

Original

HEREDITARY ELLIPTOCYTOSIS IN BAHRAIN

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Hereditary elliptocytosis an abnormality of red blood cell may provide a selective advantage to protect against malaria. We screened 2000 Bahraini blood donors and found 42 cases of hereditary elliptocytosis. Clinical and haematological aspects were analysed in 100 consecutively diagnosed cases of hereditary elliptocytosis among Bahraini patients. Their ages ranged from 46 hours to 75 hours. Female preponderance was observed in the adult age group. Majority of patients presented with anaemia. Low haemoglobin and low red cell indices were noticed in all age groups. However the condition was found to exist in three forms as clinically silent, disease with transient haemolysis, and as a chronic haemolytic process. Thus a peripheral smear examination to screen for elliptocytosis is warranted in all anaemic Bahraini patients.

Hereditary Elliptocytosis (HE) is an autosomal dominant condition in which an abnormality of the red cells cytoskeleton leads to their oval appearance. Because the condition is usually benign, many healthy people are unaware of the abnormality of their red cell. Frequent documentation of cases of elliptocytosis in routine haematology lead us to study this disorder in the Bahraini population and to evaluate the risk involved when their blood is accepted for the purpose of transfusion.

METHODS

The study was conducted in two parts. In part 1, two thousand Bahraini blood donors were screened to study the prevalence of HE in the Bahrainis. In part 2, clinical and haematological aspects were studied in one hundred consecutively diagnosed cases of HE.

RESULTS

Part 1: Between May 1993 and October 1993, peripheral blood smears stained with Geimsa stain from 2000 Bahraini blood

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donors were screened to detect elliptocytosis. There were 1984 males and 16 females. Their ages ranged from 22 years to 55 years old. Haemoglobin levels were >13.6 g/dl in the males and >12.6 g/dl in the females. Forty two cases of elliptocytosis were detected, all of whom were males. Elliptocytes ranged from 50% to 100% of the total red cells in these cases (Table 1).

Table 1: Prevalence of hereditary elliptocytosis among
Bahraini blood donors

No. of donors Age Hb No. of cases Percentage of
screened (years) (g/dl) of ellipto- elliptocytosis

				cytosis	in peripheral blood
Males	1984	22-51	13.6-16.5	42	50-100
Females	16	25-37	12.7-14.3	0	
Total	2000	22-51	12.7-16.5	42	50-100

Part 2: One hundred consecutively diagnosed cases of HE were included for this study. All these cases were detected between January 1992 and October 1993.

Clinical Findings: The age of the patients ranged between 46 hours to 75 years old. There were 13 patients less than one year of age (Infant group), 26 patients between one year to 16 years of age (Paediatric group), and 61 patients above the age of 16 years (Adult group). In patients below the age of 16 years there was a slight male preponderance (males 23, females 16) which changed to a female preponderance in patients above the age of 16 years (males 14, females 47).

Pallor was the single most common complaint and clinical finding (59 cases), for which haematological investigations were undertaken. Asymptomatic carrier states were detected in the blood donors and in patients during routine preoperative clinical examination. Minimal and mild HE was detected as being associated with ENT problems, bronchial asthma etc. HE with transient hemolysis was detected in patients with fever and infections. HE with neonatal poikilocytosis was seen in children of less than one year of age.

Haematological findings: Table 2 shows the relevant haematological data in all three age groups. Low haemoglobin was a feature in all age groups. However, wide difference in haemoglobin levels was observed between the males and females in the adult age group. The MCV and MCH were also decreased in all age groups. Red cell diameter width had a broad range in the adult female patients. Total red cell, white cell and platelet counts were within normal limits. Reticulocyte counts were slightly elevated. Elliptocytes formed 50% - 100% of the total red cells. Severe anisopoikilocytosis was present in 18 cases. In 27 cases marked hypochromia of the red cells was observed (Figs 1 & 2).

Table 2: Haematological values in elliptocytosis patients of different age groups

Age range (year)	Infant	Paediatric	Adult	
	< 1	1 - 6	males 17 - 75	females
No. of patients	13	26	14	47
Haemoglobin g/dl	9.9* (8.7-17.5)**	10.5 (7.9-11.8)	12.3 (7.0-16.1)	9.7 (6.5-12.0)
HCT %	28.9 (25-50)	28.3 (20-38)	36.1 (23-48)	29.0 (19-37)
MCV	74.0	62.1	71.6	66.4
f1	(66.0-103.8)	(50.8-72.8)	(52.7-85.6)	(51.5-83.4)
MCH pg	25.9 (22.0-36.0)	21.4 (17.0-25.6)	24.0 (19.0-29.0)	22.3 (16.1-29.8)

MCHC g/dl	34.0 (32.0-35.0)	34.1 (30.0-43.8)	33.6 (30.0-39.9)	33.4 (31.0-36.9)
RDW	17.7 (14.3-27.5)	15.1 (13.6-32.8)	14.9 (13.0-17.0)	19.7 (9.8-32.5)
RBC x 10 ¹² /l	4.03 (2.99-5.00)	4.6 (3.70-5.49)	5.08 (3.32-6.39)	4.4 (3.0-5.80)
WBC x 10 ⁹ /l	11.3 (5.9 -16.4)	9.0 (3.8-17.6)	6.7 (3.5-13.3)	6.5 (2.8-16.3)
Platelets x 10 ⁹ /l	575 (356-1073)	513 (225-1100)	284 (210-350)	329 (45-1028)
Retics %	1.7 (1.5-9.0)	2.2 (1.2-4.5)	2.4 (1.2-3.0)	3.4 (1.0-7.0)

 * Mean value ** Range

DISCUSSION

Elliptocytosis was first observed by Dresbach in 1904 and the hereditary nature of the disorder was firmly established by Hunter and Adams^{1,2}. The prevalence of elliptocytosis in the Bahraini population as observed in this study (20-22 cases per 1000) is significantly higher than the 3-5 cases per 1000 births found in the USA and the 4-6 cases per 1000 seen in the West African population^{3,4}.

One form of elliptocytosis known as hereditary ovalocytosis which occurs in South East Asia has been found in up to 30% of aboriginal populations of this region particularly among the Melanesians living in coastal parts of Papua New Guinea. This form has been recognised to confer protection against malaria and strongly favours the selection of this gene in the presence of malaria⁵. This might also be true for the Bahraini population with genetic traits such as sickle haemoglobin, red cell G-6PD deficiency, and alpha thalassemia which are known to provide advantage for resistance to malaria⁶.

In vitro studies of HE red cells have revealed increased utilisation of adenosine triphosphate (ATP) and 2,3 diphospho glycerate (2,3,DPG) leading to rapid decrease in their levels⁷. Since red cells with lower levels of ATP are postulated to be destroyed in the spleen, this will lead to shortened post transfusion survival of these red cells⁸. With the prevalence of around 2% elliptocytosis among the Bahrainis, the likelihood of a transfused patient receiving more than one unit containing elliptocytes is small and the risk of requiring additional transfusions to compensate for the shortened survival of these cells is negligible. So the need for screening of blood donors for elliptocytosis is not warranted.

The clinical expressions of HE in this study was found to be highly variable. Anaemia due to a chronic haemolytic process was however the most frequently diagnosed situation in this series.

In the present study the mean haemoglobin level and other red cell indices were significantly low in all age groups, suggesting that the haematological expressions of the disease did not change with advancing, but the haematological values significantly become worse in the females, and this may be attributed to additional factors such as menstruation and pregnancy. Thus a peripheral smear examination to screen for elliptocytosis is warranted in all anaemic patients of Bahraini origin, and especially in the female patients.

There were cases which showed striking micro poikilocytosis and with MCV as low as 50 Um. These conditions may belong to the subtype hereditary pyropoikilocytosis^{3,9}.

Several underlying abnormalities have been identified in HE indicative of the heterogenous nature of the disorder. All these abnormalities involved "horizontal interactions" between proteins of the membrane skeleton, especially spectrin-spectrin and spectrin 4.1. This weakens the skeleton and under the influence of shear stress in the microcirculation the cells progressively lose the ability to regain the normal disc shape, becoming permanently stabilised in the elliptocytic or poikilocytic shapes which are characteristically seen in cells exposed to shear stress in vitro or in the microcirculation in vivo¹⁰.

The extent of mutant spectrin in the cell and the severity of the spectrin association dictates the seriousness of HE. The molecular defects have been identified thus far are heterogenous and different mutations are described for the Southeast-Asian types and West African variants, which appear to be totally and or partially resistant to malaria⁴. It will be interesting to study the molecular defects present in the Bahraini population and their similarities and differences from elliptocytosis in other populations for any possible protection from malaria it may offer.

CONCLUSION

The prevalence of Hereditary elliptocytosis is around 2% in the Bahrainis. Malaria might be a selecting factor for its high prevalence. Anaemia is the common clinical and haematological finding in all age groups with this disorder and warrants blood smear examination to rule it out. Further details into the molecular defect need to be investigated and the results should be compared to other population.

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