Print ISSN: 2321-6379
Online ISSN: 2321-595X
DOI: 10.17354/ijss/2016/384

Original Article

Hemoglobin E in Marathwada Region of Maharashtra: Report of 14 Cases

Manjusha S Dhawle[1], Santosh Govind Rathod[2], Ashok Kumar Methwani[2], Mrunmayi M Awari[2], Ashwini R Tangde[2], R S Bindu[3]

[1]Associate Professor, Department of Pathology, Government Medical College and Cancer Hospital, Aurangabad, Maharashtra, India, [2]Medial Officer, Department of Pathology, Government Medical College and Cancer Hospital, Aurangabad, Maharashtra, India, [3]Professor, Department of Pathology, Government Medical College and Cancer Hospital, Aurangabad, Maharashtra, India

Abstract

Introduction: Hemoglobin E (HbE) (β26 glu → lys) is the most common hemoglobin variant in South East Asia and the second most prevalent worldwide. However, in India, it is prevalent in the North-Eastern region but relatively rare in the rest of country. Identification of this Hb variant is important because the double heterozygous state for HbE and β thalassemia is characterized clinically by thalassemia major. Thus, the affected individual may be symptomatic and transfusion dependent at an early age.

Materials and Methods: This paper reports 9 cases with HbE trait and another 5 cases with HbE β thalassemia. Laboratory investigations are based on red blood cell indices and high-performance liquid chromatography.

Results: We have discussed here the clinical and hematological features of this disorder. These disorders cause a public health concern due to a high level of morbidity, mortality and fetal loss in the backward, underprivileged, and vulnerable people. The main aim is to increase the awareness of this relatively rare disorder so that it can be included in the differential diagnosis of patients presenting clinically such as thalassemia intermedia or thalassemia major.

Conclusion: This awareness may also help in the prenatal diagnosis, genetic counseling, and clinical management.

Key words: Hemoglobin E, Hemoglobin E β thalassemia, High-performance liquid chromatography, Red cell indices

INTRODUCTION

Hemoglobinopathies are genetically important hematological disorder affecting millions of people worldwide. The cumulative gene frequency of hemoglobinopathies in India is 4.2%.[1] Hemoglobin E (HbE) is the second most globally prevalent Hb variant and common in South East Asia.[2] In India, it is prevalent in North-Eastern region.[3] It is relatively rare in the rest of the country, with only occasional case reports from other parts of the country. However; there are no published reports on the occurrence of this HbE variant in the region of Marathwada in Maharashtra. This is for the first time, we report the clinical and hematological profile of 14 such patients diagnosed and confirmed as having HbE/β thalassemia and HbE trait during the last 8 years in routine clinical and laboratory investigations. Since sickle cell hemoglobinopathy and thalassemia are widely prevalent in tribal as well as normal communities in Maharashtra, we focused the present study on 14 cases of HbE disorders encountered for the first time during screening and investigation for anemia and hemoglobinopathies. HbE is caused by a substitution of glutamic acid by lysine at codon 26 of the β globin gene. This mutation also activates a cryptic mRNA splice site which results in reduced synthesis of β-E chain and leads to a thalassemia phenotype. HbE disorder may be found in heterozygous (AE), homozygous (EE), and compound heterozygous states (e.g., HbE with other abnormal hemoglobin's or thalassemia) with widely variable clinical phenotype. In many countries, facilities for the control of these conditions are extremely limited. The awareness of this relatively rare Hb variant in this part of India may help in the clinical diagnosis and management of these patients and may also help in prenatal diagnosis and genetic counseling. Our present study focuses on the HbE

Access this article online

www.ijss-sn.com

Month of Submission : 05-2016
Month of Peer Review : 06-2016
Month of Acceptance : 07-2016
Month of Publishing : 07-2016

Corresponding Author: Dr. Santosh Govind Rathod, Government Medical College and Cancer Hospital, Aurangabad - 431 001, Maharashtra, India. Phone: +91-9545549174. E-mail: drsgrathod2007@gmail.com

disorders that were encountered during screening and investigation of hemolytic anemia.

MATERIALS AND METHODS

We studied a total 3707 patients from January 2008 to December 2015. Patients suspected of having thalassemia or other hemoglobinopathy were referred from the outpatient department or wards to the Department of Pathology, Government Medical College, Aurangabad. A detailed clinical and hematological evaluation and other investigations were performed in these cases. The clinical evaluations on the presence and absence of pallor, icterus, hepatosplenomegaly were carefully noted. Data pertaining to age, sex, place of origin, caste, history of blood transfusion, and hospitalization were also recorded. A complete hemogram with red blood cell (RBC) indices was performed on automated cell counter. High-performance liquid chromatography (HPLC) using variant β thalassemia short program (Biorad Laboratories) was carried out in all cases. HPLC was used as confirmatory test for identification of hemoglobinopathy in all cases. Each type of Hb has a characteristic retention time. HPLC utilizes the principle of cation exchange based on differential retention time. The introduction of HPLC for detection of hemoglobinopathies is an important advancement for hematology laboratories. All together 14 cases with HbE trait and HbE β thalassemia were identified. HbE has the same elution time as HbA2 on HPLC, but HbE can be distinguished by its higher concentration.

RESULTS

Here, we report total 14 cases, of which, 9 cases of HbE trait and 5 cases of HbE β thalassemia. All the cases of HbE β thalassemia had splenomegaly. The size of spleen varied from 1 to 8 cm below the left costal margin. Whereas 4 out of 5 cases had hepatomegaly (1-4 cm). Total Hb level varied from 5 to 7.2 g/dl with mean of 5.6 g/dl. Mild to moderate icterus was observed in 3 cases. History of multiple transfusion was given by 4 patients from the age of 1 year onward and needed 1-10 units of whole blood. The peripheral smear examination revealed a microcytic hypochromic blood picture with predominant target cells. The age variation of our patient was between 3 months and 33 years. The age of onset, clinical presentations and disease course of all the cases were such as β thalassemia major patients of this region. While the 9 cases of HbE trait did not have any symptoms. They had mild anemia with mean Hb level of 11.1 g/dl. Peripheral smear revealed mild hypochromia and microcytosis as seen with β thalassemia trait. There was no history of blood transfusion. The RBC indices of all these patients were available, and the diagnosis was confirmed by HPLC (Figures 1 and 2).

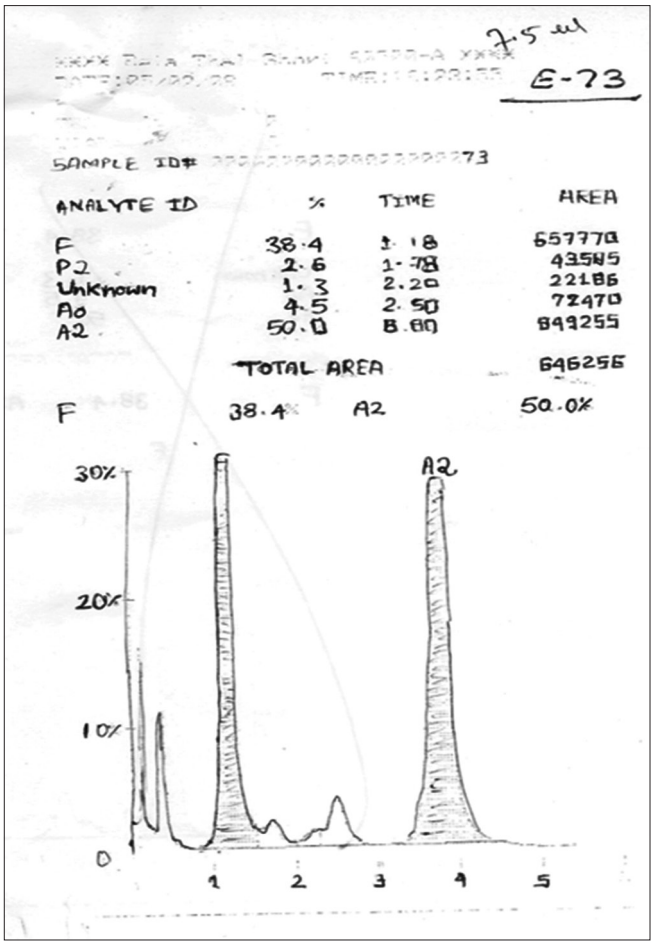

Figure 1: Hemoglobin E β thalassemia

Table 1: Mean values of Hb, RBC, mean corpuscular volume, mean corpuscular Hb, HbA2, and HbF in a tabular form

Mean values	Hb	RBC count	MCV	MCH	HbA2	HbF
HbE trait	11.1	4.4	68.2	22.5	29.2	0.4
HbE β thalassemia	5.6	2.5	66.4	20.9	47.5	22.8

Hb: Hemoglobin, RBC: Red blood cell, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, HbA2: Hemoglobin A2, HbF: Hemoglobin F

Table 1 shows the mean levels of RBC indices, Hb A2/HbE, and HbF levels in the two groups of patients in HbE trait and HbE β thalassemia, and the same is represented in multiple bar charts (Figure 3).

The mean HbA2 level in HbE trait cases was 29.2 and that with HbE β thalassemia patients was 47.5, whereas the mean value of HbF in HbE trait patient was 0.4 and that with HbE β thalassemia patients was 22.8. It is known that a raised HbF value reduces the severity of symptoms.

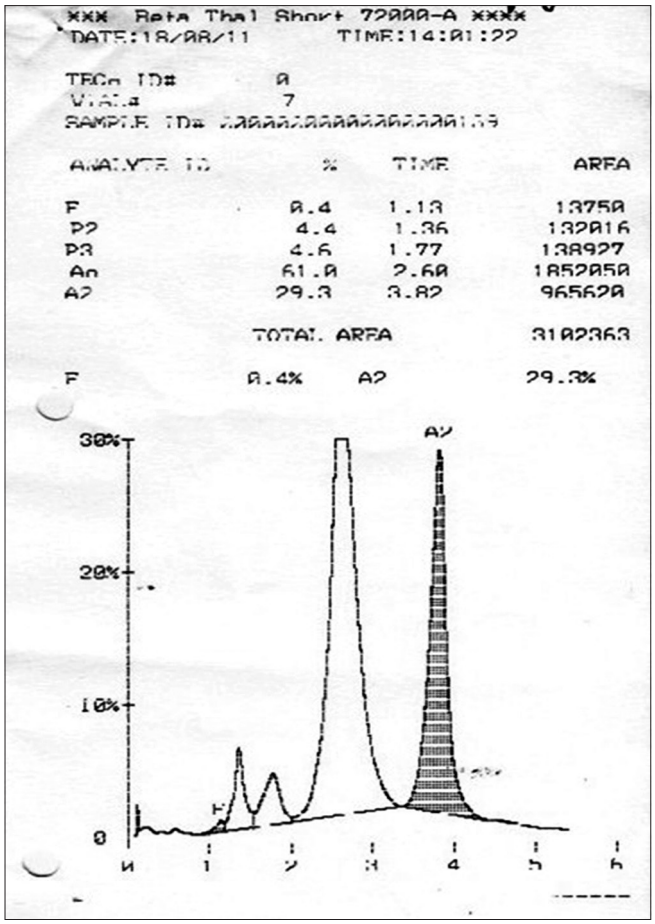

Figure 2: Hemoglobin E trait

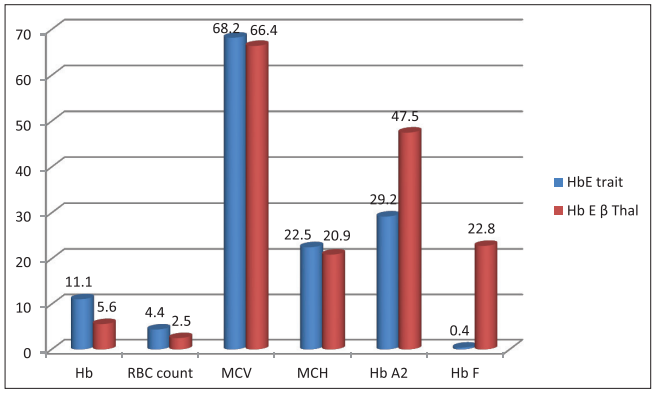

Figure 3: Multiple bar diagram in the two group of patients

DISCUSSION

Hemoglobinopathies are a growing global public health problem with an estimated 9.00,000 births of clinically significant thalassemia disorders expected to occur in next 20 years.[4] This growth will occur in disorders previously uncommon in many parts of the world. Although hemoglobin disorders are of a worldwide occurrence, yet some communities and geological regions have high prevalence of specific hemoglobin variants either due to practice of consanguinity or natural selection against malaria.[5]

HbE (Glu→ lys) is the most common Hb variant in South East Asia[2] and second most prevalent Hb variant worldwide. In India, it is mostly prevalent in the North-Eastern states[3] and Bengal. Case reports are also available from North India.[6]

Although the incidence of HbE disease is increasing which may be as a result of increased awareness, still little is known about the natural history, the reasons for clinical diversity or management of patients having this variant.

HbE is variant hemoglobin with a mutation in β globin gene causing substitution of glutamic acid for lysine at position 26 in β globin chain. HbE disease presents in 3 forms namely heterozygous state (genotype AE or HbE trait) homozygous state (genotype EE or HbE disease) and compound heterozygous state HbE β thalassemia (EB thalassemia), sickle cell/HbE disease (shared epitope genotype).[7-9]

Pathophysiology is complex which involves ineffective erythropoiesis, apoptosis, oxidative damage, and shortened red cell survival. HbF is the strongest predictor of morbidity.

Blood count, Hb, red cell indices, HPLC, and DNA analyses are the various diagnostic modalities which are used worldwide to assess the prevalence of thalassemia and hemoglobinopathies. HPLC provides effective separation of hemoglobin and detects a majority of hemoglobin variants.[10]

Clinical features of HBE β thalassemia range from that of β thalassemia minor through thalassemia intermedia to thalassemia major. It has been documented that the symptoms start usually before the age of 5 years. Most severely affected individuals are transfusion dependent and have hepato-splenomegaly, intermittent jaundice, and growth retardation.[7-9] Death from infection in childhood is common, but some patients live until adult life.[11] In our study, out of 5 cases, 4 cases were transfusion dependent from the age of 1 year onward and needed multiple transfusions varying from 1 to 10 units.

All of these patients had pallor, intermittent jaundice, fatigue, recurrent fever, splenomegaly, and 4 cases had hepatomegaly of varying grades and degrees. The clinical feature in our study is compatible with the other studies reported from other parts, especially from North-Eastern

region of India where the frequency is reported to be very high.[3,5,12,13] The peripheral blood smear examination revealed a hypochromic and microcytic picture with predominance of target cells.

Individuals with HbE trait are usually not anemic and have no symptoms. Hematological investigations of these individuals reveal mild microcytosis and hypochromia as seen with β thalassemia trait. Even in our study, the patients did not suffer from any symptoms.

However, identification of these individuals is of crucial importance as they may be the transmitters of the abnormal gene, giving rise to various combinations of hemoglobinopathies and thalassemia in their progeny.

These new insights into the knowledge of these diseases are important because they are gradually becoming a global health problem and impart diagnostic challenges to all the experts involved in the treatment of patients with thalassemia. Many cases have been misdiagnosed and misinterpreted as hemolytic anemia and met premature death without adequate diagnosis and management. The awareness of HbE, relatively rare Hb variant in this part of India, may have utility in clinical management and genetic counseling, and thus reducing the burden of this disease.

CONCLUSION

HPLC forms a rapid, accurate, and reproducible tool for early detection and management of hemoglobinopathies and variants. Findings must be supplemented by hemogram findings, family studies, hemoglobin electrophoresis, and molecular studies.

REFERENCES

1. Sarnaik SA. Thalassemia and related hemoglobinopathies. Indian J Pediatr 2005;72:319-24.
2. Lukens JN. The abnormal hemoglobins: General principles. In: Lee GR, Foerster J, Lukens J, Paraskevas F, Greer JP, Rodgers GM, editors. Wintrobe's Clinical Hematology. 10th ed. Baltimore: Williams and Wilkins; 1993. p. 1329-45.
3. Piplani S. Hemoglobin E disorders in the north east India. J Assoc Physicians India 2000;48:1082-4.
4. Vichinsky EP. Changing patterns of thalassemia worldwide. Ann N Y Acad Sci 2005;1054:18-24.
5. Balgir RS. Emerging trends in genetic epidemiology of hemoglobinopathy in the seven sister states of North Eastern India. In: Kanti DR, Debashish B, editors. North East India in Perspectives: Biology, Social Formation and Contemporary Problems. New Delhi: Akansha Publishing House; 2005. p. 17-37.
6. Kakkar N. Hemoglobin E-thalassaemia in a Sikh child: A case report. Indian J Pathol Microbiol 2005;48:408-10.
7. Weatherall DJ. Introduction to the problem of hemoglobin E-beta thalassemia. J Pediatr Hematol Oncol 2000;22:551.
8. Fucharoen S, Winichagoon P. Clinical and hematologic aspects of hemoglobin E beta-thalassemia. Curr Opin Hematol 2000;7:106-12.
9. Olivieri NF, Muraca GM, O'Donnel A, Premawardhena A, Fisher C, Weatherall DJ. Studies in haemoglobin E beta thalassaemia. Br J Haematol 2008;141:388-97.
10. Galanello R, Barella S, Gasperini D, Perseu L, Paglietti E, Sollaino C, *et al.* Evaluation of an automatic HPLC analyser for thalassemia and haemoglobin variants screening. J Automat Chem 1995;17:73-6.
11. Weatherall DJ, Clegg JB. Genetic disorders of hemoglobin. Semin Hematol 1999;36:24-37.
12. Pati AR, Bhargava M, Rath PK, Kochupillai V. Unusual features of haemoglobin-E thalassaemia. Indian J Med Res 1985;81:409-12.
13. Agarwal S, Gulati R, Singh K. Hemoglobin E-beta thalassemia in Uttar Pradesh. Indian Pediatr 1997;34:287-92.

How to cite this article: Dhawle MS, Rathod SG, Methwani AK, Awari MM, Tangde AR, Bindu RS. Hemoglobin E in Marathwada Region of Maharashtra: Report of 14 Cases. Int J Sci Stud 2016;4(4):102-105.

Source of Support: Nil, **Conflict of Interest:** None declared.