SCREENING FOR THALASSAEMIA AND HAEMOGLOBINOPATHY IN ADULT PATIENTS

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SYNOPSIS

316 patients were studied for thalassaemia and haemoglobinopathy from February 1978 to August 1980 by the Division of Haematology, Department of Pathology, University Kebangsaan Malaysia. The diagnosis was suspected from the clinical features, red cell indices, osmotic fragility, red cell morphology, determination of the discriminant function, and serum ferritin levels. Definitive diagnosis necessitating family studies and haemoglobin analysis.

INTRODUCTION

The diagnosis of thalassaemia and haemoglobinopathy is dependent upon a number of laboratory parameters; including the determination of red blood cells indices, red cell morphology, red cell osmotic fragility, demonstration of red cell intraerythrocytic inclusions, haemoglobin electrophoresis, quantitation of HbF and HbA2, determination of serum ferritin and family studies.

MATERIALS AND METHODS

316 patients, 12 to 60 years old were studied from February 1978 to August 1980. Suspected patients screened from routine haemograms on the Coulter S and with characteristic red cell morphological appearance were subjected to haemoglobin analysis. Included in the study were patients with a family history of thalassaemia and haemoglobinopathy, unexplained anaemia, jaundice or hepatosplenomegaly.

Haemoglobin analysis consisted of electrophoresis on cellulose acetate Tris-EDTA boric acid (CEAE) buffer pH 8.9 and phosphate buffer pH 6.0. Homemade haemolysate consisting of Hb AA2 (adult blood) and Hb AF (cord blood) are usely routinely as controls. Hb A2 and other haemoglobin components are quantitated on CEAE (4). HbF levels are estimated by the alkali resistant method (6) and its distribution in red cells by the acid elution cytochemical tests. Osmotic fragility, sickle cell and solubility tests, intraerythrocytic inclusions by incubation with brilliant cresyl blue are procedures included (1) and determination of serum ferritin levels by radioimmunometric assay (7, 3).

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TABLE I

The Distribution of Patients with Thalassaemia and Haemoglobinopathy

Total Number of Patients 316

RACES	MALAYS	CHINESE	INDIANS
Total Number Studied	166	105	11
B thalassaemia trait	9	5	1
B thalassaemia major	0	0	0
B thalassaemia intermedia	0	2	1
Hb EA	10	2	0
Hb EE	3	0	0
Hb EB+ thalassaemia	3	0	0
Hb H	0	6	0
Hb ES	1	0	0

Patients with associated iron deficiency and suspected thalassaemia were treated with haematinics and haemoglobin analysis repeated; family studies providing confirmatory evidence.

A similar study of sixty normal adult males and female were analysed as controls.

RESULTS

The racial distribution of thalassaemia and haemoglobinopathy in adult patients are summarised in Table I. The normal range of HbA2 being 1.5 - 3.5%; in B thalassaemia trait 3.5 - 7.5%; Hb EA, the E from 20 - 40% and in HbEE 90 - 100% (Hb E running together with HbA2 electrophoretically); and the normal range of Hb F being 1 - 3%.

DISCUSSION

Characteristic clinical features in various thalassaemic syndromes and haemoglobinopathies are described (8). The adult patients with B thalassaemia trait, HbE trait, Hb constance springs trait and α thalassaemia^2 trait are clinically normal with mild or no anaemia at presentation and no jaundice, the diagnosis being susected from red cell indices and red cell morphology. Hb Eβ+ thalassaemia in adults seems to be a mild disease with no jaundice; Hb levels 11 - 12gm/dl, mild to moderate splenomegaly in constrast to Hb Eβ^0 thalassaemia which produces severe anaemia in children. The β thalassaemia intermedia patients have a Hb 6 - 9gm/dl, jaundiced, moderate hepatosplenomegaly, and the usual thalassaemic changes in red cell morphology. Hb H patients had a similar picture in addition to intraerythrocytic H inclusions.

Routine haemograms done on Coulter S provide accurate determination of red cell indices. Measurement of the mean cell volume (MCV) showing microcytosis provides a convenient first step in screening for thalassaemia (5). However it does not aid in the diagnosis of α thalassaemia^2 and Hb Constance Springs traits where the indices are within normal limits. The red cell morphological appearance in thalassaemia includes hypochromia, microcytosis, anisopoikilocytosis, nucleated red cells, fragmented forms, basophilic stippling and spherocytes. Similar changes are seen in iron deficiency but are grossly abnormal only if haemoglobin is below 10gm/dl. The determination of the discriminant function and serum ferritin values are useful in differentiating iron deficiency from thalassaemia. In suspect cases of thalassaemia with associated iron deficiency a course of iron therapy with repeat analysis, and family studies provide a definitive diagnosis. In the Chinese the commonest thalassaemia in adults was HbH - 6 patients; β thalassaemia trait — 5 patients and 2 patients each of β thalassaemia intermedia and Hb EA. In the Malays, the commonest was Hb EA — 10 patients, followed by β thalassaemia trait — 9 patients, and 3 each of Hb EE and Hb EB + thalassaemia. There was a patient with β thalassaemia trait and β thalassaemia intermedia in the Indians.

Peptide mapping and studying the rates of chain synthesis in suspected individuals and their families would provide further knowledge of the thalassaemia syndromes and haemoglobinopathies present in adults in the future.

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REFERENCES

1. Dacie J.V., Lewis S.M.: Practical hematology. 4th Edition. Churchill, London 1968.
2. England J.M., Fraser P.M.: Differentiation of iron deficiency from thalassaemia trait by routine blood count. Lancet 1973; 1: 449-452.
3. Jacobs A.: Ferritin in serum of normal subjects and patients with iron deficiency and iron overload. Br Med J 1972; 4: 206-208.
4. Marengo-Rowe A.J.: Rapid electrophoresis and quantitation of haemoglobin on cellulose acetate. J. Clin Path 1965; 18: 790-792.
5. Pearson M.A., O'Brien R.T., McIntosh S.: The Screening for Thalassaemia trait by electronic measurements of