A STUDY ON PREMARITAL SCREENING FOR SICKLE CELL TRAIT IN HILLY AREAS AROUND SALEM

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Background: Sickle cell disease is a genetic disease which is more prevalent in many developing countries. A genetic blood disease due to the presence of an abnormal form of hemoglobin, namely hemoglobin S. In southern India sickle cell anemia varies around 1 to 40% among tribal population. Early detection and genetic counselling to the high risk group is the need of the hour to control this disease burden. Aims and Objectives: To evaluate the prevalence of sickle cell trait in premarital population in hilly areas around Salem and to estimate the sensitivity and specificity of the screening test. Methods: A cross-sectional study was carried out and the study is based on the evaluation of data available from the screening programme for prevention of hemoglobinopathies. All the 10th and 12th std students in hilly areas (yercaud, kolli hills, kalrayan hills) were included and known case of thalassemia and other hemoglobinopathies were excluded. Data was analyzed by using SPSS software. Result: This study shows that the prevalence of sickle cell trait in hilly areas around salem was 4.4%. Among the three hilly areas around salem, Kolli hills shows the highest prevalence of about 2.2%. Second highest prevalence of about 1.9% was found in Yercaud hills and Kalvarayan hills showed a prevalence of 0.3%. Sickling test shows 100% sensitivity and 100% negative predictive value. Specificity was only 25%. Conclusion: This study emphasizes the importance of premarital genetic counseling and effective screening for sickle cell anemia in hilly areas. However, more number of screening need to be done to increase public awareness. The present study shows the need for formal pre-marital counseling and screening for sickle hemoglobin among the youth to help them take informed decision about their marriage to prevent procreation of children affected by sickle cell disease.

Article Info

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urinary tract infection in women, complications of hyphema, splenic infarction with altitude hypoxia or exercise, and life-threatening complications of exercise. Hematuria is the most common manifestation of sickle cell trait. People with sickle cell trait are more susceptible to complications following treatment of hyphema. The slow flow of relatively hypoxic fluid in the chamber of the eye out of the filtration apparatus is a location in which both polymerization of hemoglobin S and obstruction of flow by rigid erythrocytes is likely. All this can result in glaucoma and secondary hemorrhage.

If both the partners are having sickle cell trait, their child will have 25% chance of being born with sickle cell anemia. If only one of the partner is having sickle cell trait, their child would not be born with sickle cell anemia, but there is a 50% chance the child will be born with sickle cell trait.

If one parent has sickle cell disease and one parent has sickle cell trait, there is a 50% chance their children will be born with sickle cell disease.

As a part of the ongoing school screening programme for haemoglobinopathies, blood samples were collected from 10th and 12th school children in 30 selected tribal blocks in Tamil Nadu. Our Medical College Hospital receives samples from three tribal blocks around Salem namely Yercaud hills, Kolli hills and Kalayan hills. This study aims at estimating the prevalence of sickle cell trait in these three hilly areas around Salem and to validate the screening test for sickle cell trait.

MATERIALS AND METHODS

Study design: It is a cross sectional study. Ethical clearance was obtained from the institutional ethical committee. After getting assent from the parents, blood sample of 2ml each in two vacutainers (EDTA tube) are collected by the tribal mobile medical unit on every Monday. Complete Blood Count, screening tests and solubility tests are carried out by Tribal Mobile Medical Unit. Second sample of screening positive cases are transported using ice carrier to Government Medical College Hospital. HPLC is performed in the Biochemistry Department of Govt. Mohan Kumaramangalam Medical College, Salem to confirm screened positive cases. HPLC is performed with Bio Rad D10 Analyser available in our department. HPLC reports in excel format are sent to Tribal Medical Medical Unit, Block Medical officer, District Early Intervention Centre Medical officer and State nodal officer every week and a register is maintained in our Department. The HPLC results of samples collected from the three hilly areas around Salem for period of one academic year (2018-2019) were analyzed. Sensitivity and specificity of solubility test was also calculated. Known cases of thalassemia's and other hemoglobinopathies were excluded in this study.

RESULTS AND DISCUSSION

Data of samples collected during the academic year 2018-19 was analyzed. Total number of samples collected from 10th and 12th school children were 1,984. Total number of children, males and females screened block wise is shown in Table-1. Block wise number of beta thalassemia carriers identified is shown in Table-2. Block wise prevalence of sickle cell trait is shown in Table-3 and a bar diagram, Figure-1. The overall prevalence in three hilly areas around Salem is shown in a pie chart Figure-2.

Solubility test was used as a screening test for identifying sickle cell trait. Of the 1,984 samples collected, only 551 samples which were SICKLING positive were subjected to HPLC for confirming the sickle cell trait status. Hb S elutes in the S window. For a S trait, A2 will be normal F will be normal Hb S will be between 30-40% was considered as sickle cell trait. It was further confirmed by parental screening and DNA analysis. 80 random samples which were SICKLING (solubility) negative was also subjected to HPLC to find out the sensitivity of the screening test. Screening test result by diagnosis is shown in Table-4. The sensitivity of SICKLING test was found 100% and specificity was found to be only 25%. It has 100% negative predictive value and 37% positive predictive value.
Method:

Mix 1 drop of blood with 1 drop of 2% sodium metabisulphite solution on a microscope slide. Cover with a cover slip and seal the edge with wax/Vaseline mixture or with nail varnish. Allow to stand at room temperature for 1 to 4 hours. Examine under a microscope with the dry objective.

Interpretation: In positive samples the typical sickle-shaped red blood cells will appear. Occasionally the preparation may need to stand for up to 24 hours. In this case put the slides in a moist Petri dish. False negative results may be obtained if the metabisulphite has deteriorated or if the cover slip is not sealed properly. Sickling test achieves the criteria of a good screening test. A good screening test must have high sensitivity, repeatability and high negative predictive value. NESTROFT test shows 100% sensitivity and 100% negative predictive value. Specificity is only 25%.

Hb S elutes in the S window For a S trait A2 will be normal(<4.0%) F will be normal (<1%), Hb S will be between 30-40%

Haemoglobin will be normal, MCV 80-90fl

The first description of sickle haemoglobin in India was by Lehman and Cutbush in 1952 in the tribal populations in the Nilgiri hills in south India. Sickle cell disease (SCD) is a life-threatening genetic blood disorder that affects over 6 million newborns annually \[7,8\]. It is an autosomal recessive disorder most commonly caused by homozygosity for the A to T mutation in the sixth codon of the hemoglobin β-subunit (i.e. homozygosity for the S variant of hemoglobin β-subunit; SS). It can also be caused by compound heterozygosity for the S and C variants (SC) 9. Individuals with sickle cell trait (SCT) are heterozygous for the S variant (AS) and hence are unaffected carriers. SCT is a heterozygous carrier state, not a disease. In SCT, sickle hemoglobin S accounts for only 35% to 45% of total hemoglobin10. The presence of normal hemoglobin A dilutes mutated hemoglobin S and greatly reduces the probability of sickling and hemolysis 10. However, erythrocytes stiffness, increased blood viscosity, and in extravascular thrombosis have been reported in individuals with SCT in situations of severe volume depletion, hyperthermia, and reduced oxygen tension12. In extreme circumstances of high-intensity sports and military training, SCT has been shown to increase the risk of rhabdomyolysis and exercise-related sudden death13. Structural changes of red blood cells and impaired endothelial function account for other rare SCT complications such as venous thromboembolism and kidney damage. However, the magnitude of the clinically relevant red blood cell sickling and intravascular thrombosis is much less in SCT persons than in SCD patients11. For these reasons, SCT individuals do not display chronic vaso-occlusive complications and have a life expectancy similar to that in general population. Hemoglobin S is a predominant type in SCD, and normal hemoglobin A is absent. When exposed to conditions of low oxygen, red blood cells, containing hemoglobin S, become inflexible and assume a sickle shape10. Chronic sickling, vaso-occlusion, and hemolysis are hallmarks of SCD10. SCD affects every major organ system, causes significant morbidity, and reduces the life span of the affected individuals by almost 30 years13. If results indicating the presence of SCT are not directly
reported, the opportunities to counsel families on potential SCT—related complications and future family planning might be overlooked. Knowledge of their SCT status may affect lifestyle and reproductive choices not only of the newborn at puberty and beyond but also of the parents, other children of the parents—full and half-siblings, and extended family members.

Conclusion:

Our study shows the prevalence of sickle cell trait in the hilly areas and sensitivity of sickling test to be 100% in detecting sickle cell disease and it can be very well used as a simple tool of screening for Sickle cell disease screening. Carrier status increases the risk of having an offspring with SCT, and if the partner also has SCT, SCD. Although SCT was long considered as benign, knowledge is accruing of uncommon but potentially severe complications associated with the SCT carrier status. However, with the high prevalence of SCT, it is important that NPs be aware of these comorbidities. The present study emphasizes the need for establishment of centres for formal pre-marital counselling and screening for sickle hemoglobin among the high risk groups to help them take informed decision about their marriage to prevent procreation of children affected by sickle cell disease.

REFERENCES


