ORIGINAL

Alpha-Thalassaemia in Bahrain: Haemoglobin H Disease - Not So Benign

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ABSTRACT

A retrospective analysis of the records of 76 in-patients seen at Salmaniya Medical Centre, Bahrain, during the period 1985-86 was carried out. The aim of the study was to determine the clinical manifestations of haemoglobin H disease. These patients were classified into three groups; their clinical and haematological details were carefully recorded. The study has revealed one important finding: contrary to old-held belief, haemoglobin H disease can have diversified and at times severe clinical manifestations. However, haemoglobin H disease still remains intriguing and requires the collaborative research efforts of Arabian Gulf countries.

Until recently, little attention was paid to α-thalassaemia in the countries of the Arabian Gulf, in marked contrast to β-thalassaemia. This observation may partly be attributed to two factors. Firstly, β-thalassaemia in its homozygous form is usually a severe chronic disease with variable morbidity and high mortality; and secondly, α-thalassaemia in its most common form seems to be mild clinically. The latter impres-sion has been propagated by haematology textbooks published in the West.[1,2]

We have recently observed in our study that α-thalassaemia does not only confuse the picture of iron deficiency anaemia on the basis of low red cell indices (MCV, MCH), but also emulates β-thalassaemia inter-media or even β-thalassaemia major in presenting as moderate to severe haemoglobin H disease respectively. The purpose of this publication is to render a brief account on the salient features of the clinical spectrum of haemoglobin H disease in a Bahraini population and to make an attempt to clarify some of the confusion around the subject.

METHODS

Seventy-six of 200 case-records reviewed retrospec-tively from the registers of Salmaniya Medical Centre formed the basis of this study. Laboratory registers of Salmaniya Medical Centre were consulted and some of the data were obtained from these records. The rest were obtained by screening the parents of children diag-nosed to have haemoglobin H disease. These findings are shown in Table 1.

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Table 1
Data of Hb-H disease from laboratory registers and Paediatric Haematology Clinic of Salmaniya Medical Centre (1985 – 86)

Particulars	*Statistics*	*Comments*
No. of cases reviewed	76	
Age range	Neonates-29 years	1. Two thirds were below 18 years 2. Three were neonates
Hb-H† level (% of total Hb*)	3.0 – 50%	In over 85% of the cases Hb–H† was above 10%
Significant splenomegaly	In 40.9%	Older children
Massive hepatomegaly	In 3.8%	All neonates
Need for blood transfusion	In 63.6%	Some need regular transfusion and iron chelation

*Hb = Haemoglobin
† Hb-H = Haemoglobin H

RESULTS

Clinical Spectrum of Haemoglobin H disease

The clinical presentation of patients with haemoglobin H Disease is highly variable, ranging from severe anaemia with organomegaly in neonates to symptomless presentation in adults. Details of our findings are shown in Table 2.

The three neonates of group 1 presented with severe anaemia, massive hepatosplenomegaly coupled with heart failure. Bart's haemoglobin in these patients was very high (30–50%),of whom one had haemoglobin H noticeable on electrophoresis in the neonatal period while the other two subsequently revealed it at an older age.

At one end of the spectrum is a group of adult patients who remain asymptomatic and clearly behave like β-thalassaemia trait in their haematological manifestations with low MCV and MCH and normal to slightly reduced haemoglobin. These were picked up by screening parents of children with Haemoglobin H disease. Between these two extremes of presentation, there exists a population of Haemoglobin H disease patients, usually children in the age range of 1-10 years who have chronic haemolytic anaemia with variable range of severity but invariably need occasional to regular blood transfusion to maintain haemoglobin at 10.0 g/dl (Group 2). The base line haemoglobin in some of these patients may drop to 5.0 – 6.0 g/dl if left untransfused as happened in a few whose parents failed to bring them for periodic haemoglobin determination. 40.9% of these children had detectable splenomegaly but none had massive hepatosplenomegaly in contradistinction to what was noticed in the neonates of group 1.

DISCUSSION

The clinical manifestations of haemoglobin H disease has received minimal attention in the medical literature, particularly in reports from the Middle East. In reviewing 260 Thai patients, Wasi et al found bony changes typical of thalassaemia in 35% of the cases, and splenomegaly in 80%.[5] Acquaye et al reported the presence of slight splenomegaly in 4 out of 8 Saudi cases of haemoglobin H disease (50%) and slight hepatomegaly in a similar number of their cases, but no skeletal abnormalities.[7] In our series, splenomegaly was noted in 40.9%, but none of our patients had obvious bony changes including those who were on regular blood transfusion and iron chelation.

Variability in the clinical spectrum was emphasised by Weatherall et al who stated that some patients with haemoglobin H disease might go through life with little disability while in others the disorder might be as crippling as homozygous β-thalassaemia anaemia.[1] Such variability in the clinical presentation was clearly demonstrated in our patients: at one end of the spectrum, the abnormality was detected in asymptomatic parents of index paediatric patients on screening, while at the other end, some neonates started life with severe anaemia and massive hepatosplenomegaly.

The latter presentation is in contradistinction to homozygous β-thalassaemia where patients rarely manifest with clinical abnormalities prior to six months of

Table 2
Clinical spectrum of haemoglobin H disease in Bahrain

Group	*Age range*	*No. of cases*	*Clinical manifestation*
1	Neonates (0–1 m)	3	Severe anaemia, massive hepatosplenomegaly, high Bart's Hb* (30–50%) ± Hb-H† at birth, subsequent appearance of increase in Hb-H†.
2	Children (>1-10 yrs)	23	Moderate-severe chronic haemolytic anaemia, significant splenomegaly ± hepatomegaly.
3	Adults (>20 – <30 yrs)	50	Normal haemoglobin level to mild anaemia, incidental finding or detected on screening parents of children with Hb-H disease.

*Hb = Haemoglobin
† Hb-H = Haemoglobin H

age. We would like to highlight this extreme presentation which was observed in about 4% of the cases of haemoglobin H disease reviewed by us.

It is noteworthy to record that all these neonates had on electrophoresis, a high level of Bart's haemoglobin in the cord blood. These neonates were very sick but obviously could not be considered as Bart's haemoglobin hydrops fetalis since they all survived the neonatal period. It is indeed unfortunate that our facilities did not permit α-globin gene mapping studies to pin down the underlying genetic defect in the index cases and their parents.

Between the two end of the clinical spectrum there existed patients with a clinical picture of β-thalassaemia minor and β-thalassaemia intermedia. These were older children in the age range of 1–10 years. Such finding is suggested in several reports.[1-3,6] The molecular defect (the haplotypes) of α-thalassaemia in general has been disclosed in the Saudi population living in the Eastern and Western regions of the Arabian peninsula.[3,7-9] The majority of the cases of haemoglobin H disease in the Saudi population resulted from homozygosis of $\alpha\,\alpha^{T}/-$ (ie, non-deletion α-gene defect).[3,7,9]

Pending molecular studies, we speculate that our Bahraini population being an extension of the Eastern Province of Saudi Arabia geographically and socially, may have a similar genetic defect in patients with α-thalassaemia including its most significant clinical form, haemoglobin H disease.

CONCLUSION

Haemoglobin H disease can have diversified clinical presentations with the very severe form manifesting so early in the neonatal period at one end of the spectrum, while on the other hand, adults with the disease may go unnoticed unless detected by mere chance in the course of family screening. We still find the subject intriguing and accordingly solicit a collaborative clinical and molecular study in a larger population of patients from other countries of the Gulf.

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