

# Frequency of $\beta$ (Beta Thalassaemia) Trait and Haemaglobin E (HbE) Trait: Case Study in a Thalassaemia Carrier Detection Camp in Gurudas College, West Bengal, India

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## Abstract

Hemoglobinopathies include an array of disorders caused due to mutations in the alpha and beta chain of hemoglobin. Thalassaemia is an inherited blood disorder and is a significant public health alarm in India with many individuals not even knowing that they are carriers of this dreaded haemoglobin disorders. The South-east Asia region, which includes India, Thailand and Indonesia accounts for 50% of world carriers. Beta ( $\beta$ )-thalassaemia is the commonest single-gene disorder in the Indian population with an overall prevalence of 3-4%. This health burden<sup>1</sup> emphasizes the need for prenatal diagnosis and carrier status detection to contain the disease and reduce the load of the mutant alleles in the gene pool. A free carrier detection camp was organized by Gurudas College and conducted Thalassaemia Control Unit, (State Thalassaemia Control Programme, West Bengal), Haematology Department, Calcutta School of Tropical Medicine, Kolkata. This important event was in collaboration with the Inner Wheel Club of Cossipore, District 329. Frequency of  $\beta$  (Beta Thalassaemia) trait and HbE trait in a Thalassaemia carrier detection camp in Gurudas College, Kolkata 54 was within the national prevalence range.

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## 1. Introduction

Haemoglobinopathies are common genetic disorders of hemoglobin in which there is an abnormal production or structure of the haemoglobin molecule. World Health Organization (WHO) figures estimate that 7% of the world population is carrier for haemoglobin disorders. Hemoglobin is the oxygen carrying partner in RBC (red blood cells) and has four globin chains *viz.* two alpha and two beta each. Hemoglobinopathies include an array of disorders caused due to mutations in the alpha and beta chain of hemoglobin.

The clinical spectrum of these disorders varies from asymptomatic conditions to serious disorders like thalassemia major that requires regular blood transfusions and widespread medical care.<sup>1, 2</sup> Prevalence of haemoglobinopathies is on the rise worldwide. According to Madan *et al* in the year 2010 the frequency of beta-thalassemia trait ( $\beta$ TT) has variously been reported from 1% - 17% and it was 3.3% on an average<sup>3</sup>. This is of special importance in developing countries where it increases the burden of health care delivery system. Almost 70,000 infants are born with  $\beta$ -thalassaemia worldwide each year, and 270 million people are carriers of haemoglobinopathies<sup>4</sup>. It is estimated that 1.5% of the world's population are carriers of beta thalassemia- that is, at least there are 80 million to 90 million people with an estimated 60,000 new cases being born each year. The carrier rate varies between 0 to 17% in different ethnic groups<sup>5</sup>. The South-east Asia region (which includes India, Thailand and Indonesia) accounts for 50% of world carriers<sup>6</sup>. Beta thalassaemia carriers are asymptomatic but homozygous beta thalassaemia is a life-threatening disorder .

## 2. Thalassemia in India

Thalassaemia is an inherited blood disorder and is a significant public health alarm in India with many not knowing they are carriers of this haemoglobin disorders. India has a high prevalence of haemoglobinopathies<sup>7</sup>. Beta ( $\beta$ )-thalassemia is the commonest single-gene disorder in the Indian population with an overall prevalence of 3-4%<sup>8</sup>. About 10% of the total world

thalassemics are born in India every year<sup>9</sup>. Certain communities in India, like Sindhis, Gujratis, Punjabis, and Bengalis, are more commonly affected with beta thalassemia, the incidence varying from 1 to 17%<sup>10</sup>.

### 3. Types of Thalassaemia

Thalassaemias are genetic disorders characterized by reduced synthesis of either alpha or beta chain of hemoglobin. The two main types are called Alpha and Beta thalassemia, depending on which part of globin chain is produced in reduced amounts.

#### Alpha Thalassemia

Normally, alpha globin chain is made by four genes (two from each parent), two on each strand of chromosome 16. The alpha thalassemias are caused by a decrease in production of alpha globin chains due to deletion or mutation of one or more of the four alpha globin genes located on chromosome 16<sup>11</sup>.

#### Beta Thalassemia

There are more than 200 mutations within the beta globin gene found worldwide to produce beta thalassemia. Unlike the deletion that constitutes most of the alpha thalassemia syndromes, beta thalassemias are caused by mutation on chromosome 11 that affect all aspects of beta globin production: transcription, translation, and the stability of the beta globin production. Most of the patients with severe forms of  $\beta$ -thalassaemia i.e. thalassaemia major need lifelong treatment including blood transfusion, iron chelation etc. The thalassaemia syndromes particularly the beta thalassaemias and some alpha thalassaemias are the major cause of morbidity<sup>12</sup>. Hemoglobin E (HbE) is an extremely common structural hemoglobin variant that occurs at high frequencies throughout many Asian countries. It is a  $\beta$ -hemoglobin variant, which is produced at a slightly reduced rate and hence has the phenotype of a mild form of  $\beta$  thalassemia.

Thalassemia can be categorized into three classes depending on clinical expression:

1. thalassemia major (TMA), a severe disorder leading to transfusion dependence;
2. thalassemia intermedia (TI), relatively milder involving less transfusion dependence; and

- thalassemia minor (TMI), where individuals carry the heterozygous mutation but do not exhibit any of the symptoms and usually do not require blood transfusion and are commonly referred to as Thalassaemia carriers.

#### 4. Inheritance of Thalassaemia

The inherited genetic diseases of haemoglobin are controlled by a single gene that transmits from parents to offspring from one generation to another affecting millions of people throughout the world. The two main types of thalassemia are alpha and beta. Both types are inherited in the same manner. Parents who carry the mutated thalassemia gene can pass it on to their child. A child who inherits one mutated gene is considered to be a carrier, which is sometimes called thalassemia trait. Most carriers lead completely normal, healthy lives

If both parents have TMI there exists a 25% probability in each pregnancy that their child will have TMA, a 50% probability that the child will have TMI and a 25% probability that a child will have neither mutation<sup>2, 13</sup>.

##### **Hemoglobin E (HbE) carrier**

Hemoglobin E trait does not pose health concern, although individuals with this trait may have smaller than normal red blood cells. HbE is synthesized at a slightly reduced rate and homozygotes show mild globin-chain imbalance, similar to that observed in  $\beta$ -thalassemia heterozygotes. It is caused by a base substitution at codon 26 of the  $\beta$ -globin gene, GAG-AAG, which results in the substitution of lysine for glutamic acid. This mutation also activates a cryptic splice site that causes abnormal messenger RNA processing<sup>14</sup>. Because the normal donor site has to compete with this new site, the level of normally spliced  $\beta^E$  messenger RNA is reduced<sup>15</sup>, resulting in the clinical phenotype of a mild form of  $\beta$  thalassemia. Being a carrier of haemoglobin E will not generally cause any health problems. However, red blood cells of HbE carriers may be smaller than usual and their haemoglobin level may be slightly lower than normal. This may be confused with iron deficiency anaemia. But as a carrier, there is a chance that they could pass on the gene for haemoglobin E to any children that they have.

However if one member of a couple has hemoglobin E trait, and the other has beta thalassemia trait, there is a 25% chance with each pregnancy that their child will co-inherit both traits. This leads to a disease called hemoglobin E/beta thalassaemia in that child. These individuals make little or no normal adult hemoglobin and may need blood transfusions.

## **5. Reduction of Thalassaemia Incidence by Population Screening and Counselling**

$\beta$ - thalassaemia is a preventable disease through comprehensive strategy at community level<sup>16</sup>. In India, nearly 30 million people are carriers of beta thalassemia and 7000 babies with beta-thalassaemia major are born every year<sup>17</sup>. This health burden emphasizes the need for prenatal diagnosis and carrier status detection to contain the disease and reduce the load of the mutant alleles in the gene pool. High cost of treatment, repeated blood transfusion and chelation therapy, and economic burden on family resources, all suggest that prevention is better than cure. Thus a joint venture of antenatal and inductive screening seems to be the most fruitful strategy for beta thalassaemia in India. With improving environmental and socio-economic conditions, better public health care and medical facilities and better nutrition, children suffering from thalassaemia and hemoglobinopathies can be better managed and rehabilitated in India<sup>18</sup>. HPLC is considered as one of the best methods for screening and detection of various hemoglobinopathies with rapid, reproducible and precise results. It is recommended for detection of  $\beta$ -thalassaemia trait in population and necessary for genetic counseling to reduce the incidence and burden of thalassemia major in the society<sup>19</sup>.

## **6. Awareness Seminars and Thalassaemia Carrier Detection Camps**

The international situation changed in 2006 with the recognition by the Executive Board of the World Health Organization that thalassaemia and sickle cell anaemia were major global health problems which needed to be urgently addressed, a move reinforced by their inclusion in the current Global Burden of Disease Study. Preventive strategies involving identification of carriers, genetic counselling and prenatal diagnosis have now almost eliminated the risk of new children with homozygous thalassaemia in countries which were once known for the highest prevalence of thalassaemia. A reduction in the birth rate of babies with thalassemia major from 1: 250 to 1: 4000 over the years has been reported in Sardinia<sup>20</sup>. Accurate and timely screening

of various Hb variants including  $\beta$ -thalassemia traits before marriages of couples at risk and prenatal diagnosis can prevent the occurrence of more serious disorders like thalassemia major in newborns substantially. The carrier rate varies between 0 to 17% in different ethnic groups<sup>5</sup>.

## 7. Material and Methods

The present study attempted to find out the prevalence of  $\beta$ -thalassemia trait and other hemoglobinopathies especially HbE trait in the population screened on 19<sup>th</sup> November 2013 in Gurudas College, Kolkata 700054. An attempt was made to spread the awareness about importance of thalassaemia trait testing before marriage among the students. Awareness campaign was conducted by members of Nandana, the Women Empowerment Cell of Gurudas College. Awareness regarding thalassemia was created in the vicinity of camp site by putting up notices, distributing pamphlets, personal meetings and counseling sessions with the students. To highlight the need for this test and posters provided by the State Thalassaemia Control Programme, West Bengal were put up around the camp site. The reason behind pre marital screening was emphasized.

A total of 100 persons participated in the thalassaemia carrier camp held on the premises of Gurudas College, Kolkata 54. Among the 100 (hundred) participants 6 were faculty members and 1 non teaching staff. There were 93 students with age group ranging from 18 to 23 years who participated in this carrier detection camp and were screened for various hemoglobinopathies. This free carrier detection camp was conducted Thalassaemia Control Unit, (State Thalassaemia Control Programme, West Bengal), Haematology Department, Calcutta School of Tropical Medicine, Kolkata. This important event was in collaboration with the Inner Wheel Club of Cossipore, District 329.

## 8. Results

A total of 4 participants (4%) were diagnosed with beta ( $\beta$ )-thalassemia trait and 3 participants (3%) were diagnosed with Hb- E trait as shown in Table 1.

**Table 1. Details of the Thalassemia Carrier Detection Camp at Gurudas College**

Sl no.	Camp No.	Date	Total	Normal	Beta ( $\beta$ -thalassemia Carrier	Hb- E carrier
1	1	19/11/2014	100	93	4	3

## 9. Discussion

The carrier rate varies between 0 to 17% in different ethnic groups<sup>5, 21</sup>. The frequency of beta-thalassemia trait ( $\beta$ TT) has variously been reported from 1% to 17% and an average of 3.3%<sup>3</sup>. Frequency of  $\beta$  (Beta Thalassemia) trait and HbE trait in a Thalassemia carrier detection camp in Gurudas college campus was within the national prevalence range. Identification of carriers is an essential part of prevention programs. Education and awareness regarding thalassemia need to be accelerated urgently among medical practitioners, paramedics, thalassemic and general population to reduce the morbidity and mortality and the financial and socio-psychological burden of the thalassemic families. Prospective prevention through population screening and genetic counseling is the best possible strategy in the prevention of these disorders<sup>22</sup>. The strongest argument for prevention is that it would ensure the best possible care for the affected, by curbing the increase in their number. The siblings, parents of the carriers detected and other family members would undergo a counseling session and carrier detection in a subsequent camp.

## 10. Conclusion

Pre marital screening among students, especially college going if made mandatory could have a great impact on reducing the incidence of thalassaemia. All individuals should be aware of their haemoglobin status before they contemplate marriage. If a certain carrier does not marry another carrier then the probability of a child with thalassaemia from such marriage becomes nil. However if two carriers marry they have 25% chance of having a child with thalassaemia so in that case prenatal tests should be mandatory.

Perhaps lack of awareness among students is a major deterrent towards 100% screening amongst the students. Parallel awareness seminars that lucidly explain the inheritance and subsequent prevention of this disease will clear doubts in the minds of students. More such camps need to be carried out. As these camps by State Thalassaemia Control Programme, West Bengal is totally free of charge this could be an added incentive.

Further research on frequencies and prevalence of different traits is required in establishing regional database. Findings must be supplemented with hemogram findings, family/sibling studies, other confirmatory techniques and molecular studies based on HPLC findings. This is especially important in view of high incidence of  $\beta$ -thalassemia trait in the Indian subcontinent.

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