International Journal of Healthcare Sciences ISSN 2348-5728 (Online)
Vol. 2, Issue 2, pp: (385-388), Month: October 2014 - March 2015, Available at: www.researchpublish.com

Biochemical Patterns of Hemoglobinopathies and Thalassemia Syndrome in a Tertiary Care Hospital of Telangana

[1]Archana.A.Dharwadkar, [2]Kavita.Dharwadkar, [3]Pragna.Rao

1 Associate Professor, Department of Biochemistry, Kamineni Institute of Medical Sciences, Narketpally,Telangana
2 Assistant Professor,Department of Biochemistry, Amala Institute of Medical Sciences,Thrissur,Kerala
3 Professor, Department of Biochemistry, Kasturba Medical College,Manipal,Manipal University,Karnataka

Abstract: **In India, hemoglobinopathies are responsible for the largest number of genetic disorders and hence are of great public health hazard. Major concerned hemoglobinopathic disorders are sickle cell anemia and beta-thalassemia which are the cause of chronic ill health and financial burden to the patient. This was a hospital based study carried out at Hyderabad of Telangana state. The cases of hemoglobinopathies were identified based on clinical data, family history and red blood cell indices then hemoglobin electrophoresis was done. These disorders with genetic and biochemical components showed remarkable clinical variability ranging from mild condition to severe life threatening condition. Out of twenty eight cases, nine cases were identified as sickle cell trait, seven as sickle beta thalassemia, seven cases were suffering from beta thalassemia and three of them from sickle cell disease and two of them were identified as having hereditary persistence of fetal hemoglobin. Screening and counseling of the target population can lead to a significant reduction in affected births.**

Keywords: **Anaemia, Electrophoresis, Erythrocytes, Hemoglobinopathies, Sickle cell trait, beta-Thalassemia**

I. INTRODUCTION

Hemoglobinopathies are the cause of major morbidity and mortality in India[1] and abroad[2].The frequency of total hemoglobinopathies in India was reported to be 4.2% with 30 million carriers and 15,000 infants with hemoglobinopathies[3] commonly being sickle cell anemia and *β*-thalassemia. The inherited disorders of hemoglobin are largely prevalent in tropical countries including India. The carrier rate for beta-thalassemia gene varies from 1 to 3% in Southern India to 3 to 15% in Northern India [4],[5].Thalassemia result from a quantitative defect in the globin chain production. When no globin chain is synthesized at all they are called α0 or β0 thalassemia, when it is produced at a reduced rate, designated as α+ or β+ .Sickle cell disease (SCD) is an inherited chronic hemolytic anemia. Sickle cell anemia and thalassemia poses psychological and economical burden to the affected individual, his family and the society as a whole. These disorders comprise of genetic and biochemical entities which showed remarkable clinical variability ranging from mild condition to severe life threatening condition. Apart from genetic factors, environmental factors may also play an important role in modifying the disease expression. Hence, biochemical explication of the abnormal hemoglobin during medical help in tertiary care hospital is important in understanding the pathophysiologic basis of the disease which facilitates appropriate treatment.

The present study was carried out in a tertiary care hospital, Hyderabad situated in Telangana state. This region has unique socio-cultural practice of consanguinous marriages added with ignorance about the disease and the family influence which appears to increase genetic stability of the disease to persist in this community. The study aimed to identify the individuals with hemoglobin disorders, using the available hematological and biochemical tests.

II. MATERIALS AND METHODS

Our study included 115 cases with clinical suspicion of hemoglobinopathy, referred to the department of Biochemistry and Pathology for laboratory investigations of hemoglobinopathies. Family history was taken from the patient/relatives.

Information about previous history of hemolytic anemia and blood transfusions, any history of medications was taken, consanguinity in marriages,clinical signs and symptoms were noted . Hematologic values were determined by TC101 automated cell counter. Naked Eye single tube red cell osmotic fragility test (NESTROFT) was performed to screen the cases of beta-thalassemia trait [6, 7] .Separation of normal hemoglobins (A&A2) and detection of hemoglobin variants was done by electrophoresis on alkaline gels using sebia hydragel hemoglobin (e) k20 kit and percentages of Hb A, HbA2, HbF and HbS were assessed. The resulting electrophoretograms were evaluated visually for pattern abnormalities.Densitometry was used as an aid in the interpretation which provided relative concentrations of individual fractions. Electrophoresis on acidic gel by sebia hydragel acid(e) hemoglobin(e) k20 kit was followed to confirm the identification of hemoglobin variants. The normal range for HbA2 by this method in our laboratory is 2.78+_0.65(mean+_SD).

III. RESULT AND DISCUSSION

Out of 115 cases that were suspected of hemoglobinopathies, referred to laboratory for further confirmation,28 cases were identified as cases of hemoglobinopathies which included 19 males & 9 females in the age group of 2-46 yrs. Out of twenty eight cases, nine cases(32.14%) were identified as sickle cell trait, seven cases (25%)as sickle beta thalassemia. Seven cases(25%) were suffering from beta thalassemia and three(10.71%) of them from sickle cell disease and two (7.14%)of them were identified as having hereditary persistence of fetal hemoglobin. Hematological parameters and electrophoretic findings in the cases are given in the Table-1 and Figure -1 shows mean age and gender distribution in sickle cell disease and thalassemia syndrome.

Table-1: Characteristic electrophoretic patterns and hematological parameters in the cases

GROUPS	Hb(gm%)	MCV(fl) 80-96	MCH(pg) 27-36	HbA(%) >96%	HbA2(%) <3.5%	HbF(%) <2%	HbS(%)
Sickle cell disease N=3	8.5* (8-9)#	85.5* (80-89)#	25.3* (24-26)#	0	3.1* (2.2-4.3)#	22.5* (19.1-25.7)#	73.9* (72.1-76.6)#
Sickle cell trait N=9	9.2* (7.7-11.2)#	74.2* (70.1-78.4)#	24.7* (22.3-26.8)#	59.9* (43.6-69.7)#	1.6* (0.5-3.7)#	0	36.8* (29.5-54.4)#
Sickle beta thalassemia N=7	7.8* (6.8-9)#	71.5* (68.1-75.6)#	23.6* (22.6-25.2)#	40.2* (0-76)#	4.2* (3.6-4.9)#	7.9* (0-30)#	43.4* (19.1-65.9)#
Beta thalassemia N=7	8.7* (8.4-9.7)#	71.4* (65.2-87.6)#	26.1* (22.6-31.9)#	74.2* (0-94.9)#	4.1* (3.5-5.1)#	33.1* (0-96.8)#	0
Hereditary Persistence of Fetal Hemoglobin N=2	8.3* (7-10)#	70.6* (66.2-75.5)#	21.7* (20.1-23.5)#	0	1.5 (1-2.4)#	98.2* (97.6-99)#	0

*Values presented as mean # Range of values given

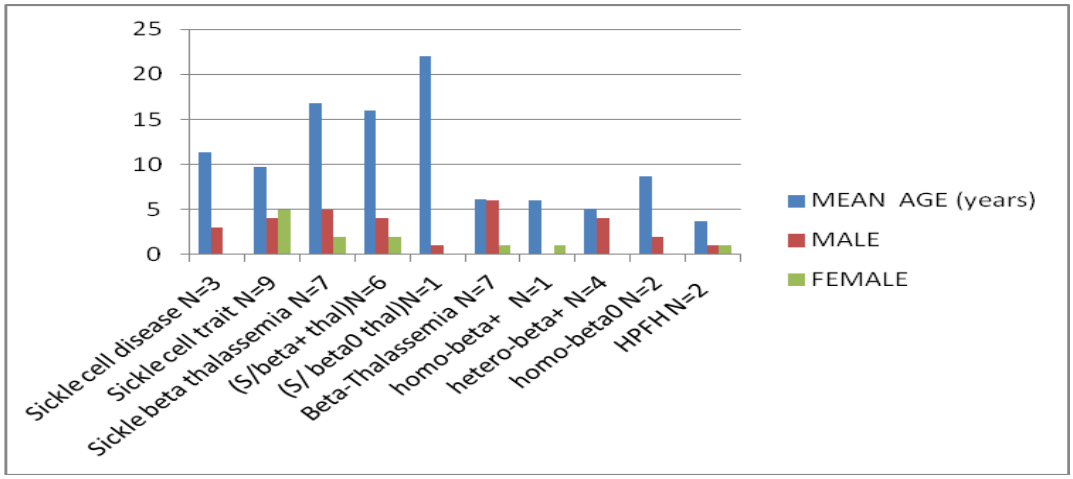

Figure-1: Mean age and gender distribution in sickle cell disease and thalassemia syndrome

Hemoglobinopathies are the most common genetic disorders affecting the millions of population worldwide. In India, due to genetic heterogeneous nature of the population, the sickle cell anemia and thalassemia gain great importance from public health point of view. There are several reports on the spectrum of mutations resulting in hemoglobin variants in different states of India [8-9] like Orissa, Gujarat, West Bengal, AndraPradesh and other states of northern and eastern parts of India. [10-15] Consanguinous marriage is the most prevalent social practice irrespective of caste, religion educational status and economical background. In our study out of 28 confirmed hemoglobinopathy cases 21(75%) of them gave the history of consanguinous marriage. Traditionally, electrophoresis has been the method of choice for identification and quantification of hemoglobin variants. Commercial, rapid electrophoretic methods have been developed that allow for separation at pH 8.4 (alkaline) and pH 6.2 (acid) on agarose gels. These provide a clear background, allowing for quantification of the hemoglobin present by densitometric scanning.

In our study mean age was high in sickle beta thalassemia group (16.7 years) as compared to other groups. Males (67.8%) were affected more than females (32.1%) in almost all the types of disorders in accordance to other studies [16] except in sickle cell trait where females(66.6%) are affected more than males(44.4%). We report high prevalence of sickle cell trait, followed by sickle beta thalassemia, beta thalassemia(minor followed by major) and lastly sickle cell disease. Some of the sickle cell disease, sickle beta thalassemia and β-thalassemia patients in our study presented with anemia, vasoocclusive crisis and splenomegaly. A considerable high level of HbF in some of our cases of sickle cell disease and β-thalassemia provides a protective mechanism in improving the quality of life. Homozygous expression of the affected gene produces sickle cell disease**,** presenting as chronic hemolytic anemia and vasoocclusive condition that is usually life threating. In beta thalassemia there is decrease in the synthesis of beta chains of globin, and net decreased synthesis of Hb A. With less Hb A, the patient suffers from microcytic anemia. Since the body cannot make enough beta globin chains, it makes an attempt to compensate by trying to increase the delta chain, thereby causing increased Hb A_2 as also seen in our study in the cases of sickle beta thalassemia and beta thalassemia**.** The diagnosis of hemoglobinopathy including thalassemia can result from either clinical suspicion or from follow up of an abnormality detected during screening.[17]Screening of healthy population is required to determine the carrier rates and gene frequencies in this region. Because of the complications associated with hemoglobinopathies and frequent health crisis these genetic disorders are becoming a growing health care problem in all regions of the developing country. There is need for community based mass screening programme at large level to target the high risk population so that implementation and monitoring can be done to reduce the prevalence of hemoglobinopathies in the country. Thalassemia can also be associated with other hemoglobinopathies, one of them being thalassemia associated with sickle cell disease where HbA levels are less than HbS.[18]Hereditary Persistence of Fetal Hemoglobin(HPFH),heterozygous, in nature with increased HbF (23.2%) and reduced HbA2 (1.4%). This is a heterogeneous group of conditions having persistent HbF production in adult life in the absence of major hematological abnormalities.In case of homozygous HPFH there is presence of 100% of HbF. The following preventive measures should be done vigorously to tackle this disorder.

1) Community level mass screening in and around Telangana to identify the target population.
2) Screening and counseling of the target population can lead to a significant reduction in affected births.
3) Prenatal diagnosis for identification of couple at risk and screening of premarital/reproductive age group people.

4) Encouraging antenatal diagnosis that enables parents to make informed and thoughtful choices regarding the outcome of pregnancies in which the fetus is severely affected.

5) Keeping in mind the cultural, religious and ethical views of an individual, genetic counseling should be planned.

IV. CONCLUSION

Though molecular techniques have a better advantage in diagnosing hemoglobinopathies these technologies are available only in few centers. Alkaline hemoglobin electrophoresis being a simple technology it can be made available even at the primary level and thus aids in diagnosis of thalassemia and sickle cell anemia. Health education and creation of awareness about the disease among the target population when done by the research bodies, health institutions along with government agencies will help in eradicating hemoglobinopathies in our community

REFERENCES

[1] Balgir RS. Genetic epidemiology of three predominant abnormal hemoglobins in India. J Assoc Physicians India, 44:25-8,1996.

[2] Borgna-Pignatti C and Galanello R.Thalassemias and related disorders.Quantitative Disorders of Hemoglobin Synthesis. In: Greer JP, Foerster J,Lukens JN, Rodgers GM, Parakevas F,Glader B, ed. Wintrobes Clinical Hematology, 11th edn. Lippincott Williamsand Wilkins, Philadelphia, 1319-65,2004.

[3] Balgir RS, The burden of Hemoglobinopathies in India and the challenges ahead. Curr. Sci., 79:1536- 1547,2000

[4] Verma IC, Choudhury VP, Jain PK. Prevention of thalassemia : a necessity in India. Indian J Pediatr ; 59: 649-654.,1992

[5] Yaish HM. Thalasemia. http://www.emedicine.com/PED/topic 2229.htm. Accessed 23rd October 2007.

[6] Manglani M, Lokeshwar MR, Vani VG, Bhatia N, Mhaskar V. ' NESTROFT-an effective screening test for b-thalassemia trait. Indian Pediatr ; 34: 703 -708,1997

[7] Wild BJ, Bain BJ.Investigation of abnormal hemoglobins and thalassemia. In: Lewis SM, Bain BJ, Bates I (Eds.), Dacie and Lewis Practical Hematology, 9th Edition. London : Churchill Livingstone; 231-268,2001

[8] Verma IC, Saxena R, Thomas E, Jain PK. Regional Distribution of Beta-Thalassemia Mutations in India. Hum Genet, 100: 109-113,1997

[9] Garewal G, Fearon CW, Warren TC, Marwaha N, Marwaha RK, Mahadik C, Kazazia HH.The molecular basis of Beta thalassemia in Punjabi and Maharashtran Indians includes a multilocus aetiology involving triplicated alpha-globin loci. Br. J. Haemotol. 86(2): 372-276,1994

[10] Balgir RS, Spectrum of hemoglobinopathies in the state of Orissa, a ten years cohort study. J Assoc Physicians India, 53:1021-6, 2005

[11] Rao S, Kar R, Gupta SK, Chopra A and Saxena R. Spectrum of hemoglobinopathies diagnosed by cation exchange-HPLC & modulating effects of nutritional deficiency anemias from northIndia. Ind J Med Research, 132(11):513-519, 2010

[12] Suprio Ray Chaudhury et al, Spectrum of hemoglobin variants in Eastern Indian population; a study of 14,145 cases Al Ameen J Med Sc i, 6(3): 243-248, 2013

[13] Patel Ashwin P et al., Prevalence of Common Hemoglobinopathies in Gujarat:An Analysis of a Large Population Screening Program, NJCM-3(1):112-116, 2012

[14] Bhawna Bhutoria Jain et al., Screening for thalassemia and other hemoglobinopathies in a tertiary care hospital of West Bengal: Implications for population screening; IJPH of public health, vol 56, issue 4 dec, 2012

[15] Haritha.P et al., Prevalence of Hemoglobinopathies among the Konda Kammaras of Visakhapatnam District, Andhra Pradesh ISSN: 2278-3008, IJPBS Volume 2, Issue 4, PP 06-08, 2012

[16] Bikash Mondal, Soumyajit Maiti, Biplab Kumar Biswas, Debidas Ghosh, and Shyamapada Paul, Prevalence of hemoglobinopathy, ABO and rhesus blood groups in rural areas of West Bengal, India, J Res Med Sci.; 17(8): 772–776, 2012

[17] Bain BJ. Haemoglobinopathy Diagnosis: Algorithms, lessons & pitfalls. Blood Reviews; 25: 205-213, 2011

[18] Henry, J.B.Clinical Diagnosis and management by Laboratory methods,19th edn. W.B. Saunders Company, Philadelphia, PA 19106. U.S.A. p. 645-647, 1996