ORIGINAL ARTICLE CLINICAL HAEMATOLOGY

Journal of Contemporary Medicine and Dentistry
www.jcmad.com

ISSN [P-2347-4513]
ISSN [O-2349-0799]
Year: 2022, Volume: 10
Issue: 2, p:20 - 24

Epidemiology of Sickle Cell Disorder in Western Maharashtra

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Abstract

Background: *Sickle cell disease is a major genetic disorder amongst Scheduled Caste (SC), Scheduled Tribe (ST), and Other Backward Communities (OBC) population groups of Maharashtra. We modified diagnosis technique and developed simple laboratory technology to identify carrier (Hb SS) and sufferer (Hb AS) suitable for field work.* ***Methods****: This cross-sectional study was done in hematology clinical laboratory of T.N Medical college and B.Y.L Ch Nair Hospital Mumbai from August 2021 to February 2022. All 287 patients were informed about the work and written informed consent was taken from each patient and following test were done. Solubility Test and Electrophoresis of Hemoglobin.* ***Results:*** *In order to find out prevalence for sickle cell disorder we screened major communities from the state and found high prevalence amongst SC, ST and OBC. The overall prevalence amongst SC, ST and OBC is 3.48 %. Severe joint pains and milder type of jaundice are peculiar symptoms amongst sicklers from the state of Maharashtra.* ***Conclusion:*** *High prevalence is observed in the rural area from Eastern part of Maharashtra and hence population is at high risk in this area. It is necessary to establish community control program involving people, doctors, social workers, and sympathizers. This program will undertake diagnosis, treatment, management and counselling. Government of Maharashtra is aware of these facts but unable to undertake major projects because of financial constraint and needs support from Central agencies.*

Keywords*: Sickle Cell, Electrophoresis, Anemia, Jaundice*

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Date of Acceptance: 17/10/2022

Introduction

Red blood cells of adult healthy human individual consist of mixture of three unique respiratory proteins known as hemoglobins. One major, with 96% concentration of the total, known as adult hemoglobin (HbA) and other two minor with less than 2% or traces are Fetal hemoglobin (HbF) and Hemoglobin A2 (HbA2). The major function of hemoglobin is to transport oxygen from atmosphere to lungs and finally pass on to all vital organs. The property of combining reversibly with oxygen is unique wonder and interesting. Hemoglobin molecule is conjugated protein and is combination of four hemes and four polypeptide globin chains. Each globin chain is attached to one heme group. There are four different types of globin chains, which are Alpha (α), Beta (β), Gamma (γ) and Delta (δ). Each globin polypeptide chain is a polymer of different amino acids. α globin chain is a polymer of 141 amino acids while β, γ and δ chains each consists of 146 different amino acids. The sequence of amino acids in each globin chain is different and is very specific for that particular globin chain. The pair of α chain is common to all hemoglobins. However, in adult hemoglobin (Hb A), the non α chain pair are β globin chains, in fetal hemoglobin (Hb F)

pair of γ globin chains and in hemoglobin A2 (Hb A2) pair of δ chains. It can be described as follows: Hb A = α2β2 Hb F = α2γ2 Hb A2 = α2δ2. The genes for α chains are located on short arm of chromosome number 16 and for β, γ and δ chains genes are located on chromosome number 11. The mode of inheritance is autosomal recessive type.

Abnormal Hemoglobins

The alteration of sequence of amino acids in either of the four globin chains is termed as abnormal hemoglobin. Abnormal hemoglobins have similar structure of that of normal hemoglobin except slight alteration in the sequence of amino acids and hence may be designated as mutant or variant hemoglobin. A well-known example of abnormal hemoglobin is

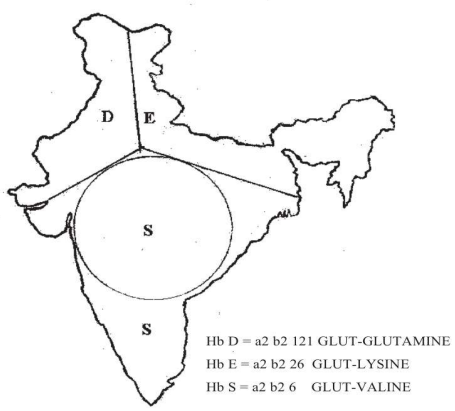

Fig. 1. Distribution of abnormal haemoglobin in India–DESH (D, E and S Haemoglobins)

sickle cell hemoglobin (Hb S) in which 6th amino acid (i.e. glutamic acid) is replaced bby valine. (Hb S = α2 β2 6-Glut-Val). During last fifty years, more than 800 abnormal hemoglobins are reported in the literature. In 90 % of these there is altered sequence of single amino acid in any of the globin chains. Of these, single base mutation reported, 55 % result in β globin chain, 35 % in α globin chain and remaining γ and δ globin chain. In rest of 10 % there may be alteration of two or multiple amino acids or sometimes addition or deletion of amino acids in either of the globin chains. It is observed that β globin gene is most sensitive to single nucleotide base changes. Abnormal hemoglobins with very high prevalence in world population are Hb C (West Africa); Hb D (North Western India); Hb E (West Bengal and North Eastern India) and Hb S (India, South Africa and Saudi Arabia). [1] Most of the abnormal hemoglobins reported today are not associated with detectable clinical manifestation. Most common clinically relevant variants are Hb C, Hb D, Hb E, Hb O (Arab) and Hb S (all β chain variants) and occur in polymorphic frequencies in different geographical areas. Amongst all abnormal hemoglobins, Sickle Cell Hemoglobin (Hb S) is more deleterious, since in hypoxic condition it alter the shape of red cells leading to early destruction of the cells and sometime clogging the sickled red cell in microcapillaries producing tremendous, unbearable pain which does not respond to any pain killer. No other abnormal hemoglobin has such ability which ultimately leads to miserable life to patients suffering from sickle cell disease.

Abnormal Hemoglobins Amongst Indian Population Of the genetic disorders prevalent in this country hemoglobinopathies have been most intensively studied both from case reports and population survey. There is more than dozen abnormal hemoglobins reported amongst different population groups from India. Some are sporadic confined to small community or family. Hb D, Hb E and Hb S are widely spread. [2] Hb D is found amongst Sindhi, Punjabi and Gujrathi population groups with origin in North West India. Hb E amongst Bengali and Assami population groups while Hb S found amongst different population groups from south and central parts of India. Distribution represented in figure 1 (DESH).

Sickle Cell Hemoglobin (Hb S)

In 1904 Prof. Herrick observed that red cells of an African origin anaemic patient acquired sickle like shape instead of normal round shape. After 40 years of research it was found that hemoglobin inside the sickle red cell is mutant variant of normal hemoglobin in which 6th amino acid in β chain is replaced by valine. This was first abnormal hemoglobin reported in literature and labeled as hemoglobin B (Hb B), but because of its sickling property it is relabeled as Sickle Cell Hemoglobin (Hb S). The population survey conducted thereafter found high prevalence of sickle cell hemoglobin in different African tribal groups. [3-15] Prior to 1952, no information was available about existence of Sickle Cell Hemoglobin in India. In 1952 it was recorded for the first time

simultaneously amongst tribal population groups of Nilgiri Hills and laborers in the tea gardens of Assam1,2. Now it is firmly established that this gene harbor amongst different caste groups but very high prevalence amongst Scheduled Caste (SC), Scheduled Tribe (ST) and Other Backward Communities (OBC). [3-15]

Sickle Cell Disorder Scenario in the State of Maharashtra

Taking into our huge population size, more than 50 % of the world's sickle cell anemia cases are in India. [3-15] It is estimated that most of the cases are in the Central and South India. During last 50 years, because of simple, reliable and inexpensive laboratory methods are available18, the large number of population genetic surveys conducted by different scientific groups and data on geographical distribution, clinical manifestation along with its variations, available from the state of Maharashtra. [3-15]

Materials and Methods

This cross-sectional study was done in hematology clinical laboratory of T.N Medical college and B.Y.L Ch Nair Hospital Mumbai from August 2021 to February 2022. All 287 patients were informed about the work and written informed consent was taken from each patient and following test were done.

Solubility Test

Deoxygenated Sickle cell hemoglobin has an abnormally low solubility. A fibrous precipitate is formed when a concentrated solution of sickle cell hemoglobin is deoxygenated (This precipitate deforms red cells and gives them their sickle shape. The rate of fiber formation is proportional to about the tenth power of the effective concentration of deoxyhemoglobin S. Thus, fiber formation is a highly concerted reaction). HbS is deoxygenated form and is insoluble in phosphate buffer (giving turbidity to the solution) while other hemoglobins are completely soluble (giving clear solution).

Electrophoresis of Hemoglobin

Each of the major hemoglobin types has an electrical charge of a different degree, so the most useful method for separating and measuring normal and abnormal hemoglobins is electrophoresis. This process involves subjecting hemoglobin components from dissolved red blood cells to an electrical field. The components then move away from each other at different rates, and when separated, form a series of distinctly pigmented bands. The bands are then compared with the other samples on the same membrane strip called as control. Quantitation of different hemoglobins can also be made to indicate severity of any abnormality. Electrophoresis of Hemoglobin at Alkaline pH (pH 8.6) Using Cellulose Acetate Membrane as Supporting Medium: Hb A has faster mobility than Hb Awhich is slower. Hb D and Hb S have similar mobility in between Hb A and Hb A2 . In case of Hb S solubility test is positive. Criteria used is as follows: Combination of electrophoretic technique with solubility test is a golden standard for detecting sickle cell hemoglobin in carrier and sufferer state. It is very cost effective (about Rs.10/- per hemoglobin blood samples) hence screening on large scale can be undertaken by different institutions. From the available data [5-10, 14]. it is found that Sickle cell gene is widely spread in all districts of Eastern Maharashtra (known as Vidarbha region), North Maharashtra (Satpuda ranges) and some parts of Marathwada region. [15-17]

Results

Age-wise prevalence of sickle cell disorders is shown in table I.

SL. No	Age	Number	Prevalence
1	11-15	58	20.2%
2	16-20	162	56.4%
3	21-25	35	12.19%
4	26-30	20	6.96%
5	31-35	1	0.34%

Sexwise prevalence was 2.8% in males and 3.0% in females. The overall prevalence of SCD was 2.9%. The prevalence was maximum in Nandurbar (7.0%) followed by 4.6% in the Pune region and 3.4% in Mumbai and Konkan regions. In all 31 castes were encountered. No case of SCD was found in Bari, Bhoi, Chambhar, Dhangar, Halba, Jain, Kalar, Khati, Komti, Koshti, Maheshwari, Mana, Muslim, Navi, Oza, Powar, Shimpi, Sonar, Sutar, and Thakur. The prevalence was maximum in Bheel (50%) followed by Macchi (20 %) and Vanjari (10 %). The prevalence in Bouddha was found

to be 10%. The electrophoresis pattern revealed that 94.4% were Sickle Cell Traits and 5.6% were Sickle Cell Anemia.

Discussion

The prevalence of the disorder was found to be 3.48 %. Deshmukh et al., [18] reported prevalence to be 5.6% from a few villages. Kamble et al., [19] reported prevalence to be 5.7% in a clinic-based study. The differences may be attributed to the differences in study designs. In the present study, the prevalence of sickle cell disorders was maximum in the age group 11-20 yrs. and it increased with increasing age. Leikin et al., [20] in their cooperative study also had patients with sickle cell disorders which were distributed more in higher age groups. Kamble et al., [19] also noted similar findings. The prevalence of the disorder was 2.8% in males and 3.0% in females. As regards to sex distribution of the disorder, Wintrobe stated that the sickle cell trait is more common in females. [21] In the present study also such a correlation could not be found. The reason for the higher prevalence in a few blocks may be attributed to a greater number of Matang, Pradhan, and Bouddha populations in the blocks. The prevalence of Sickle Cell Disorders in tribals was highest in Bheel at 50% followed by mavchi at 20% and 10% by vanjari. In scheduled castes, the prevalence in Bouddha was 10%. These observations support the hypothesis that Sickle Cell Disorders are present in scheduled castes, tribals, and a few communities of OBCs and not found in so-called higher castes; though the review of literature says it is present invariably in all castes [20]. In the present study, the prevalence of Bheel was found to be 50%. Negi reported a prevalence of 19.38%, Sathe reported 15.92%, and Bankar 6.6%. [2] Deshmukh reported a prevalence of 5.3% in Gond and Gowari together. [18] In Mavchi, the prevalence was 10.6% and Ahmed reported 9.0%, Rao reported 30.5%. [23] In Banjara, the prevalence in this study was found to be 10 % while Bankar has reported a 5.6% prevalence. [2] In Bouddha, the prevalence was 10 % in the present study. But Shukla and Solanki reported prevalence in Bouddha to be 22.22% and Deshmukh reported prevalence to be 12.4% in the same caste. [18]

Conclusion

High prevalence is observed in the rural area in the Eastern part of Maharashtra and hence population is at high risk in this area. In this rural area, general practitioners have very little knowledge about this disease. Moreover, diagnostic and treatment facilities are not available. Modern interventions like Bone Marrow Transplantation (BMT), Gene Therapy (GT), Preimplantation Genetic Diagnosis (PGD), and Prenatal diagnosis is beyond their capacity (the population with sickle cell anemia inheritance). Lack of knowledge and awareness enhances superstitions about the disease. It is necessary to establish a community control program involving people, doctors, social workers, and sympathizers. This program will undertake diagnosis, treatment, management, and counseling. The government of Maharashtra is aware of these facts but unable to undertake major projects because of financial constraints. Similarly, there is a need to have Central Institute to study epidemiology and clinical course aspects in detail. It needs support from Central agencies.

***Conflict of Interest*: None**
***Source of support*: Nil**
***Ethical Permission*: Obtained**

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