

# Distribution Pattern of Haemoglobinopathies in Northern Areas of Pakistan.

Pages with reference to book, From 106 To 109

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## Abstract

Of 1187 cases of refractory anaemias, 305 (25.69%) had thalassaemia and/or abnormal haemoglobins. Eighty three percent of these had B-thalassaemia and 17% abnormal Hbs with or without B-thalassaemia.

Seventy three percent cases with B-thalassaemia were homozygous and 27% heterozygous. Mean age in homozygous group was 2.9 years for males and 2.4 years for females.

Frequency of abnormal Hbs was higher in northern areas. Hb-s alone or with B-thalassaemia was found in 47%, Hb-E in 12% and Hb-D trait in 10% of cases. Hb-D punjab was found mainly in pathans. (JPMA 35: 106, 1985).

## Introduction

Hereditary disorders of Hb-synthesis, e.g. thalassaemias, and of Hb-structure e.g. Hb-S, Hb-C and Hb-D have a worldwide distribution. Thalassaemias are probably present in every racial and ethnic group if efforts are made to look for it, whereas Structural Hb defects are distributed within certain geographical and racial limitations, e.g. Hb-S and Hb-C is primarily an African and Negro characteristic whereas Hb-E is present mainly in the Far East and South East Asian populations. There is relatively little information about the incidence of thalassaemias and abnormal Hbs in Pakistan. Studies done in Karachi<sup>1-3</sup> suggest an incidence of 1.5% for beta-thalassaemia trait. About 4% Pathans in NWFP are similarly affected<sup>4</sup> and Hb-D Punjab has also been described in Pathans<sup>4</sup>.

The present study was done to determine the distribution pattern of hereditary Hb defects by a retrospective analysis of the cases referred to Armed Forces Institute of Pathology (AFIP), Rawalpindi, over a period of more than 10 years starting from 1972.

## Material and Methods

A total of 1187 cases of refractory anaemia with or without splenomegaly were referred to AFIP for Hb studies from July 1972 to December 1982 from Armed Forces as well as from the civilian population.

Complete blood count and reticulocyte counts were done by standard techniques<sup>5</sup>.

Hb-F was estimated initially by Alkali denaturation technique<sup>6</sup> and later by its modification of Betke<sup>7</sup>.

Hb-A<sub>2</sub> was estimated by the modified M orongo-Rowe method using cellulose-acetate strips and TRIS-EDTA-BORATE Buffer pH 8.9.

Hb-Electrophoresis was carried out on cellulose-acetate strips for 1 hour using TRISEDTA-BORATE Buffer pH 8.9. Sickling test, using sodium metabisulfite as a reducing agent, and sjckledex test, whenever available, were used to differentiate between Hb-D and Hb-S.

Appropriate controls were used at all stages.

## Results

A total of 305 cases (25.69%) of both thalassaemias and abnormal Hbs were detected. Male to female ratio was 2.2: 1. The cases were spread over a wide area extending from NWFP, including the tribal areas, to the Northern areas of Punjab upto Jhelum mainly and parts of Western Azad Kashmir. Thalassaemias had a more general distribution as compared to abnormal Hbs which came mostly from NWFP (mainly from tribal areas).

Of 305 cases with abnormal findings, 254 (83.23%) belonged to B-thalassaemia group and 51(16.73%) to abnormal Hbs either alone or in combination with B-thalassaemia. There was 1 case of Hb-H disease. Thus alpha-thalassaemia group had a very small representation (0.4%).

Of 254 B-thalassaemia cases, 185 (72.80%) were homozygous and 69 (27.20%) were heterozygous.

### Homozygous Beta-thalassaemias

Of 185 homozygous B-thalassaemia cases 122 were males and 63 were females, giving a male to female ratio of approximately 2: 1 (Fig. 1).

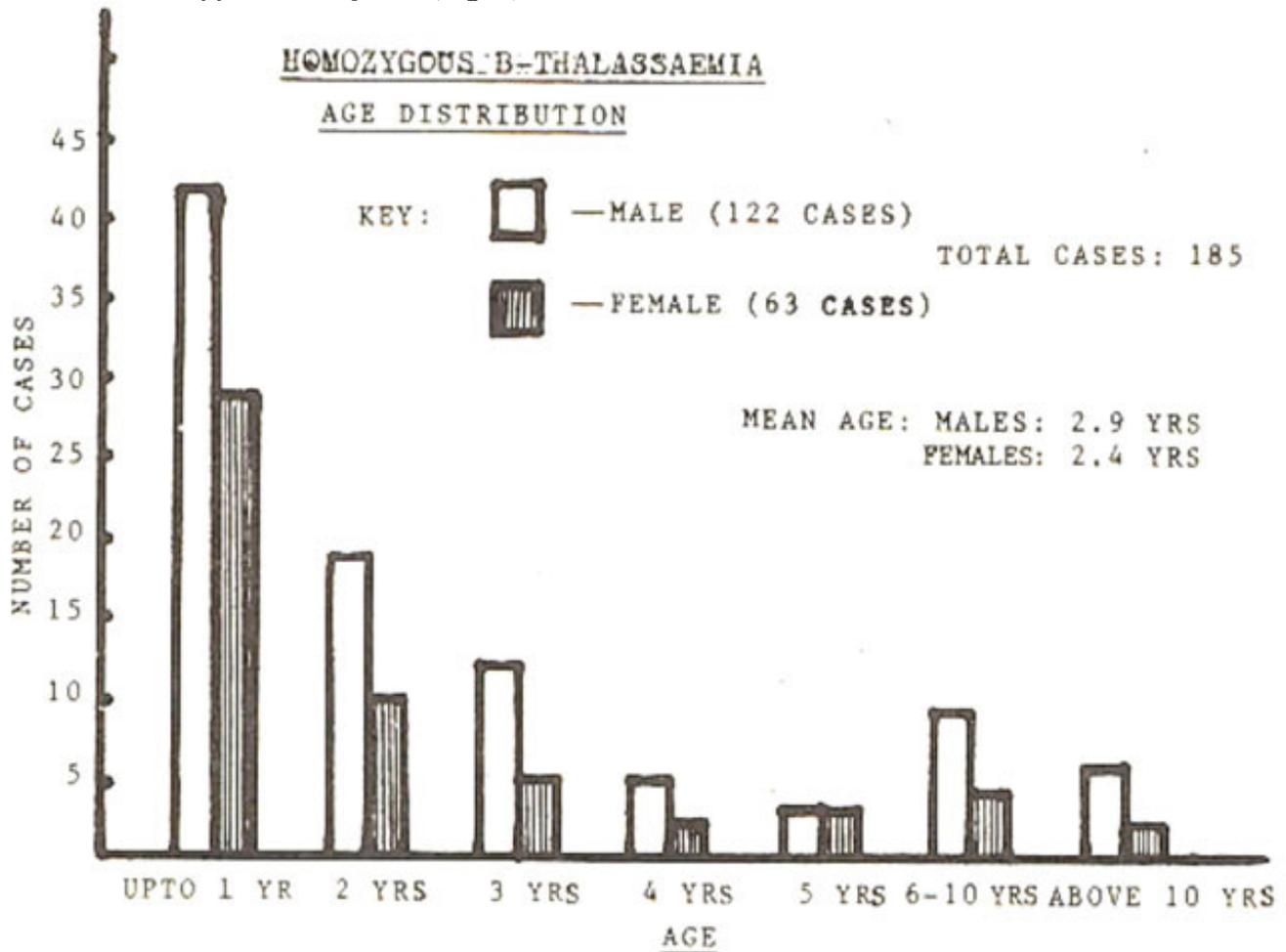


Fig - 1

Age at the time of presentation varied from 6 months to 10 years or even more the mean age being 2.9 years in males and 2.4 years in females (Figure 1). Hb-level at the time of presentation varied from 1.5 g/dl to 9.0 g/dl (mean Hb 4.6 g/dl).

Reticulocytosis was a persistent feature varying between 5% to as high as 30%.(mean 10%).

Hb.F level varied between 30-90%, mean level at presentation being 55% (Fig - 2).

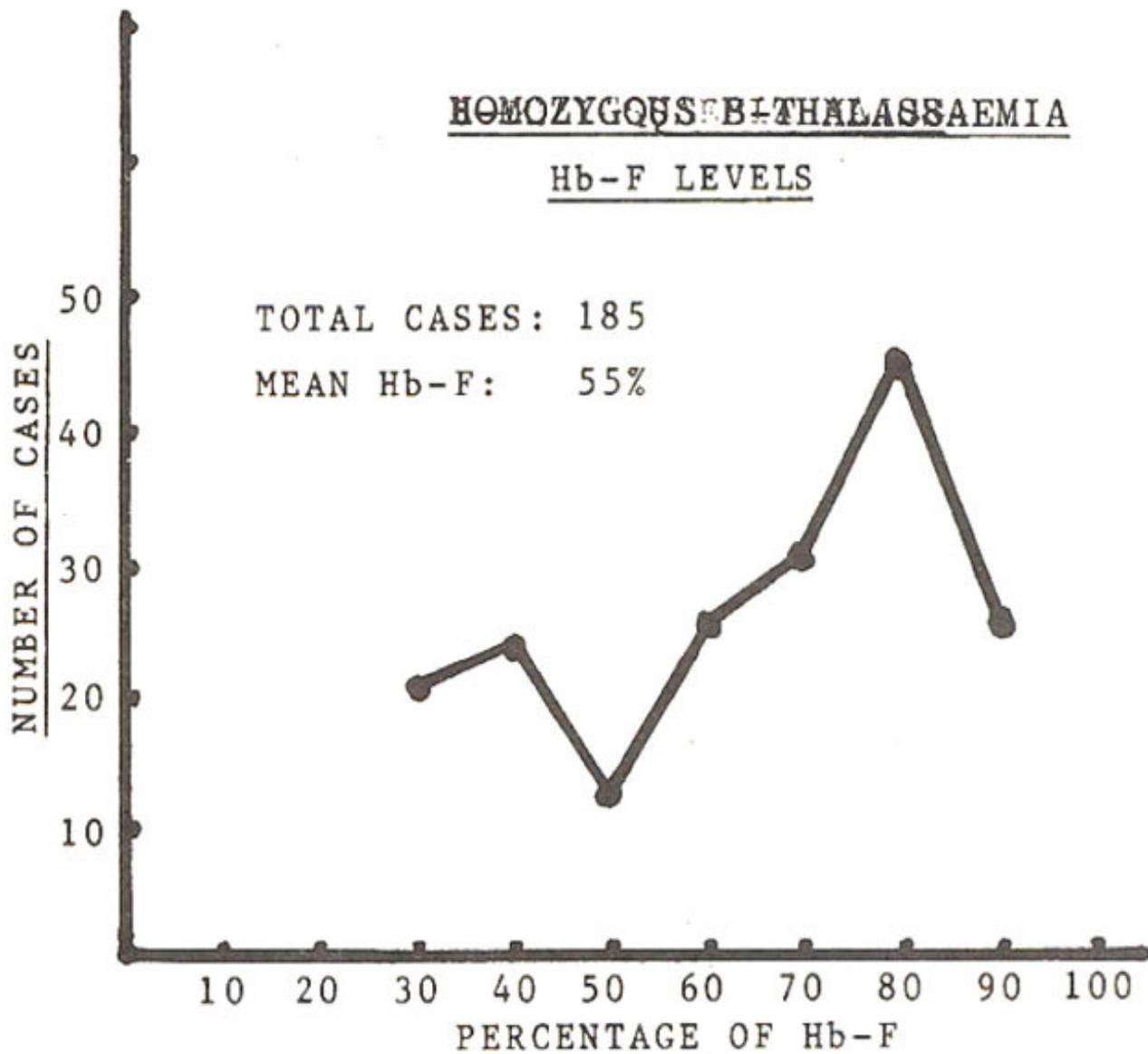


Fig 2

**Heterozygous Beta-thalassaemias**

Diagnosis of heterozygous B-thalassaemia in 69 cases was made either as part of family study or in pregnant women having unusually low Hb despite adequate administration of haematinics.

Hb-level in these cases varied from as low as 7.0 g/dl to as high as 15.0 g/dl (mean 10.8 g/dl).

Reticulocytosis was not a persistent feature though in occasional cases it was as high as 10%. fib-A<sub>2</sub>

level varied from 3.5 to 7.0% - mean A<sub>2</sub> level being 5.3%. One family had unusually high A<sub>2</sub> levels of between 8-9% (Fig - 3).

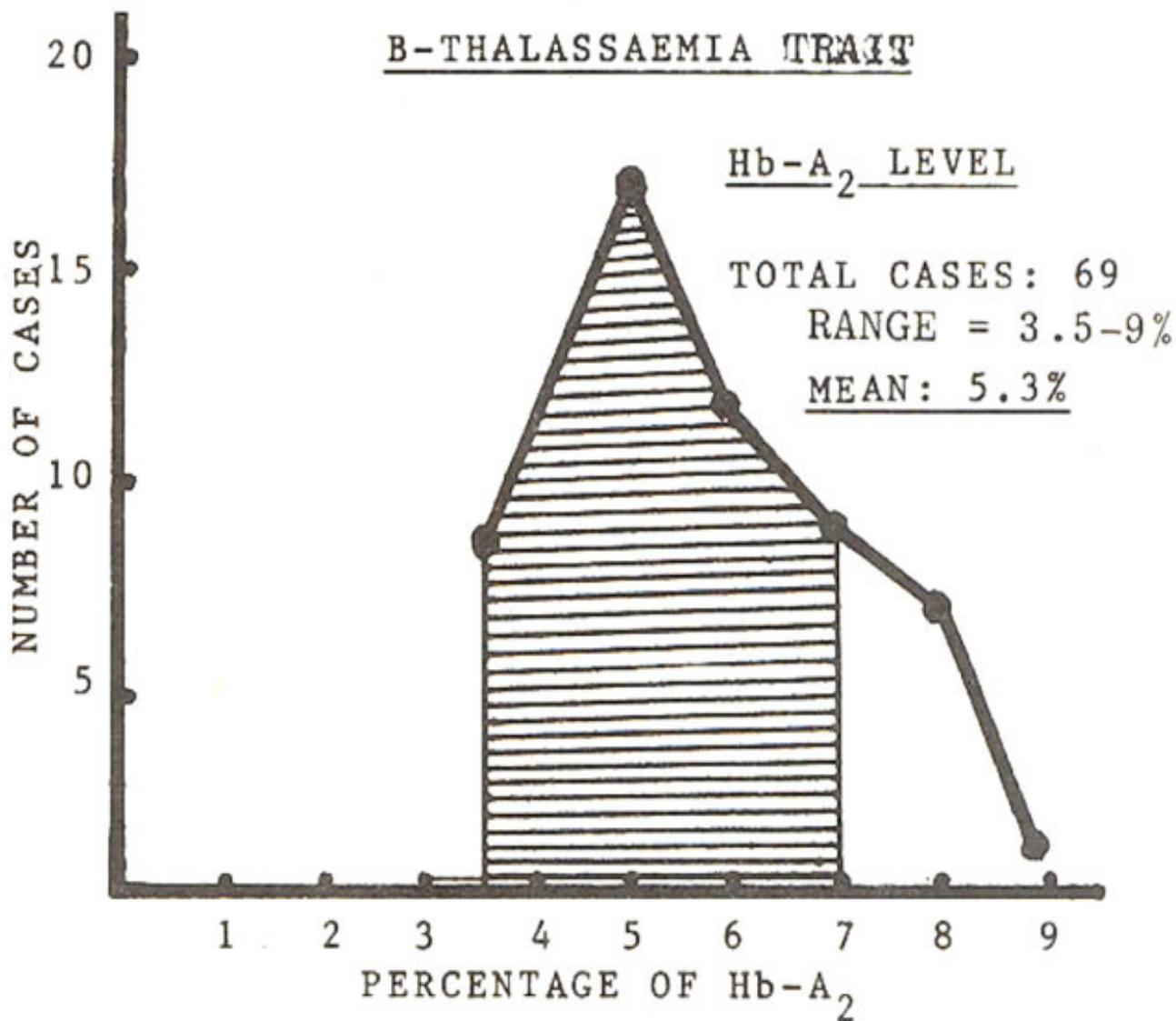


Fig 3

**Structural Hb defects**

The pattern of distribution of 51 cases of structural Hb defects is shown in Table- I.

**Table – 1**                      **Pattern of Distributuion**

Structural Hb Defects		
Hb–S Thalassaemia	11	21.56%
Hb–S Homozygous	01	1.96%
Hb–S Heterozygous	12	23.52%
Hb–C/E Thalassaemia	08	15.69%
Hb–C/E Homozygous	04	7.84%
Hb–C/E Heterozygous	03	5.89%
Hb–D	05	9.80%
Hb–H	01	1.96%
Hb–E Thalassaemia	01	5.89%
Hb–E Heterozygous	03	5.89%
<b>Total:</b>	<b>51</b>	<b>100.00</b>

Hb-S alone or in combination with B-thalassaemias, was present in 24 cases (47.0%).

Hb-E alone or with B-thalassaemia was present in 6 cases (11.76%) Hb-E was confirmed from WHO Reference Lab at Cambridge, U.K.

Hb-C/E was diagnosed when Mb-C could not be distinguished from Mb-F due to non-availability of Agar gel electrophoresis. Such cases, with or without B-thalassaemia, numbered 15 (29.4%).

**Five cases (9.80%) had F1b-D trait.**

Majority of Mb-S and Hb-D came from NWFP mainly from the tribal areas. Hb-E cases were from a family whose ancestors had migrated from Iran. Hb-C/E cases were from Punjab as well as NWFP.

### **Discussion**

This study reveals that hereditary defects of Hb synthesis are not uncommon in Northern areas of Pakistan. In fact there has been a gradual and progressive rise in the number of cases being diagnosed at AFIP with the present average being 50 cases per annum. Previous studies<sup>2,4</sup> have reported a 4% incidence of B-thalassaemia trait amongst Pathans and 1.5% amongst the population of Karachi. Our studies seem to support the more common prevalence of B-thalassaemia but the incidence appears to be

as common in Pathans as in non-Pathan population.

Mean age of homozygous B-thalassaemia cases in our study (2.9 years for males and 2.4 years for females) is higher than in other studies<sup>8,9</sup> where mean age was 13.1 months and more than 60% patients presented under the age of 1 year. The late presentation in this series appears to be related to the delay in realisation by the medical practitioners of the nature of underlying disease process with consequent administration of haematinics, especially iron, for long periods of time. The levels of Hb-F and presence of Mb-A in these cases is indicative of the presence of both and B<sup>o</sup> type of thalassaemia in our country.

Abnormal Hbs (Hb-D, Mb-C & Hb-S) have been reported to be present in 0.9% of the Karachi population<sup>2</sup>. Our study indicates a probably higher incidence in Northern areas of Pakistan, especially of Hb-S, amongst the tribal people of NWFP.

The presence of Hb-D Punjab reported previously in Pathans<sup>4</sup> has also been confirmed by this study. Presence of this Hb in Pathans is intriguing as it may help to form a link between its Eastern presence in Sikhs of India and its Western occurrence in Iran.

Hb-E has not been previously reported from this part of the world although it is known to occur in Bengalis<sup>10</sup>. No data are available about the prevalence of alpha-thalassaemia in Pakistan although the finding of Mb-H disease indicates that some form of abnormal alpha-thalassaemia gene does occur in our country.

Very scanty, if any, data are available about the prevalence of the hereditary defects of Mb synthesis in Pakistan. Organised and detailed studies are required to determine the exact gene frequencies of defects in order to assess their over-all impact at the national level. Not only is there a need for the establishment of special diagnostic and treatment centres but an effort has to be made to make the medical profession more conscious of the existence of these maladies. This would help in an early diagnosis of such cases so that the unnecessary and harmful effects of iron administration can be avoided. Proper treatment can, therefore, be instituted in time so as to prevent the gross Ramolies of growth and development from which these patients suffer and which are a source of great misery, not only to the patients themselves, but to the family as a whole.

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