

# To Determine the Frequency of Beta Thalassemia Trait in Siblings of Beta Thalassemia Major patients

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## ABSTRACT

**Aim:** To determine frequency of beta thalassemia trait in siblings of beta thalassemia major patients.

**Setting:** Sir Ganga Ram Hospital Lahore, Institute of Blood Transfusion, Children Hospital and Services Hospital Lahore

**Methods:** A total of 400 subjects were included in the present study and divided into two equal groups. Group I comprised of asymptomatic siblings of beta thalassemia major (BTM) patients and were further divided into two groups: IA with normal siblings of BTM patients and IB with beta thalassemia trait (BTT) siblings of BTM patients. Group II were age and sex matched healthy controls. Asymptomatic siblings of diagnosed cases of beta thalassemia major were included in this study and patients with history or diagnosis of any acute or chronic illnesses were excluded. Osmotic fragility, mean cell volume (MCV), haemoglobin electrophoresis were done.

**Conclusions:** Out of 200 siblings of beta thalassemia major (BTM) patients, 78% (156) were diagnosed as beta thalassemia trait (BTT). MCV was decreased in BTT siblings as compared to control group. Median corpuscular fragility (MCF) was reduced in BTT siblings (IB) as compared to control group.

**Keywords:** Beta thalassemia trait, Osmotic fragility, Hb electrophoresis.

## INTRODUCTION

The diagnosis of beta thalassaemia trait cases is essential to prevent births of homozygous cases by genetic counseling<sup>1</sup>. By this method alone the birth rate of thalassaemia major children can be reduced by as much as 90%<sup>2</sup>. Peripheral blood film of these cases shows microcytosis, hypochromia and anisopoikilocytosis and target cells<sup>3</sup>. It is based on finding microcytic red cells, target cells and basophilic stippling in peripheral blood film<sup>4</sup>. The red cell indices give a more reliable diagnosis. In the thalassaemia trait cases MCV and MCH are low while MCHC is normal<sup>5</sup>. The red cell count is often more than  $5.0 \times 10^{12}/L$ <sup>6</sup>. Haemoglobin electrophoresis is essential for definite diagnosis of beta thalassaemia trait. Raised HbA<sub>2</sub> >3.5% confirms diagnosis<sup>7</sup>. Fetal hemoglobin is also high in  $\beta$ -thalassaemia minor cases as was seen in 64% of subjects with  $\beta$ -thalassaemia minor<sup>3</sup>.

## METHODOLOGY

This study was carried out at thalassemia center, Sir Ganga Ram Hospital Lahore, Institute of Blood Transfusion, Children Hospital and Services Hospital, Lahore. A total of 400 subjects were included in the present study and divided into two equal groups. Group I comprised of apparently asymptomatic

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siblings of beta thalassemia major patients and was further divided into two groups i.e. IA with normal siblings of BTM patients i.e. HbA<sub>2</sub><3.5% and IB with BTT siblings of BTM patients i.e. HbA<sub>2</sub>>3.5%. Group II was age and sex matched healthy control subjects in Lahore. Asymptomatic siblings of diagnosed cases of beta thalassemia major were included in the study. Patients with history or diagnosis of any acute or chronic illness were excluded from the study. 200 subjects were selected. They were brothers and sisters of BTM patients.

## RESULTS

The detail of results is given in tables 1, 2, 3, 4, 5 & 6

Table 1: MCV In Group IA, IB, and II

MCV(fl)	IA	IB	II
Mean± SD	72.4± 5.4	62.8± 4.7	84.8± 6.71
Ranges	63.5-89.0	50-76	80-91
Total	44	156	200

IAvsIB p<0.01(HS) IBvsII p<0.01(HS) IAvsII p<0.05(s)  
IA=Normal Siblings of BTM patients, IB=BTT Siblings of BTM patients  
II=Normal Controls

Table 2: MCF In Group IA, IB, and II

MCF (%)	IA	IB	II
Mean±SD	0.40±0.04	0.34±0.04	0.42±0.03
Ranges	0.35-0.45	0.20-0.38	0.40-0.45
Total	44	156	200

IAvsIB p<0.05(s) IBvsII p<0.05(s) IAvsII p<0.05(s)

Table 3: HbA<sub>2</sub> In Group IA, IB, and II

HbA <sub>2</sub> (%)	IA	IB	II
Mean±SD	2.14±0.72	4.59±0.94	2.02±0.51
Ranges	0.8-3.4	3.6-7.1	1.2-2.9
Total	44	156	200

IAvsIB p<0.01(HS) IBvsII p<0.01(HS) IAvsII p>0.05(NS)

Table 4:HbF In Group IA, IB, and II

HbF (%)	IA	IB	II
Mean±SD	0.72± 0.12	2.1±0.69	0.91±0.69
Ranges	0.3-0.8	0.4-3.4	0.2-0.9
Total	44	156	200

IAvsIB p<0.05(s) IBvsII p<0.05(s) IAvsII p>0.05(NS)

Table 5: Siblings of BTM Patients

Normal Siblings (IA)		BTT Siblings (IB)	
n	%age	n	%age
44	22	156	78

## DISCUSSION

Out of 200 siblings of beta thalassaemia major patients, 156(78%) were detected to have beta thalassaemia trait, so the incidence of beta thalassaemia trait in the siblings of beta thalassaemia major patients is 78% in this study. Each offspring of a carrier couple at risk of having a child with thalassaemia major has a 25% chance of being normal, a 50% chance of heterozygosity and a 25% of thalassaemia major<sup>8</sup>. Beta thalassemsias occur in persons of Mediterranean origin, and to a lesser extent, Chinese, other Asians and African Americans<sup>9</sup>. A study was carried out on 200 thalassemic families in Bombay and the incidence was 48% among the siblings<sup>10</sup>. In Pakistan, among the various hemoglobin disorders, the heterozygous beta thalassemsias were commonest (59.15%) followed by the homozygous beta thalassemsias (30.99%)<sup>11</sup>. In Pakistan, the thalassaemia trait is quite frequent with a carrier rate of 5.4%.The disease is commoner in pathans (7.96%) than Punjabis (3.26%). The higher incidence in pathans is attributed to a higher rate of consanguineous marriages in them<sup>12</sup>.

In the present study, the MCV of beta thalassaemia trait subjects was 62.8±4.7fl (51—70fl). Mean corpuscular volume in the range of 49--74fl in 312 beta thalassaemia trait cases were observed by Pootrakul et al (1973)<sup>13</sup> whose values are in close agreement with the present study. In other studies, MCV in BTT subjects was decreased (67.1—71.1fl) by Tatsumi et al (1989)<sup>6</sup>, 59 --62fl by Calero et al (1990)<sup>14</sup>, 46--60fl by Galanello et al (1990)<sup>8</sup>, 58 --82 fl by Khattak and Saleem (1992)<sup>12</sup>, and 66.5—70.2fl by Saleem (1995)<sup>2</sup>. Raised HbA<sub>2</sub> level is the most important finding in the confirmation of beta thalassaemia carrier state. Some studies show that

HbA<sub>2</sub> level is affected by iron deficiency which decreases its level below the values for the diagnosis of carrier state<sup>8</sup>.

The mean±SD values of HbA<sub>2</sub> of beta thalassaemia minor subjects was 4.59±0.95 (3.6--8.4%) in the present study. These values are in agreement with the findings of various studies carried out in Pakistan and outside Pakistan i.e., 3.1-- 7.78% by Pootrakul et al(1973)<sup>16</sup>. While higher values were observed by Hashmi et al (1975)<sup>3</sup> i.e., 3.5—13.6% and lower values were in the range of 3.6—6.0% by Galanello et al (1990)<sup>8</sup> and Khattak and Saleem (1992)<sup>12</sup>. In the present study, the mean value of HbF was 2.1±0.69% (0.6—6.6). These results are in agreement with the values of other studies. The range of HbF by different studies was 0--7.8% by Pootrakul et al (1973)<sup>13</sup>, while lower HbF levels were reported in which its level was <1%<sup>14</sup>.

Moinuddin et al (2004)<sup>15</sup> conducted a study in the Institute of Hematology, Baqai Medical University, Karachi evaluating a modification of MCF as a screening tests for beta thalassaemia trait. In this study, hemolysis was measured by recording the optical density after centrifugation. The osmotic fragility index was calculated to be the ratio of the optical density of the hemolysate in 0.36% saline to the optical density(OD) of the hemolysate in distilled water, multiplied by 100. 95% (57 out of 60) of the hematologically normal donors had OD higher than 70%. Samples drawn from fathers of children with beta - thalassaemia major registered OD <70% in 75 % cases.

## CONCLUSION

Out of 200 siblings of Beta thalassaemia major (BTM) patients, 78% (156) are diagnosed as Beta thalassaemia trait (BTT).

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