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Haemoglobin E Disease in Bahrain

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Objective: To report the presence of abnormal haemoglobin E (Hb E) in the Bahraini population and study its interaction with other haemoglobinopathies prevalent in Bahrain.

Study Design: a) Identification of Hb E during routine haemoglobinopathy screening and subsequent confirmation by various biochemical methods. b) Analysis of haematological data of all cases of Hb E detected during the year 1997.

Results: Seventeen cases (families) with Hb E were identified in Bahrainis in 1997. They consisted of 13 cases of Hb E trait, 3 cases of Hb S-E disease and one case of Hb E-Beta thalassaemia. Haematological data showed normal to mild disease in the trait form and a severer picture when in combination with Hb S and or Beta thalassaemia.

Conclusion: This is the first report of the existence of Hb E in the Bahraini population. When in combination with other haemoglobinopathies namely Hb S and Beta thalassaemia, both of which are highly prevalent in Bahrain, it can produce a clinical disorder, similar to Sickle Cell disease or Beta thalassaemia major, requiring close monitoring, treatment and genetic counseling.

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Haemoglobin E (Hb E) is an abnormal haemoglobin found principally in the south east Asian countries such as Burma, Thailand, Cambodia, Laos, Malaysia, Indonesia and eastern states of India[1]. In some of these areas the carrier rate is as high as 30%. This abnormal haemoglobin has rarely been seen in Arab countries[2] and has never been reported in Bahrainis. We report here 17 cases of HbE disease in trait form and in combination with other haemoglobinopathies in Bahrainis detected in the year 1997.

METHODS

All HbE cases were detected by initial screening in cellulose acetate electrophoresis at pH 8.6 (Helena Laboratories, UK) and then by HPLC (Beta-thal short programme variant haemoglobin testing system, Biorad USA). Samples were also subjected to acid agar gel electrophoresis (Paragon acid haemoglobin electrophoresis, Beckman, USA) and immunological detection with anti HbE antibodies (Isolab Haemocard, UK).

Complete blood counts were done in Coulter and Giemsa stained peripheral blood smears were examined.

RESULTS

In 1997 a total of 11870 haemoglobin electrophoresis were conducted in the haematology laboratory at the Salmaniya Medical Complex. Seventeen cases (families) with HbE were detected in Bahrainis, comprising of 13 cases of HbE trait, 3 cases of HBS-E disease and one case of HbE-Beta thalassaemia. An additional 7 cases of HbE were detected in non-Bahrainis (Bangladeshi - 6, Indian - 1), which are not included in this report.

Table 1. Haemoatological values of 13 cases of Hb E trait in Bahrain

Sr No.	Age (sex) (M/F)	Hb g/dl	MCV	MCH	RDW	Retics %	Hb A %	Hb E %	Hb F %
1	Newborn (M)	15.3	105.0	35.0	17.2	3.0	8.3	4.8	72.0
2	4 months (M)	10.2	80.0	25.0	12.9	1.2	56.2	15.5	21.5
3	4 months (M)	11.1	69.0	20.9	14.0	1.0	60.5	20.7	8.2
4	4 months (M)	12.2	84.0	29.0	19.4	1.2	62.8	28.0	0.4
5	9 months (M)	9.9	54.5	16.8	19.5	1.5	64.1	18.7	4.1
6	2 years (F)	10.0	67.2	23.5	15.2	1.5	61.1	20.9	2.0
7	3 years (F)	10.9	78.0	25.9	13.1	1.2	64.6	27.5	1.2
8	6 years (M)	12.1	70.0	23.3	13.6	0.4	61.3	31.2	0.8
9	7 years (M)	11.0	75.1	24.1	14.5	0.5	63.7	28.2	0.9
10	22 years (F)	10.8	73.2	22.5	15.3	1.2	61.2	31.6	0.5
11	31 years (M)	14.0	70.0	25.0	13.5	1.0	57.0	28.9	0.6
12	44 years (F)	11.0	70.1	21.5	19.4	0.5	69.9	22.1	0.3
13	67 years (F)	8.7	76.0	24.0	15.1	0.6	65.2	29.8	0.5

Haemoglobin E trait: Table 1 gives the haematological details of the 13 cases of HbE trait. Age ranged from newborn to 67 years. The newborn was detected during cord blood

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screening and the other 12 cases presented to the hospital with some complaints. Eight were in paediatric age group and 4 were adults. All except one adult case had low haemoglobin levels (median llg/dl). MCV was low in all cases and all cases showed microcytosis and target cells. Hb E levels ranged from 18.7 to 31.6 with a median value of 27.5%. Fetal haemoglobin (Hb F) was less than 1% in all patients above one year of age (Fig 1).

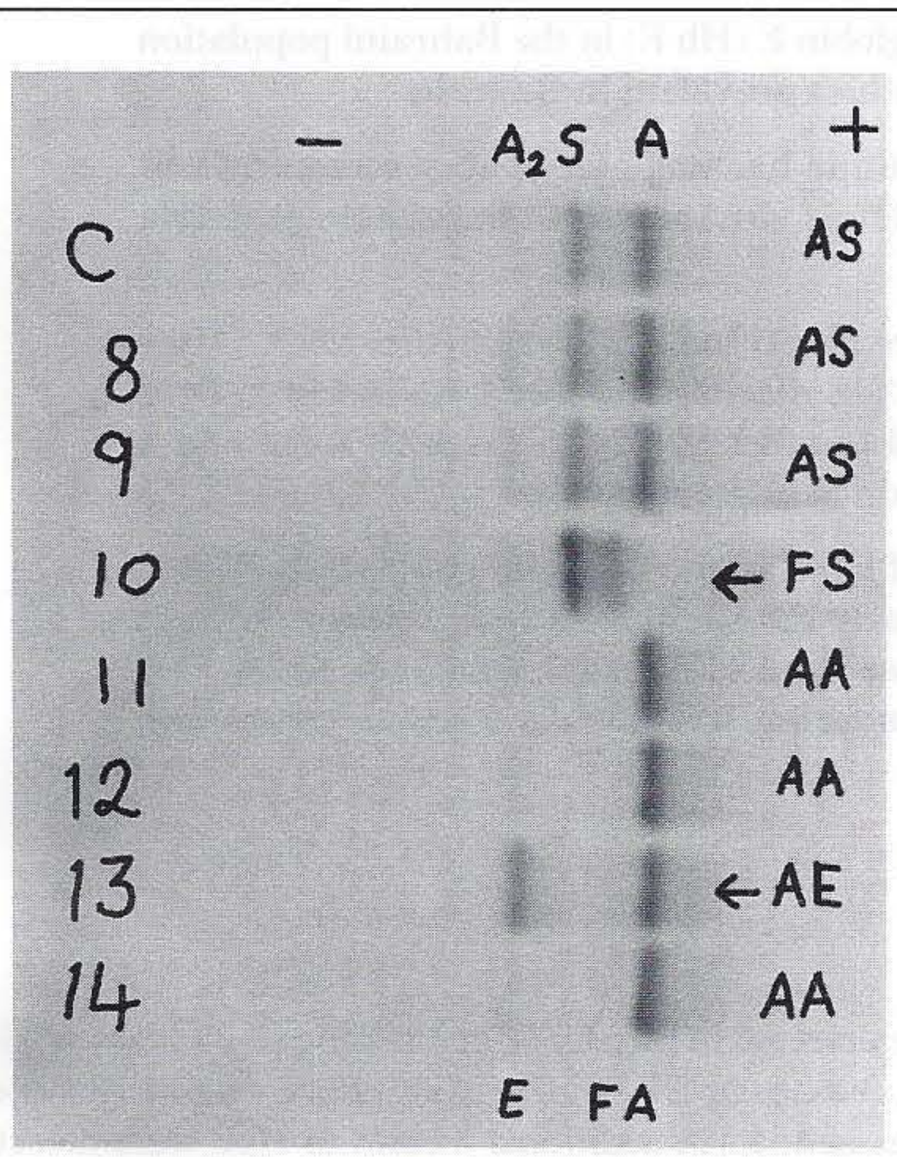

Figure 1. Hb electrophoresis at pH 8.6 in-cellulose acetate showing separation of Hbs S, E, F and A. Sample No.13 is a case of Hb E trait.

HbE - Beta thalassaemia: One case of double heterozygosity for HbE and Beta thalassaemia was seen during 1997. This was a 3 year old male child with moderate to severe haemolytic picture. His haemoglobin was 6.9 g/dl, peripheral smear showed marked anisopoikilocytosis with microcytes, hypochromia and target cells. HbE was 75% with 18.5% Hb F. Investigation of parents revealed HbE trait in the mother and Beta thalassaemia trait in the father.

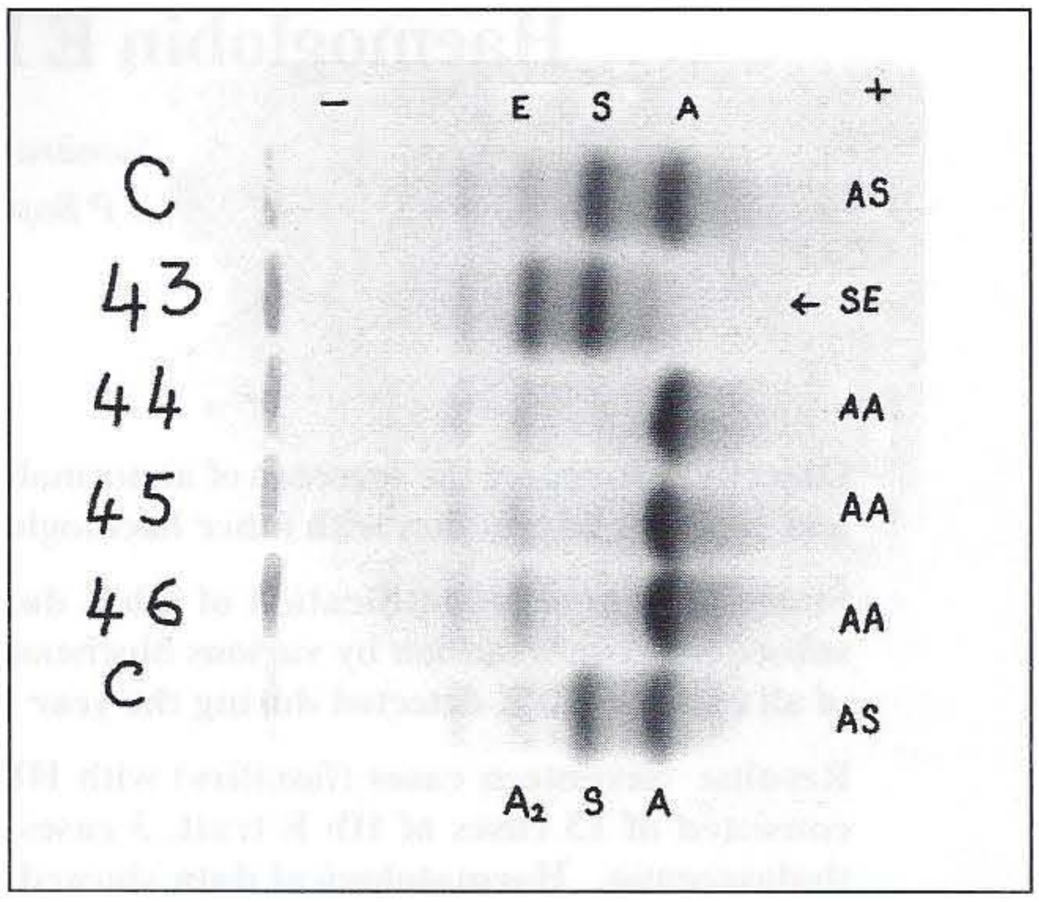

Figure 2. Hb electrophoresis at pH 8.6 in cellulose acetate showing separation of Hb bands. Sample No. 43 is from a case of Hb S-E disease.

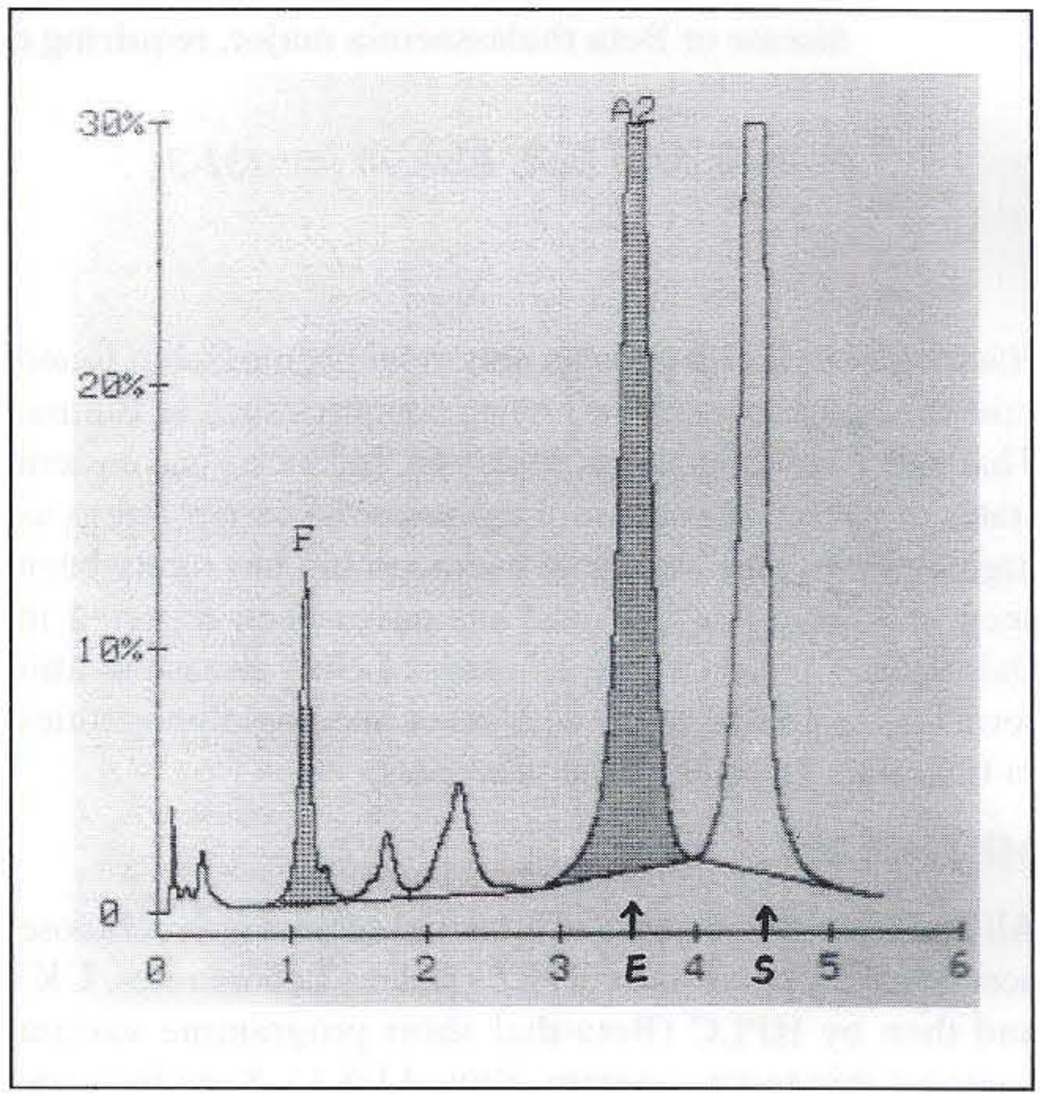

Figure 3. HPLC of haemoglobin showing Hb S and Hb E which is eluted with Hb A2 from a case of Hb S-E disease.

Table 2. Haemoatological values of 3 cases of HbS-E disease

Sr No.	Age (sex) (MIF)	Hb gldl	MCV	MCH	RDW	Hb S %	Hb E %	Hb F %
1	18 years (F)	9.2	63.0	22.5	15.2	53.7	38.1	5.2
2	25 years (F)	8.8	79.9	27.0	14.8	55.1	37.1	3.8
3	54 years (M)	11.1	68.0	23.0	14.4	58.0	35.7	2.5

Hb S - E disease: There were 3 cases with double heterozygosity for Hb S and Hb E (Table 2). All 3 were adults. All had low haemoglobin levels, low MCV, microcytosis and target cells. Hb E was 35.7 to 38.1%, Hb S 53.7 to 56.0% and Hb F 2.5 to 5.2% (Figs 2 & 3).

DISCUSSION

Hb E is the result of a Beta globin chain mutation, lysine replacing glutamic acid at position 26 of the Beta chain[3]. This base substitution not only produces a haemoglobin that is somewhat unstable when subjected to oxidative stress[4], but also creates a new potential splicing sequence giving rise to a thalassaemia like situation[5,6].

In the trait form this abnormal haemoglobin is symptomless. The red cells show slight but significant reduction in MCV and MCH although the blood film is usually relatively normal . Most of our cases however showed low Hb levels and abnormal red cell morphology. The homozygous state

for Hb E is characterised by a very mild degree of anaemia with slightly reduced red cell survival[8]. The clinical manifestations of heterozygous state between Hb E and Beta thalassaemia is more severe than homozygous Hb E disease which usually presents with moderate anaemia and splenomegaly[9].

Double heterozygosity for Hb S and Hb E is extremely rare. The reported cases were less than 10 till today[10]. Clinical features in children are either insignificant or equivocal[2]. Older patients however sometimes have symptoms suggestive of a major sickling disorder[11]. Patients with Hb S-E disease may not require the vigorous infection prophylaxis and counseling that is required for those with more severe sickle haemoglobinopathy. However they must be monitored closely for any worsening of their haematologic condition as they grow older.

CONCLUSION

This is the first report of the existence of Haemoglobin E in Bahrainis. These cases can be misdiagnosed in screening methods of haemoglobin electrophoresis. Better separation techniques such as HPLC and immunological methods are required to identify this abnormal haemoglobin. When in combination with other haemoglobinopathies namely Hb S and Beta thalassaemia, it can produce moderate to severe clinical disorder, similar to sickle cell disease and B-thalassaemia major, requiring close monitoring and treatment.

REFERENCES

1. Flatz G. Haemoglobin E: Distribution and population dynamics. Hum Genet 1967;3:189-234.
2. Hardy MJ, Ragbeer MS. Homozygous Hb E and Hb S-E disease in Saudi family. Hemoglobin 1985;9:47-52.
3. Hunt JA, Ingram VM. Abnormal human haemoglobins VI. The chemical difference between haemoglobins A and E. Biochim Biophys Acta 1961;49:520-36.
4. Frischer H, Bowman J. Hemoglobin E, an oxidatively unstable mutation. J Lab Clin Med 1975;85:531-9.
5. Orkin SH, Kazazian HH Jr, Antonarakis SE, et al. Abnormal RNA processing due to the exon mutation of Beta globin gene. Nature 1982;300:768-9.
6. Weatherall DJ, Clegg JB, Higgs DR, et al. The Haemoglobinopathies. In: Scriver CR, Beaudet AL, Sly WS, et al (eds). The metabolic and molecular basis of inherited diseases. New York: McGraw Hill, 1995:3417-74.
7. Fairbanks VF, Gilchrist GS, Brinhall B, et al. Hemoglobin E trait re-examined. A cause of microcytosis and erythrocytosis. Blood 1979;53:109-15.
8. Wong SC, Ali MAM. Hemoglobin E diseases: Hematological, analytical and biosynthetic studies in homozygotes and double heterozygote for alpha thalassaemia. Am J Hematol 1982;13:15-21.
9. Dash S, Dash RJ. Hemoglobin E-thalassaemia in Punjab. J Assoc Physicians India 1980;28:315-8.
10. Rey KS, Unger CA, Rao SP, et al. Sickle cell-hemoglobin E disease: Clinical findings and implications. J Pediatr 1991;119:949-51.
11. Engelstad BL. Functional asplenia in hemoglobin SE disease. Clin Nucl Med 1982;7:100-4.