed to very small sample size, secondly most of the sickle cell patients could have succumbed to the disease in early age and thirdly, we were failed to attract higher age group persons towards screening camps.

The study has documented SCD from all Hindu categories along with Muslim, Boudh and Christian religious people. This demonstrates that sickle cell anemia is no longer confined to specific ethnic groups (Urade B, 2012).

CONCLUSION

Our study suggests that in urban parts of Eastern Maharashtra, the frequency of sickle cell trait is quite high irrespective of caste and creeds. The study further reveals that the urban and rural parts of this area have similar frequency of SCD. The study provides, for the first time, a comprehensive database on the spectrum of sickle cell disease in urban region that will be helpful to future community based studies especially epidemiological studies.

Thus for maintaining good urban health, the steps have to be taken to restrict the further spread of sickle cell trait by proper management, treatment and creating awareness. Management might be involved screening of people with sickle cell trait and positive results needs to be treated with antibiotics promptly and rigorously. Severe pain should be considered medical emergency that prompts timely and aggressive management until the pain is tolerable. Genetic counselors should be focused on premarital screening. Positive individuals should be informed about their implications and family planning.

There is no specific treatment for individuals with sickle cell disease; however, there are prophylactic measures that

that help to limit the factors that may trigger sickling crisis episodes and complications. Thus, treatment likely will involve the use of different agents alone or in combination to produce optimal results. Capacitating the basic healthcare centers should be made a priority, since simple interventions, such as neonatal screening, prophylactic penicillin, immunization and education can have a great impact on public health.

Prevalence of SCD would be avoided through increasing awareness of the people. Awareness should be created by inclusion of relevant information in the school curricula has been adopted. Article should be published in news papers. Talk shoes on radio and TV, workshop, symposia and special days for SCD should be organized.

ACKNOWLEDGEMENT

We thank Dr. Arun Khurad, Head, Post Graduate Department of Zoology, Rashtrasant Tukdoji Maharaj Nagpur University, Nagpur, for providing necessary laboratory facilities during this investigation. We are also thankful to local leaders, social workers and technicians for their help.

CONFLICT OF INTEREST: Author's declare that they have no conflict of interest.

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