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Sickle cell disease and associated problems: Case study of Homozygous sicklers

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ABSTRACT

This paper is focused on the problems faced by homozygous individuals of sickle cell disease. In a survey of 500 household of 17 villages of district Mandla, a total of 2316 individuals were covered out of which 13 were found homozygous for the disorder; whereas 3 homozygous children were reported died preceding to one year of the survey. In depth case studies of these children were recorded. The highest age of surviving homozygous individual was 30 years. After 4-5 years of age their survival is very difficult and they require frequent blood transfusion. They face frequent episodes of various infections and unbearable pain. The findings are based on longitudinal and cross sectional study as well as empirical field investigation. It was found that the homozygous children have to face multiple problems, acute pain, priapism, alienation, frequent hospitalization, economic constraints. The families of homozygous children have to face frequent emotional shock as well as economic burden. The problem of homozygous sicklers can be categorized as clinical, educational, economic etc. and is a challenge for achieving the goal of human development. Further to understand the relationship of the prevalence of gene and Human Development, district and state wise gene (HbS) frequency were computed. The bivariate correlation analysis between the district wise prevalence of gene and human development index was found positive but insignificant (r^2=0.065, p>0.8). At the same time, the correlation of prevalence of the HbS gene and human development index for 11 states was found negative and insignificant (r^2=-0.237, p>0.5). It leads to conclude that there is no apparent correlation between the prevalence of gene and the human development in that particular region, although there is lack of sufficient data.

Keywords: *Sickle cell, clinical symptoms, priapism, economic status, pain, blood transfusion, Human development, aneamia.*

INTRODUCTION

Today, Genetic disorders and life style diseases are great challenge for humanity. With the advent of science and technology including medical science we conquered the communicable disease viz. small pox, diphtheria, pertussis etc., even polio is near to eradication. At the same time, life style diseases like heart attack, hypertension, obesity, diabetes etc. as well as genetic disorders are posing new challenge for humanity. the sickle cell disease (SCD) is a widely spread genetic disorder characterized by red blood cells assuming an abnormal, rigid, sickle shape that results in a risk of serious complications. The sickling occurs due to a mutation in the hemoglobin gene. Homozygosis of the gene, contributed by both the parent, results into sickle cell disease, whereas persons with one recessive gene are called carrier or trait shows asymptomatic sicklemia (Neel 1951).

The homozygous individuals are aneamic and susceptible to many infections. They are prone to early death. In medical terminology it is called Sickle-cell disease (SCD), or sickle-cell anaemia (or anemia; SCA) or drepanocytosis. The sickling occurs because of a mutation in the Hemoglobin gene. Life expectancy is shortened, with studies reporting an average life expectancy of 42 in males and 48 in females. (Platt et *al.* 1994).

Sickled hemoglobin polymerizes under deoxy condition and therefore obstructs small blood vessels. Thus poor perfusion results in acute and chronic tissue damage. The problems of SCD arise in people from their early childhood, deteriorating the quality of life and also reducing the life expectancy of the patients. Person with trait leads a normal life but the diseased person suffers from various complications throughout the life such as anaemia, bone & joint pain,

swelling on joints, recurrent infection, osteomyelitis, necrosis of bone, aplastic crises, abdominal pain, splenic sequestration crises, hepato-splenomegaly etc. (Serjeant & Serjeant, 2001).

Among SCD patients Anaemia, hepato-splenomegaly and vaso-occlusive crisis in the form of bone and joint pains and infections are very common. The symptoms include jaundice, fever, gall stones, epistaxis, priapism and leg ulcers are not common in India as reported by Mohanty and Mukherjee (2002).

Little information is available on the causes of death at different ages but several symptoms have been reported in sickle cell disease (SCD) cases from different parts of India. Sarma et al. (1986) studied 1812 cases of SCD and reported 33 deaths (1.81%) due to SCD. The causes of mortality were septicemia, acute splenic sequestration, severe anemia and hemolytic crisis. In a study from Central India, it has been shown that the prevalence of malnutrition and non-compliance to medications increased their susceptibility to infection (Patel and Athavale 2004).

Sickle cell occurs in high frequency in many tropical countries of the world. About 50% of world's population of SCD cases is found in India (Mohanty & Pathare 1998). The prevalence rate of this trait has been reported in Madhya Pradesh ranging from 10- 30% among different castes and tribal groups (Bhatia & Rao 1987 and Kar 1991).

In central India various clinical case studies on SCD have been conducted by different workers especially in Madhya Pradesh, Maharastra, Orissa and Chhattisgarh (Patra et al. 2008). Gautam (1998) have reported the prevalence of 43% among Mehra of Madhya Pradesh. Approximately three million population of central India belong to the high risk communities of sickle cell traits.

The objective of present study is to highlight the problems faced by homozygous individuals of sickle cell disease. The second objective is to test a hypothesis- whether the

prevalence of gene have negative effect on human development or not? The paper is based on longitudinal and cross sectional study as well as empirical field investigation among Mehra a scheduled caste of Mandla District of Madhya Pradesh. Simultaneously, district and state wise prevalence of gene were computed on the basis of secondary/published data available.

MATERIAL AND METHOD

In a cross sectional survey of 500 household of 17 villages of district Mandla, a total of 2316 individuals were covered out of which 13 were found homozygous for the disorder; whereas 3 were reported died preceding to one year of survey. The paper is based on detailed case study of these homozygous individuals. The survey was conducted during summer and winter of 2012, 2013 and 2014 as part of post doctoral programme (PDF), funded by University grant commission (UGC). To find out the presence of sickle cell gene, couples were screened through rapid slide test method. The homozygous individuals were already confirmed by the standard laboratories viz. Regional Medical Research Centre for Tribal, Jabalpur (MP). In spite of living homozygous children information were also collected from the parents of those homozygous children who were died recently.

The state wise prevalence of Sickle cell gene was drawn from a metadata analysis done by Jhariya et.al. On the basis of all India review, the detail would appear elsewhere.

Human development index (HDI) is a composite index of three important aspect of human society and widely used as a parameter to understand the phenomenon of human development. It is based on achievement obtained in health, education and wealth. It can be computed for any country, state, region or population on the basis of these three indicators i.e. health (infant mortality rate), education (literacy rate) and wealth (gross domestic product). Here district and

state wise HDI was obtained respectively from Madhya Pradesh India Human Development Report (2007) and India Human Development Report (2011).

District wise prevalence of Sickle cell gene for 17 district of Madhya Pradesh was computed on the basis of 43 studies conducted by 18 Investigators as given below:

District	References
Balaghat	RMRCT, Jabalpur 2009
Betul	Gupta RB et al. 2006; Singh MPSS et al; Gupta RB, 2006
Chhindwara	RMRCT, Jabalpur 2009
Damoh	RMRCT, Jabalpur 2009
Dhar	Kumar, 1966
Dindori	Ahmad & Choudhury 1980; RMRCT, Jabalpur 2009
Indore	Kumar 1965; Kumar, 1966
Jabalpur	RMRCT, Jabalpur 2009
Jhabua	Ahmad & Choudhuri, 1980; Ahmad, 1984; Papiha et al., 1978
Khandwa	Ahmad, 1984
Khargone	Bhatia & Rao, 1986
Mandla	Gautam and Sharma, 2002
Panna	RMRCT, Jabalpur 2009
Satna	RMRCT, Jabalpur 2009
Seoni	RMRCT, Jabalpur 2009
Shahdol	RMRCT, Jabalpur 2009
Ujjan	Kumar and Ghosh 1967

RESULTS

This paper is based on case studies conducted among 13 surviving homozygous individuals for sickle gene (HbSS). At the same time, information were also gathered about 3 died children. Out of 13 surviving individuals there were 10 male and 3 female, their age ranges from 5 to 30 years.

The younger one was detected for the disease at the age of 3 years. At the time of interview he was 5 year old. The father of the child is a railway employee and career for the gene. When the child suffered from fever and anemia, the doctor at Railway hospital Jabalpur send the blood sample to Regional Medical Research Centre (RMRC) Jabalpur, where it was found that the child is homozygous for the gene. After, this diagnosis, the child fell ill repeatedly

and the father has donated blood 2 times at an interval of 6-8 months. Since then 4 blood transfusions were taken place. Currently the child is enrolled in Class-1st and continuously taking medicine on the prescription of a Doctor (D.K. Agrawal) of District Durg (Chhattisgarh). He frequently suffered from fever and acute pain.

The 2nd child was 7 years old and diagnosed for the disease at the age of 2 years, when he suffered from fever and anaemia, the doctor at the district hospital Mandla suspected sickle cell disease. On serological investigation, it was confirmed that the child is homozygous for the gene. After two blood transfusions, the child is surviving, taking medicine on the prescription of same doctor of district Durg (Chhattisgarh) as described in case one.

The 3rd case study was carried out on a 9 year old boy, who is studying in class-3rd in Government School of the village Deogaon. In general, he doesn't give normal impressions. He looks like a diseased child from his facial gesture as well as from thin and lean body built. His parents are normal in first look except short statures of father. But the serological investigation carried out in the district hospital indicates that they are carrier or heterozygous for sickle cell gene. Their economic condition is not so good. The father of child is middle passed pity entrepreneur. His mother is primary educated house wife. The child was diagnosed as sickler at the age of 5years.

The 4th case study was carried out on an 11 year old boy. He was studying in class 5th. He was diagnosed at the age of 6 years. He has regularly required blood transfusion and till the date more than 4 blood transfusions was taken place. He was diagnosed at the district hospital Mandla. He often suffers from acute pain.

The 5th case study was carried out on an 11 year old girl. She is studying in class 5th. In this family there are two homozygous children. Her younger brother also diagnosed homozygous, who is described as third case study. This girl looks like a diseased child.

The 6th case study was carried on a girl student of age 11 years. She is studying in fifth standard. Alike other sicklers; she also give an impression of diseased child. She was diagnosed at age of 6 years. Her mother is school teacher. The father of girl had died. Since her first diagnosis at 7 year of age, she required blood transfusion and till the date more than 2 blood transfusions were taken place. She is on regular medicine. She often suffers from acute pain.

The 7th case study was carried on a 14 year old girl. She was studying in eighth standard. She was diagnosed at age of 2 years. Her Mother is middle passed and Father is science graduate. The father of girl was quite aware about the disease. Since her first diagnosis, she is regularly required blood transfusion and till the date more than 10 blood transfusions were taken place. She is on regular medication, both Allopathic and Homeopathic medicine is being given to her.

The 8th case study was carried out on a girl of 15 years of age. She is studying in class-9th. She was diagnosed at age of 4 years. Her parents are school teacher. Her parents are aware about the disease. Since her first diagnosis she required regular blood transfusion and till the date more than 20 blood transfusions was taken place. She is on regular medication, both Allopathic and Homeopathic medicine is given to her.

The 9th case study was carried out on an 18 years old male. He is a student of class 10th. He was diagnosed for the disease at age of 9 years, when he fell ill and admitted at the district hospital Mandla. His level of haemoglobin fell down and required blood transfusion. The doctor

at district hospital suspected sickle cell and referred to Regional Medical Research Centre (RMRC) of ICMR Jabalpur, where, it was confirmed that he is homozygous for the gene.

The 10th case study was taken on a 20 year old male. He was detected for the disease at the age of 5 years at district hospital Mandla, when he was suffering from pain, swelling and fever. At age of 5 he required blood transfusion, in districts Hospital. Right now he is struggling with the disease with many complications and regular medicine. He often suffers from acute pain. After class 8th he could not continue his education.

The 11th case studies were taken on a 22 year old male. He was detected for the disease at the age of 12 years at district hospital Mandla; when he was suffering from pain, swelling and fever. At age of 21 he got first blood transfusion in the district hospital. Till date, 2 blood transfusions were taken place. Right now he is struggling with the disease with many complications. He often suffers from acute pain. He always keeps pain killer tablets. He is doing graduation (B.Sc.). In his family, there are two homozygous boys. His younger brother is also homozygous, who is described as twelfth case study. This boy is also look like a diseased boy. After two blood transfusions, the boy is surviving, with frequent occurrence of infections and episodes of pain and fever.

The 12th case study was taken on a 24 year old male. He was detected for the disease at the age of 11 years at district hospital Mandla when he was suffering from pain, swelling and fever. Till date he has received 4 blood transfusions. Right now he is struggling with the disease with many complications. He often suffers from acute pain. He always keeps pain killer tablets. After middle school (8th standard) he could not continue his education.

The 13th case study was taken on a 30 year old male. He was detected for the disease at the age of 3 years in 1991-92 at district hospital Mandla, when he was suffering from pain, swelling and fever. At age of 4, he was donated blood, after that he was referred to medical college Jabalpur, where again blood transfusion was taken place repeatedly. Upto age of 20 he required more than 10 blood transfusions. Last blood transfusion was taken during February 2014 and second last was during October 2008 at age of 23 years on the condition of Priapism. After a suffering of more than six months he recovered from Priapism, after blood transfusion. Right now he is struggling with the disease with many complications and regular medication. He often suffers from acute pain. He always keeps pain killer tablets and injections in his pocket and sometime he himself prick injections in the condition of crisis. Sometime he also takes tablet and capsules of hydroxyl urea.

Three case studied were recorded of died homozygous children. One was died at the age of 9 years and the second was died at the age of 14 years and third was died age of 22 year of age. They were diagnosed around 4 years of age. They were frequently suffered from fever and acute pain. Younger one was got two blood transfusions where as the second was got 10 blood transfusions, third also got 7-8 blood transfusion and suffering from leg ulcer.

The clinical problems reported by homozygous sicklers are presented in Table 1. It is apparent Joint pains, fever, abdominal pain, joint swelling, chest pain, body pain, bony pain, pallor, Icterus, blood transfusion, general weakness, fatigue and giddiness were reported by cent percent cases; whereas priapism is reported by 7.7 per cent cases.

Table 1: Clinical problems reported among sickle cell patients.

S.No.	Clinical Problems	Present study (HbSS) %
1.	Joint pain	100
2.	Fever	100
3.	Abdominal pain	100
4.	General weakness, fatigue & giddiness	100
5.	Joint swelling	100
6.	Chest pain	100
7.	Body ache	100
8.	Bony pain	100
9.	Pallor	100
10.	Icterus	100
11.	Blood Transfusion	100
12.	Priapism	7.7

DISCUSSION

For further understanding the clinical problems faced by homozygous sicklers, the present finding are compared with Yadav et al. (2006), they studied 310 SCD patients attending sickle cell clinic at Medical college Jabalpur, they reported similar problems in different frequency Icterus (69.0%), Joint pains (59.7%), bony pains (51.6%), fever (51.3%) and abdominal pain (30.3%). About 16% of patients had joint swelling, 10.6% of patients had the complaint of chest pain and 13% reported priapism. For comparative understanding these finding are presented in Table 2.

Further to understand the role of the sickle cell gene in human development. The district wise prevalence of gene was computed as displayed in the Table 3. The highest mean prevalence (43%) was reported for the District Mandla whereas lowest prevalence (1.4%) was reported for District Ujjan. The bivariate correlation analysis between the district wise prevalence of gene and human development index was found positive but insignificant (r^2=0.065, p>0.8).

Table 2: Clinical problems reported among sickle cell patients.

Clinical Problems	**Present study (HbSS) %**	**Patient (%) (after Yadav et al. 2006)**
Joint pain	100	59.7
Fever	100	51.3
Abdominal pain	100	30.3
General weakness, fatigue & giddiness	100	27.4
Joint swelling	100	16.4
Chest pain	100	10.6
Body pain	100	11.0
Bony pain	100	51.6
Pallor	100	91.0
Icterus	100	69.0
Hospitalization	100	38.1
Blood Transfusion	100	-
Priapism	7.7	-

Table 3: District wise Mean and SD of prevalence of sickle cell gene.

S.No.	District	No. of Studies	HbAS% Mean	SD	HDI
1	Balaghat	2	16.1	1.8	0.544
2	Betul	4	19.3	9.4	0.537
3	Chhindwara	7	16.6	6.8	0.578
4	Damoh	2	25.5	10.6	0.571
5	Dhar	1	5.7	-	0.596
6	Dindori	3	17.1	12.0	0.565
7	Indore	3	8.9	3.3	0.710
8	Jabalpur	4	13.9	9.4	0.589
9	Jhabua	6	11.3	4.7	0.396
10	Khandwa	3	14.1	2.8	0.519
11	Khargone	1	12.8		0.525
12	Mandla	1	43.0		0.587
13	Panna	1	6.7		0.479
14	Satna	1	4.1		0.516
15	Seoni	2	19.9	2.0	0.596
16	Shahdol	4	14.3	10.1	0.564
17	Ujjan	1	1.4		0.626

Similarly, State wise prevalence of gene was obtained for 11 states (Table 4). The highest mean prevalence of gene (22±9.9%) was reported for the State of Assam, whereas lowest prevalence (0.6%) was reported for State of Goa. The correlation of prevalence of the HbS gene and human development index for these states was found negative and insignificant (r^2=-0.237, p>0.5). For further elaboration scattered plot diagramme is constructed (Figure 1).

Table 4: State wise Mean and SD of prevalence of sickle cell gene

S. No.	State	No. of study	Mean	SD	HDI
1	Andhra Pradesh	26	11.3	9.0	0.473
2	Assam	2	22.0	9.9	0.444
3	Chhattisgarh	54	13.4	9.8	0.358
4	Goa	1	0.3		0.617
5	Gujarat	12	16.7	7.0	0.527
6	Madhya Pradesh	57	14.2	8.8	0.375
7	Maharashtra	115	11.1	9.2	0.572
8	Manipur	1	9.6		
9	Orissa	16	8.3	4.8	0.367
10	Tamilnadu	18	18.1	13.0	0.570
11	West Bengal	1	0.6		0.492

Although the correlation between human development index (HDI) and prevalence of gene (HbS) is contradictory, still it cannot be ignored that the morbidity have negative impact on economics status education and income of the nation as whole. One reason behind this contradiction is insufficient data. The second is the fact that the HbS gene is largely limited to scheduled caste and tribe (SC/ST) population of the districts. Third reason is limited studies of the problem. In some of the districts, population of SC/ST is insignificant as compared to the total population of that district. Hence, large scale screening of gene is needed, which is missing, as this is the problem of poor who can't raise their voice, whereas a similar problem known as thalassemia had got wide attention at every level as the gene is prevalent among dominant group of peoples.

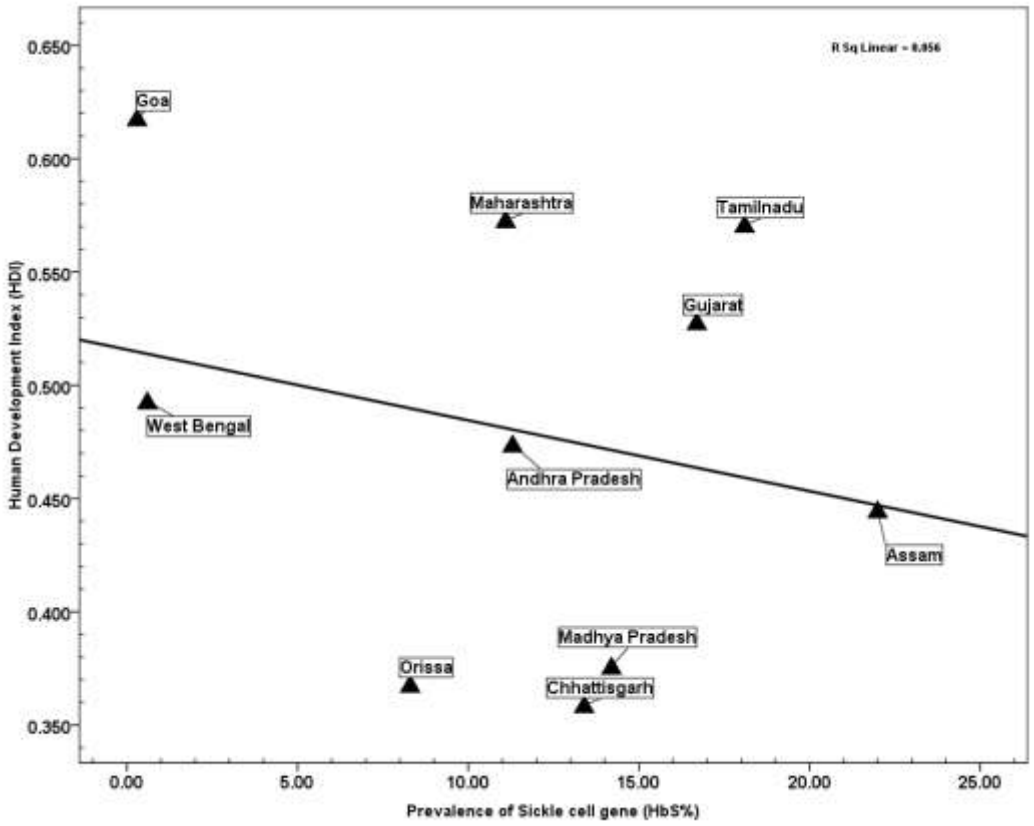

Figure 1. Scattered plot diagramme showing distribution of states as per prevalence of sickle gene and value of human development index

Conclusion

Homozygous sicklers have many clinical problems; still they survive with the help of frequent hospitalization and blood transfusion. They experience unbearable acute and chronic pain. They are always anaemic and susceptible to different infections. Their parents and family are always in trouble, they have emotional shock, economic burden of treatment and frequent hospitalization. In case of hospitalization, they lost wages and cream season of agriculture viz. sowing, harvesting etc. which again cause economic loss to family. These losses further become cause of their sufferings which affect their accessibility to good health. The sufferings are not

limited to the only family of homozygous children, but it also affects the neighborhood, horizontal and vertical relatives and society as a whole. The frequent hospitalizations of these children also affect the school of their own as well as their affinal brothers and sisters and a cause of dropouts. In this way, the sickle cell is posing a challenge for the humanity. Although the correlation of prevalence of sickle cell gene do not have significant correlation with human development index; but it can't be ignored. It should be given place in the National Health Policy. Nationwide survey of the problem would give more appropriate understanding of the problem which is still missing even after Human Genome Project.

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