DETECTION OF HETEROZYGOUS BETA THALASSAEMIA IN PARENTS AND GRAND PARENTS OF KNOWN BETA THALASSAEMIA MAJOR CHILDREN

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SUMMARY

One hundred (100) families of known beta thalassemia major children were analysed at Postgraduate Medical Institute, Lady Reading Hospital, Peshawar for the detection of beta thalassaemia trait. The screening was performed in the parents and grandparents (both maternal as well as paternal). Beta thalassaemia trait was detected in all the families. The overall 415 cases (69.2%) out of 600 subjects were beta thalassaemia carrier trait.

INTRODUCTION

The thalassaemias are heterogeneous group of genetic heritable disorders of haemoglobin synthesis.[1] Beta thalassaemia probably is the most common single gene disorder causing a major genetic health problem in the world.[2] Pakistan lies in the thalassaemia belt and b-thalassaemia is common here.[3] If an average of 5.4% is taken as the national carrier rate,[3-4] there would be approximately 5-6 million carriers in Pakistan.

The average cost of treating one thalassaemic patient is Rs. 10,000 per annum in addition to blood requirements which is unaffordable with our limited resources.[5] An alternative long term approach would be to reduce the number of these patients through prenatal screening and genetic counselling.[6] Identification of b-thalassaemia carriers and provision of prenatal diagnosis of homozygous conception using oligonucleotide probes and restriction enzyme analysis,[7-8] followed by termination of pregnancy will allow couples at risk to avoid

HAEMATOLOGICAL DATA IN SUBJECTS HAVING HETEROZYGOUS BETA THALASSAEMIA AND HEALTHY SUBJECTS

Figures in parentheses shows the range values

Haematological parameters	Beta thalassa-emia (n=415)	Healthy popula-tion (n=185)	P value
Hb (g/dl)	12.08±1.34 (6.1-15.5)	14.5±0.73 (12.5-15.5)	HS
TRBC ($x10^{12}$/L)	5.94±0.64 (3.95-7.39)	5.01±0.50 (4.05-6.65)	HS
PCV (L/L)	0.358±4.21 (0.211-0.476)	0.400±0.023 (0.370-0.460)	HS
MCV (fl)	61.73±4.55 (48.3-75.6)	80.2±6.50 (78-91)	HS
MCH (pg)	20.33±1.76 (15.4-26.4)	29.2±2.101 (27.2-29.9	HS
MCHC (g/dl)	33.12±1.45 (27.7-38.0)	33.5±1.5 (30.7-36.2)	S
HbF (%)	0.89±0.15 (0.6-1.4)	0.9±0.22 (0.6-1.3)	NS
HbA2 (%)	5.36±0.57 (4.0-6.9)	3.1±0.27 (2.5-3.4)	HS
Retic (%)	1.6±0.45 (0.8-4.0)	1.8±0.66 (0.8-2.5)	S
Serum ferrtin (ng/ml)	43.0±18.5 (2-104)	74.0±30.5 (6-136)	HS

Key

HS = Highly significant (P<0.001)
S = Significant (P<0.05)
NS = Non-significant (P>0.05)
n = Number of subjects

TABLE – 2

hundred and ninety nine (96.1%) out of 415 subjects with heterozygous beta thalassaemia were Pathans and 16 (3.9%) belonged to miscellaneous group (Table 1).

Haemoglobin A_2 level ranged 4.0-6.9%, MCV of less than 77 fl was found in 100% and MCH of 26.4 pg or less in all subjects of beta thalassaemia trait (Table 2).

Altered red cell morphology such as hypochromic, microcytosis and anisopoikilocytosis were seen in all the cases. The frequency of consanguineous marriage in parents were first cousin 72%, second marriage 5%, distant cousin 4% and not relative 19% (Table 3).

DISCUSSION

The occurrence of hereditary haemoglobin disorders in Pakistan has been known for long time although the data is limited.[12] The actual magnitude of these hereditary disorders in Pakistan has been marked by infections and nutritional deficiencies. If this country overcomes these acquired diseases successfully, hereditary disorders including haemoglobinopathies would become important national problems.[13] The prevalence of beta thalassaemia carrier state found in the relative of beta thalassaemia major children is more than 50%.[14] The latest study done on the siblings of beta thalassaemia major children showed that the incidence of beta thalassemia trait among the sibling were 58% and male to female ratio of 0.9:1.[15] Consanguineous marriages are quite common in Pakistan and especially in Pathans. This social practice may have compounded the problems.[16]

All the ɓ-thalassaemia heterozygotes showed some degree of hypochromia with MCH ranging between 15.4-26.4 pg (median 20.33). Similarly 100% (415/415) of the carriers had MCV value of less than 77 fl. This finding is in concurrence with early study at Armed Forces Institute of Pathology, and with the major work done

FREQUENCY OF CONSANGUINEOUS MARRIAGES IN 100 FAMILIES

Relationship	No. of families	Percentage
First cousin marriage	72	72.0
Second cousin marriage	5	5.0
Distant cousin marriage	4	4.0
Not relative marriage	19	19.0
Total	**100**	**100.0**

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HbA2 (%)	5.36±0.57 (4.0-6.9)	3.1±0.27 (2.5-3.4)	HS
Retic (%)	1.6±0.45 (0.8-4.0)	1.8±0.66 (0.8-2.5)	S
Serum ferrtin (ng/ml)	43.0±18.5 (2-104)	74.0±30.5 (6-136)	HS

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TABLE – 3

HAEMATOLOGICAL DATA IN HETEROZYGOUS BETA THALASSAEMIA IN DIFFERENT STUDIES

(Figures in parentheses show the range values)

Authors	Race	Sex	No.	Hb (g/dl)	RBCx (1012/L)	MCH (pg)%	MCV (pg)
		M	32	11.8±1.5 (8.7-14.7)	5.60±0.60 (4.6-6.6)	21.5±1.3 (18.6-25.6)	70.5±4.2 (63.1-77.1)
Weatherall and Clegg (1981)	British						
		F	51	10.8±0.9 (8.4-12.5)	5.10±0.50 (4.30-6.70)	21.8±1.4 (18.8-25.1)	70.3±4.8 (63.0-82.1)
		M	64	11.6±1.5 (7.8-15.7)	5.2±0.7 (3.9-6.7)	22±2 (18-25)	74±5 (66-82)
Dincol et al (1979)	Turkish						
		F	81	10.3±1.2 (7.8-13.0)	4.7±0.6 (3.8-6.3)	21±2 (18-24)	74±4 (66-81)
		M	43	13.3±0.8 (11.4-15.3)	6.1±0.5 (5.0-7.4)	22±2 (14-25)	66±4 (59-85)
Galanella et al (1979)	Sardinian						
		F	107	11.8±0.9 (9.1-14.0)	5.4±0.4 (4.0-6.7)	22±2 (18-26)	66±4 (55.78)
		M	14	13.6±1.04 (11.6-15.1)	6.7±0.67 (5.1-7.58)	20.3±1.35 (17.9-22.7)	63.4±5.1 (58-76)
Khattak and Saleem (1992)	Pakistani						
		F	13	11.6±1.56 (9.1-13.8)	5.24±0.75 (4.15-6.64)	22.35±2.23 (18.6-25.3)	71.77±6.46 (62-82)
		M	26	9.54±1.46 (5.7-13.4)	4.77±0.98 (2.5-7.5)	21.15±4.67 (10.1-31.0)	90.75±11.25 (51-120)
Anjum (1999)	Pakistani						
		F	32	9.98±1.54 (4.2-13.9)	4.82±0.85 (3.0-6.6)	21.78±4.68 (8.4-36.0)	87.35±13.5 (51-125)
		M	210	13.02±1.22 (9.1-15.5)	6.3±0.66 (4.01-7.39)	20.5±1.57 (17.1-25.0)	62.1±4.43 (51.0-71.6)
Present study (2000)	Pakistani						
		F	205	11.07±0.78 (6.1-13.6)	5.63±0.62 (3.95-6.75)	20.16±1.76 (15.4-26.4)	61.35±4.45 (48.3-75.6)

TABLE – 4

earlier by Italians where MCV value of 77 fl or less was used as the main parameter for preliminary screening of thalassaemia trait[17] (Table 4). The estimation of MCV and MCH by electronic haematology analyzer appears to be extremely cost effective method of screening for b-thalassaemia heterozygotes.

Haemoglobin A2 level of 4.0% or more appears to be highly significant level for the diagnosis of heterozygous b-thalassaemia in the present study. This was supported by low MCV, low MCH and abnormal red cell morphology. Cousin marriages were found to be present in 77% (77 families) parents of the subjects in this study. This can be minimized by nation-wide inductive screening/population surveys and establishing special care centres in major cities where facilities for diagnosis, genetic counselling, prenatal diagnosis

and genetic studies using modern techniques of restriction enzyme analysis and treatment and health education of population are available.[18]

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