PREVALENCE OF HETEROZYGOUS B-THALASSEMIA IN NORTHERN AREAS OF PAKISTAN

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ABSTRACT

Five hundred apparently healthy adults from northern parts of Punjab and NWFP were screened for the prevalence of heterozygous fi-thalassemia. The trait was detected in all ethnic groups with an overall prevalence rate of 5.4% (27/500). Pathans had significantly (P <0.02) higher prevalence rate (7.96%) than Punjabis (3.26%) (JPMA 42: 32, 1992).

INTRODUCTION

Beta-thalassemia probably is the most common single gene disorder causing a major genetic health problem in the world. There are at least two hundred and forty million carriers for hemoglobinopathies throughout the world[1-3]. In a developing country like Pakistan, which has a large number of B-thalassemia major patients, the cost of instituting hypertransfusion and chelation programme on national scale is prohibitive. An alternative long term approach would be to reduce the number of these patients through prenatal screening and genetic counselling[4]. Identification of B-thalassemia carriers and provision of prenatal diagnosis of homozygous conception using oligonucleotide probes and restriction enzyme analysis[5,6]. followed by termination of pregnancy will allow couples at risk to avoid having children with B-thalassemia disease[7,8]. Presence of hereditary hemoglobin disorders in Pakistan has been known for last thirty years though the datais not so extensive[8-18]Present study was undertaken to find out the overall frequency of healthy carriers of B-thalassemia in northern Pakistani population.

PATIENTS AND METHODS

Five hundred healthy adult studentvolunteers aged seventeen to twenty-four years (mean 19 years) from educational institutions of Rawalpindi and Peshawar were studied (males 326, females 174). Ml were thoroughlyinterviewed and clinically examined specially for jaundice, hepatosplenomegaly and lymphadenopathy. The relevant information regarding age, sex, ethnic origin (caste/tribe) and place of birth/inhabitance, family history and consanguinitywere properly recorded. Anticoagulated whole blood was collected from antecubital vein. Dipotassium salt of ethylene diamine ten-acetic acid (K2-EDTA) at a concentration of 1.5 mg/nil of blood was used as anticoagulant. The samples were stored at 4°C until tested. Blood counts and red cell indices were measured by Coulter S7 haematology cell counter. The efficiency of this counter was monitored daily by internal as well as external controls from Coulter UK (4C). Red cell morphology was observed on Leishman stained blood film. Hemoglobin A2 level was measured by elution from cellulose acetate membrane and spectrophotometry by the method of Marengo-Rowe[19]. Hemoglobin F was measured by modified Betke method[20] based on its resistance to denaturation at alkaline pH. Serum ferritin was estimated by RIA method in all cases having microcytic/hypochromic blood picture with low MCV (<77 11) and B-thalassemia trait. Reticulocyte count was performed by brilliant cresyl blue vital staining. The criteria used for diagnosis of B-thalassemia trait were hemoglobin A2 level of _ 4.0% supported by MCV _ 7711, MCH _ 26 pg, altered red cell morphology and normal or raised serum ferritin level. The significance of difference in

distribution of cases in various categories was calculated by one sample Chi-square (x2) Non Parametric Statistical test using an IBM compatible PC and Statemode2 statistical package (Copyright 1986, 1987, G.J. & S.C. Coleman) based on Siegel[21].

RESULTS

Heterozygous B-thalassemia trait was detected in 5.4% (27/500) cases in this survey of apparently healthy adults (Table I).

TABLE I. Distribution of β-thalassemia trait in major ethnic groups.

Ethnic group	Males	Females	Cases	.(%)	P value
Punjabi	5/175	3/70	8/245	3.26	
Pathan	7/113	9/88	16/201	7.96	<0.02
Miscellaneous	2/38	1/16	3/54	5.55	
Total	14/326	13/174	27/500	5.4	

Sixteen out of 27 (59.3%) subjects with heterozygous B- thalassemia were Pathans and 8 (30%) were Punjabis. Hemoglobin A2 level ranged between 4.0-6.6%. MCV of 77 fi or less was found in 92.6% and MCH of 26 pg or less in all subjects of B-thalassemia trait (Table II).

TABLE II. Summary of hematological findings in β-thalassemia trait (n=27).

Haematological Indices	Median	Range
Hb (G/dl	12.9	9.1-15.
TRBC ($X10^{12}$/1	6.02	4.15-7.58
PCV (1/1)	0.411	0.322-0.508
MCV (Fl)	67	58-82
MCH (pg)	20.9	17.9-25.3
MCHC (G/dl)	31.6	28.9-33.3
Hb F (%)0.6	0.3-0.9	
Hb A2 (%)	4.8	4.0-6.6
Retics (%)	2.0	0.2-6.0

Altered red cell morphology such as hypochromia, microcytosis and anisopoilcilocytosis were seen in all the cases. The frequency of consanguineous marriages in parents of Pathans was more than in Punjabis, Pathans: 32.9% (66/201); Punjabis: 16.8% (41/245) (P<0.005).

DISCUSSION

The occurrence of hereditary haemoglobin disorders in Pakistan has been known for long time although the data is limited[18]. The actual magnitude of these hereditary disorders in Pakistan has been masked

by infections and nutritional deficiencies. If this country overcomes these acquired diseases successfully, hereditary disorders including haemoglobinopathies would become important national problems[22]. In the present study no population subgroup out of those screened was found to be free of this abnormal gene. But heterozygous B- thalassemia was found to be more prevalent in Pathans than Punjabis; Pathans: 7.96% (16/201); Punjabis: 3.26% (8/245) (P<0.02). Further, pattern of this disorder showed a uniform distribution in almost all Pathan tribes. The distribution in Punjabi population appears to be uneven that is less prevalent in main Punjabi ethnic subgroups of 'Rajput' and 'Arain'. Out of twenty-eight children of non-Punjabi immigrants included in present study only one carrier was detected. He had history of distant Pathan ancestry. Similarly, out of eight Punjabi carriers two had similar Pathan ancestry. This observation coupled with high prevalence of this defect in Pathan tribes of NWFP makes the earlier anthropological hypothesis of Caroe[9] and others about the racial ancestry of Pathans more convincing. They tried to connect the racial origin of Pathans and Kashmiris to the early invaders of this area throughout the history including Alexander's Greek army. Beta thalassemia trait has been found to be more frequent in Sayyad population of both Punjabis and Pathans which may be due to middle eastern ancestry and a higher incidence of intermarriages amongst the members of this subgroup. The only well organized study having comparable data on a healthy population of northern Pakistan is derived from asmall survey[9] which reported an incidence of 4% heterozygous B-thalassemia in 114 unrelated subjects of local Pathan tribes in Peshawar district of NWFP. Earlier studies at Lahore[16] and Rawalpindi[18] were carried out either on the anaemic patients attending clinics or their relatives undergoing family studies. This could be a reason for relatively higher prevalence reported (9.61% and 5.8% respectively) as compared to few small but organized population surveys done at Karachi (1.4%)[12] and Lahore (1.6%)[17]. All the B-thalassemia heterozygote showed some degree of hypochromia with MCH ranging between 17.9-25.3 pg (median 20.9). Similarly 92.6% (25/27) of the carriers had MCV value of 77 fi or less (Table II). This finding is in concurrence with the major work done earlier by Italians where MCV value of 77 fi or less was used as the main parameter for preliminary screening of thalassemia trait[23]. The estimation of MCV and MCH by electronic counter appears to be extremely cost effective method of screening for B-thalassemia heterozygote[24,25]. Haemoglobin A2 level of 4.0% or more appears to be highly significant level for the diagnosis of heterozygous B-thalassemia in the present study. This was supported by low MCV, low MCH and abnormal red cell morphology. Heterozygous B-thalassemia is present in almost all population groups of the country but its prevalence is higher in northern parts of Punjab and NWFP as compared to southern part of the country. In north Pakistan its prevalence is significantly higher in Pathans (7.96%) than Punjabis (3.26%) (P< 0.02). Cousin marriages were found to be present in 25% parents of the subjects in this study. This can be minimized by nationwide 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.

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In their study also Beta thalassaemia heterozygous was the most common hemoglobinopathy in that area closely followed by hemoglobin E heterozygous. In their study no outreach screening was there and they advocated a routine premarital screening program for identification and prevention of high-risk marriages.Â Documents Similar To Prevalence of Thalassaemia and Other Hemoglobinopathies In A Northern District Of West Bengal, India. Carousel Previous Carousel Next. 36366745k. The b-thalassemias are widespread throughout the Mediterranean region, Africa, the Middle East, the Indian subcontinent and Burma, Southeast Asia in-cluding southern China, the Malay Peninsula, and Indonesia. Estimates of gene frequencies range from 3 to 10 percent in some areas.9 Within each popula-tion at risk for b-thalassemia a small number of common mutations are found, as well as rarer ones; each mutation is in strong linkage disequilibrium with specific arrangements of restriction-fragmentâ€“. From the University of Toronto, Toronto.Â As a result of the decline in the synthesis of g-globin chains in patients with b-thalassemia, fetal hemoglobin production becomes insufficient to compensate for the excess of a-globin chains, the production of which is unaffected in b-thalassemia.