

## Impact of consanguinity marriage on developing type 1 diabetes in beta thalassemia children

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### ABSTRACT

**Objective:** To find impact of consanguinity marriage on developing diabetes in a group of thalassemia children.

**Methodology:** A cross sectional study carried out from October 2016 to June 2017 at thalassemia centers of Lahore city. One hundred and fifty beta thalassemia major children with age range 4 to 8 years receiving regular blood transfusion were recruited by purposive sampling. Structured questionnaires were filled by the consented parents of children.

**Results:** Among total number of thalassemia patients, the frequency of male was 100 and of female was 50. The frequency of male and female diabetic thalassemia children was 25 (25 %) and 25 (50%) respectively. Frequency of general consanguinity was 148(98.66%). Weak correlation of fasting blood sugar with consanguinity in diabetic thalassemia children was observed.

**Conclusion:** Consanguinity marriages may have a role on developing diabetes in thalassemia children.

**KEYWORDS:** Beta thalassemia, Consanguinity marriages, Diabetes.

### INTRODUCTION

Thalassemias are the known hereditary ailments worldwide. Globally, 15 million individuals have the disorder of thalassemia and its incidence is very high in developing countries like Pakistan, Bangladesh, India and other Asian countries, where thalassemic children require regular blood transfusions to withstand life, as this may be reason of overload of iron resulting dysfunction of liver, pancreas etc.<sup>1,2</sup> Consanguineous marriages (CM) are very common globally especially in Pakistan, Lebanon, Turkey, North America, Africa, Australia and Europe and it is the main reason for increasing the occurrence of the

thalassemia. Consanguinity is demarcated as marriage between first /second cousins.<sup>3</sup> The Consanguinity is a complex and multifaceted characteristics with biological and socio cultural debates on its advantages and disadvantage. The negative effects of CM are the late development of multifaceted disease including the diabetes, heart problems, schizophrenia and others as these are heterogeneous etiologically in many of the families.<sup>4,5</sup> Highly susceptible genes may have an important role in expression of these multifaceted diseases, and if these genes are spread in an autosomal recessive style then consanguinity may be a causative factor.<sup>6</sup> In well-chelated thalassemia children the incidence of diabetes was 9% which may increase further from 20 to 30 %, depend on the age and chelation intensity.<sup>7</sup> Diabetes is more suspected in thalassemia children due to iron-induced toxicity. It is proposed that accumulation of iron in pancreatic beta cells of thalassemia patient may alter glucose tolerance resulting in overt diabetes. However, the actual mechanisms of iron-stimulated diabetes are not known. It is proposed that deficiency of insulin, resistance of insulin, dysfunction of liver and genetic issues may be the reason of developing diabetes in thalassemia patients.<sup>8,9</sup> It is experimentally proved that altered fasting blood glucose is seen in subjects having consanguineous marriages and this may increase the risk of developing diabetes in their generation.<sup>10</sup> The biological outcome of consanguinity comprises the increased level of homozygosity, which may increase the risk of genetic diseases at the level of population and family.<sup>2</sup> Regular transfusion of blood raises the chances of endocrinological link diseases like type 1

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diabetes. Iron over load is the main reason of complication of endocrinopathy in patients of thalassemia. In some patients, iron may accumulate in pancreas and may interrupts the function of pancreatic cells that may results diabetes.<sup>6</sup> Besides consanguinity may have a role to increase the chances of developing diabetes by consolidation of the genetic effects on fasting blood glucose.<sup>7</sup> Number of studies were carried out to observe the association between consanguinity and genetic conditions /health problems like diabetes, heart disease, mental disorder, immunodeficiency disorders, hypertension, beta-thalassemia, low birth weight and Down syndrome. This proves the role of genetic elements across the complete spectrum of ailments.<sup>5</sup> Studies showed that many organs like liver, pancreas and others may be effected. However we tried to find out the relationship of consanguinity with type 1 diabetes in thalassemia children which may be an extra burden in the management of health issues in thalassemic children. This study may help the medical experts to plan chelating procedure, and tried to prevent the children to develop diabetes and other complications. Study was tried to found the impact of consanguinity marriage on developing diabetes in a group of thalassemia children.

## METHODOLOGY

A study based on correlation analysis of frequency distribution was carried out from October 2016 to June 2017 at thalassemia centers of Lahore city after obtaining ethical approval from the institute (F-39 /NHRC/ admn /IRB/). One hundred and fifty beta thalassemia major children with age range 4-8 years receiving regular blood transfusion were included through purposive sampling technique. Children with co-existing medical conditions have co morbidity of other chronic disease like cardiac and renal diseases were excluded from the study.

A detailed history and physical examination were done. Liver size and spleen sizes were noted. Questionnaire was filled by consented parents of children. Thalassemia major was diagnosed by sign and symptoms and electrophoretic report of hemoglobin. Children with no history of diabetes were included in the study.

Blood samples of all children was drawn after overnight fasting ( 8- 10 hour). Estimation of blood glucose was carried out by standard kit using Auto analyzer. Level of serum insulin was estimated by

ELISA. HOMA-IR index was used to calculated insulin resistance (fasting blood sugar x fasting insulin /22.5) and cut off value was taken as 2.27. Fasting blood glucose less than 100 mg/dL was taken as indicator of standard glucose tolerance. Altered fasting blood was found, when the level of fasting blood glucose is in between of 100 & 126 mg/dl.<sup>14</sup>

**Statistical analysis:** The data was analyzed by SPSS version 20. Categorical variables were expressed as frequency and percentages. Pearson Correlation Coefficient was used to find the correlation between fasting blood sugar and consanguinity in diabetic thalassemia children.  $P < 0.05$  is taken as significant.

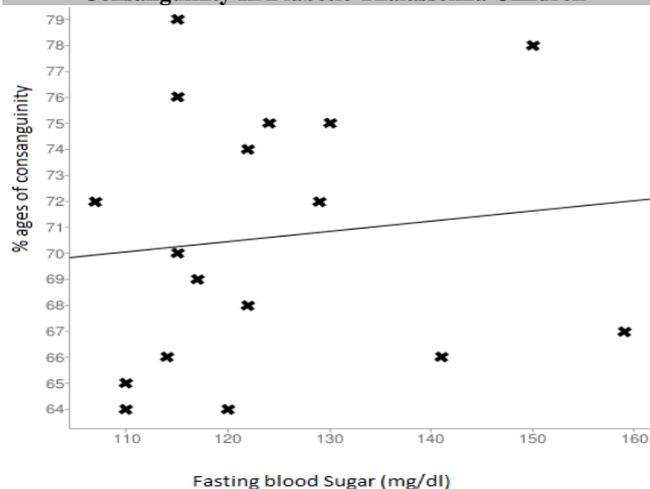
## RESULTS

Distribution of thalassemia children in relation of consanguinity and progression of diabetes is tabulated as table1. Among total number of thalassemia patients, the frequency of male was 100 (66.66 %) and of female was 50 (33.3 %). Frequency of Family history of thalassemia was observed in 70 (46.66 %).

**Table 1: Distribution of Thalassemia Children in Relation of Consanguinity and Progression of Diabetes (N=150)**

Characteristics	Frequency (n)	Percentages (%)
Male thalassemia children	100	66.6
Female thalassemia Children	50	33.3
Family history of thalassemia	70	46.66
Diabetic male thalassemia children	25	25
Diabetic female thalassemia children	25	50
General Consanguinity	148	98.66
Consanguinity		
First cousin	100	67 %
2nd cousin	48	33 %
Consanguinity ratio in male /female	2:1	-

The frequency of male and female diabetic thalassemia children was 25 (25 %) and 25 (50%) respectively. Insulin resistance was more frequently found in female as compared to male diabetic

**Figure 1: Correlation Of Fasting Blood Sugar With Consanguinity In Diabetic Thalassemia Children**

Weak correlation of fasting blood sugar with consanguinity in diabetic thalassemia male /female children ( $r = 0.11$ ).

thalassemic children (2.9 versus 1.3). Frequency of general consanguinity was 148 (98.66%) (Table1). Frequency of first cousin consanguinity was 100 (67 %) and of 2<sup>nd</sup> cousin were 48 (33 %). The consanguinity ratio in male / female was 2:1. Fasting blood glucose of diabetic thalassemic children was  $135.50 \pm 10.50$  mg/dl. Weak correlation of fasting blood sugar with consanguinity in diabetic thalassemia children was observed with  $r$  value 0.11 with  $p$  value 0.58 (Fig1).

## DISCUSSION

Endocrine complications are the known complications in  $\beta$ -thalassemia and are mostly credited to overload of iron. Regular blood transfusion may increase the risk of developing type 1 diabetes, as excess of iron deposition in  $\beta$  cells of pancreas. This iron deposition may decrease the secretion of insulin and results in hyperglycemia.<sup>15</sup> Among total number of thalassemia patients, the frequency of thalassemia in male was greater than female. We agreed with a study who observed that majority of thalassemia patients were males<sup>16</sup>. However studies found that gender differences in expression profiles of thalassemia patients proposing that females and males are differentially pretentious by the  $\beta$  thalassemia.<sup>17,18</sup> The frequency /percentage of both male/female diabetic thalassemia children were 33%. However a study found 16.1% of thalassemic patients had diabetes.<sup>19</sup> Another study noted that the incidence of diabetes in thalassemia children was 17.5%.<sup>9</sup> Frequency of first cousin consanguinity was 100 (67 %) and of 2<sup>nd</sup> cousin were 48 (33 %). According

to an Iranian study the incidence of thalassemia is 3.6% and consanguinity based incidence is 0.6%.<sup>20</sup> According to some studies the frequency of cousin marriage is 133(74%) and 135 (74%). It is stated that consanguineous marriages possibly play an vital role in the spreading of  $\beta$ -thalassaemia.<sup>21,22</sup> A Sri Lankan study found that consanguinity rate in beta thalassemia patient was 14.5%, in Tamil population it was 44 % and 12 % in Sinhalese.<sup>23</sup>

According to our study the frequency of male/female diabetic thalassemia children was 25 (25%) and 25 (50%) respectively with impaired fasting glucose and insulin resistance. Insulin resistance was more in female as compared to male diabetic thalassemic children. According to study carried out in Iran, the incidence of diabetes in Iranian thalassemic major patients was 9.0 % and estimated degree was 12.60% for thalassemic males and 10.80 % for thalassemic females. In these patients there are high percentages of impaired fasting glucose and glucose tolerance.<sup>24</sup> A study also reported that Diabetes is link with Thalassemia Major. Study found that long term blood transfusion may be the reason of impaired fasting glucose and diabetes in thalassemia patients.<sup>25</sup> It is proposed that pancreatic iron is a powerful predictor for glucose metabolism and also for cardiac iron and complications. Impaired fasting blood glucose, blood glucose tolerance, and diabetes in thalassemic patients is also noted.<sup>7,9</sup>

Weak correlation of fasting blood sugar with consanguinity in diabetic thalassemia children was observed. Number of studies observed the incidence of diabetes in thalassemia children. It is proposed that accumulation of iron in pancreas may be a reason of the risk of diabetes depend on the duration of iron overload.<sup>9</sup> Another study state that there may be role of deficiency of insulin, dysfunction of liver and genetic impact of consanguinity that may start in early.<sup>11,19</sup> Additionally a study found that due to regular transfusions, pancreatic iron may cause impaired glucose tolerance and overt diabetes.<sup>9</sup>

**Limitations:** Study has no information of iron load, only estimated via the iron take through transfusion.

## CONCLUSION

Consanguinity marriages may have a role on developing diabetes in thalassemia children. However, more studies are needed to find the impact of Consanguinity marriages on developing diabetes in beta thalassemia children.

**Recommendations:** It is suggested that there is a need of awareness of risk of complications of beta-

thalassemia after family marriage via pre-marriage psychotherapy is necessary.

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***Author's Contribution:***

<b>Rukhshan Khurshid</b>	Concept, study design, data collection, literature search, analysis, first draft write- up
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<b>Muhammad Shahroz Hamza</b>	Data analysis, final review, overall supervision
<b>Shakil Ahmad</b>	Data analysis, revised and approved the article
<b>Iram Fayyaz</b>	Data analysis, revised and approved the article for intellectual content.
<b>Huma Ashraf:</b>	Manuscript drafting, data analysis, revised and approved the manuscript.
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