



## KNOWLEDGE OF THALASSEMIA AND CONSANGUINITY: A MULTICENTER HOSPITAL BASED RETROSPECTIVE COHORT STUDY FROM METROPOLITAN CITY OF KARACHI, PAKISTAN.

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**ABSTRACT... Objectives:** To find the association between consanguinity and frequency of b-thalassemia and to assess the knowledge of parents regarding disease as well as inclination towards premarital carrier screening (PMCS), pre natal diagnosis, pre conception genetic counseling. **Study Design:** A retrospective cohort study. **Setting:** Patients with beta thalassemia attending Fatimid Foundation and PNS Shifa Hospital, Karachi. **Period:** Six Months July – December, 2017. **Materials and Methods:** Data was collected by pre tested questionnaire which include basic demographic profile, frequency of consanguineous marriages and knowledge regarding disease from parents of children suffering from thalassemia. The study was approved by ethical review committee. Data was analyzed using SPSS version 21. Chi square test was applied. **Results:** Data was collected from 200 study participants including parents of thalassemia. Males were 52% and 48% were the females. 78.5% were relatives ( $p=0.001$ ) out of these related, first degree relatives were 61% and 17.5% were distant relatives ( $p=0.009$ ). Only 25% were aware of genetic counseling, 65% know that thalassemia had genetic mode of transmission ( $p=0.005$ ), 24% were aware of screening modalities available for thalassemic patients ( $p=0.001$ ). About 63.55% agreed that premarital screening can prevent thalassemia ( $p=0.001$ ), majority (83%) of parents were not aware of pre natal diagnosis of thalassemia ( $p=0.001$ ) more than half of study participants (52%) were still in favor of cousin marriages in future. **Conclusion:** Thalassemia was found most prevalent among first degree familial relatives. Parents have inadequate knowledge regarding disease. Lack of knowledge and trends consanguineous marriages are strong contributory factor for causation of disease.

**Key words:** Autosomal Recessive Disorder, Consanguinity, Thalassemia.

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## INTRODUCTION

Thalassemia is group of autosomal recessive disorder characterized by low production of hemoglobin due to defective synthesis of alpha and beta chain leading to increase destruction of red blood cells. Depending upon involvement of globin chain it is classified as alpha and beta thalassemia.<sup>1</sup> Globally it is second most common hemoglobinopathy after sickle cell disease.<sup>2</sup>

Thalassemia has emerged as significant public health issue. According to World Health Organization (WHO) report, this is the most prevalent genetic blood disorder in the world. Recent study documented that approximately 9 million thalassemia carrier women become pregnant annually and 1.33 million children are

at risk of thalassemia major.<sup>3</sup> It has been also estimated that globally 56, 000 conceptions cause thalassemia, out of these 30,000 are affected by beta thalassemia.<sup>4</sup>

Frequency of beta thalassemia is higher in tropical and sub-tropical regions of Mediterranean countries, South East Asia, Middle East and Indian subcontinent. The highest carrier frequency is reported in Cyprus (14%), Sardinia (10.3%), and Southeast Asia (1-9%).<sup>5</sup> In Pakistan it is most common inherited disorder. There is no documented national registry of patients however data from different centers report that around 22,000 registered patients which are being treated at different thalassemia centers.<sup>6</sup> More than this figure is of children residing in villages

which are not registered to any Centre. Due to lack research at national level accurate data is nonexistent at population level. Data available is mostly from hospital based and selective small scale studies at local level.<sup>7</sup> Data from these studies suggest that prevalence rate of beta thalassemia is around 5-9% and approximately 9 million carriers of beta thalassemia producing around 4,000 to 9,000 new births every year of transfusion dependent thalassemia with average life expectancy of patient is 10 years.<sup>8</sup>

Consanguineous marriages are culturally and socially favored and constitute 20–50% of all marriages with first cousins unions accounting for almost one-third of all marriages among populations.<sup>9</sup> It is estimated that currently around one billion of world population has preference for consanguineous marriage.<sup>10</sup> Consanguineous marriage is defined as marriage between two individuals related as cousin or close family relation with the inbreeding coefficient equal to or more than 0.0156. Inbreeding coefficient is measure of the proportion of loci to which offspring can inherit identical genes from both parents. The incidence of thalassemia in children born to parents who have consanguineous marriages is relatively high and depends on the genotype of disease.<sup>11</sup> There are high number of children in Pakistan with transfusion dependent thalassemia due to high frequency of the gene mutation, consanguineous marriages, high birth rate and large population size.<sup>12</sup> Recent studies have shown that social cultural factors like low-income status, lack of awareness, marriages in same ethnic groups are also contributing towards the high frequency of this disease in the Pakistani population.<sup>13,14</sup> Consanguinity and low literacy rate accounts for highest contributory factor (more than 81%) for the risk factors for high incidence of thalassemia in South Punjab.<sup>15</sup> Cultural beliefs and misinterpretation of religious commands by the general population has resulted in increasing rate of thalassemia prevalence in our country.<sup>16</sup> Pakistan is developing country with per capita income \$1380. Whereas treatment of thalassemia per child per year cost estimated \$6000. Therefore prevention of thalassemia is demanding as well as challenging.<sup>17</sup>

Since there is no permanent cure for this disease and treatment depends on lifelong blood transfusion which impose huge financial and emotional burden on families and health system of country. Best strategy to reduce burden of thalassemia is prevention and parental knowledge regarding disease is crucial in long term prevention. As major burden of thalassemia is attributed to consanguineous marriages. Aim of our study is to find the association between consanguinity and frequency of b-thalassemia and to assess the knowledge of parents regarding disease as well as inclination towards pre natal diagnosis, pre conception genetic counseling in the city of Karachi which is the largest state of the country and where social and casts based marriages are very common.

## **MATERIAL & METHODS**

### **Study Design**

A retrospective cohort study.

### **Study Setting**

Patients with beta thalassemia attending Fatimid Foundation and PNS Shifa Hospital Karachi.

### **Study Duration**

Six Months July – December, 2017.

### **Sample Size**

184 which was inflated to 200. Sample size was calculated by taking the prevalence of Thalassemia as 14 %<sup>9</sup>, margin of error 5% ( $\alpha=0.05$ ) and 95% level of significance.

### **Inclusion & Exclusion Criteria**

Children having other Hemoglobinopathies such as Sickle cell disease and Hereditary Spherocytosis were excluded. Inclusion criteria includes parents of children suffering from thalassemia major, either gender and willing to participate in study while all those having serious illness, associated complication or having systemic illness were excluded from study.

### **Data Collection and Analysis Methodology**

Data was collected from parents of children suffering from thalassemia which were selected

from data of hospital record after consensus method. Participants were approached after taking informed written consent. Pre tested questionnaire was administered, which include basic demographic profile, frequency of consanguineous marriages parents of children suffering from thalassemia, awareness about preconception genetic counseling, screening modalities, genetic mode of transmission and preventable nature of thalassemia and opinion about future cousin marriages. Anonymity and confidentiality was maintained. Questionnaire was piloted among 20 randomly selected participants seeking thalassemia treatment from same medical facility. This was done in order to assess its feasibility, validity and reliability. Data analysis was done using SPSS version 23 with frequencies, percentages. Chi-square test was used to prove associations between categorical variables. Data was analyzed using the standard statistical software packages. P-value less than 0.05 was considered as statistical significant.

### Ethical Consideration

Study was approved by Ethical Review Committee of Bahria Medical and Dental College, Karachi.

### RESULTS

Table-I shows the socio demographic characteristics results of our study showed slight male predominance with 52% males and 48% females. Mean age of study participants was 10.2 years. Education status of parents ranged between matriculation to post graduation, 15% were illiterate, 30% had done matriculation, 15% were intermediate, 12% were graduates and 18% had completed post-graduation.

Out of total study participants 78.5% were relatives ( $p=0.001$ ), out of these 61% were first relatives and 17.5% were distant relatives ( $p=0.009$ ). Regarding awareness about pre-conception genetic counseling only 25% ( $p=0.001$ ) were aware of it, 65% knew that thalassemia had genetic mode of transmission ( $p=0.005$ ), 24% were aware of screening modalities available for thalassemic patients ( $p=0.001$ ). About 63.55% agreed that premarital screening can prevent thalassemia ( $p=0.001$ ). Result of study showed that majority (83%) of parents were not aware of pre natal diagnosis of thalassemia ( $p=0.001$ ). On inquiring about their perception about consanguineous marriage after having thalassemic child only 48% ( $p=$  discouraged cousin marriage for their next generation and more than half of study participants were still in favor of cousin marriages in future. (Table-II)

### DISCUSSION

Thalassemia is the common monogenetic disorder, resulting from absence or decrease production of globin chain. The World Health Organization (WHO) has recognized the urgent need of control of this genetic disease. In our study 78.5% parents were relatives and rest were not related. Our study is in line with previous study which reported the total consanguinity rate as 77.3% among parents of thalassemic children.<sup>18</sup>

In our study out of total 78.5% related, 61% were first degree familial relatives and rest of 17.5% were unrelated. These results are in accordance with previous study in which frequency of thalassemia among first cousin marriages was reported to be 73%.<sup>7</sup>

Variable	Frequency	Percentage (%)	Chi Square	P-Value
Gender				
Male	104	52	4.593	0.217
Female	96	48		
Education status				
Illiterate	30	15	1.371	1.541
Matric	60	30		
Intermediate	30	15		
Graduation	24	12		
Masters	36	18		
Post graduation	20	10		

Table-I. Socio demographic profile of the participants (n=200)

Questions Asked	Frequency (n )	Percentage (%)	Chi Square	P-Value
Are You And Your Spouse related				
Yes	157	78.5		
No	43	21.5	0.717	0.001
First Cousin	122	61		
Distant Cousin	35	17.5	1.231	0.009
Unrelated	43	21.5		
Hereditary mode of transmission of Thalassaemia				
Yes	130	65	3.125	0.005
No	70	35		
Awareness/Heard about Pre-Conception Genetic Counseling :				
Yes	50	25	0.152	0.001
No	150	75		
Knowledge about Screening modalities				
Yes	48	24	1.156	0.001
No	152	76		
Usefulness of premarital carrier screening (PMCS) in prevention of Thalassaemia				
Yes	127	63.5	0.131	0.001
No	73	36.5		
Knowledge about prenatal diagnosis				
Yes	34	17	1.931	0.001
No	66	83		
Opinion about future cousin marriages				
Yes	104	52	6.175	2.314
No	96	48		

**Table-II. Parental knowledge regarding thalassaemia**

In recent study at Islamabad, Pakistan, consanguinity was seen in total 95% participant out of those 97% was first cousin.<sup>19</sup> While study at Bannu, Pakistan, reported that 74% parents were cousins.<sup>9</sup> Another study reported the rate of thalassaemia to be 63% among the first cousin marriages.<sup>20</sup>

Regarding hereditary nature of disease only 65% of the total participants had knowledge about hereditary nature of Thalassaemia. This is in accordance to study conducted in India in which 60% participants had adequate knowledge regarding genetic mode of transmission of thalassaemia.<sup>21</sup> These results are contradictory to study conducted at Bengal by Srivastava et al in which 22.2% participants reported that Thalassaemia is genetic disorder.<sup>22</sup> Similarly study conducted at Iran reported that only 20%

participants had knowledge regarding hereditary nature this disorder.<sup>23</sup> Another study from Lahore reported that 44.6% participants knew that thalassaemia is genetic disorder.<sup>24</sup> This issue needs to be addressed as these results suggest that parents don't have adequate knowledge regarding thalassaemia and its mode of inheritance. This is the main reason for continuous increase in prevalence of this disease.

In our study male (52%) were found to be affected more as compared to females (48%). This is in consistent with result of previous study which reported 56% males were having thalassaemia.<sup>9</sup> Another study conducted at Turkey reported thalassaemia in 56.7% males.<sup>25</sup>

In our study only 25% had awareness regarding pre conception genetic counseling and almost

same (24%) had knowledge about premarital screening detection of thalassemia and majority had no idea about its importance. These results strongly contradict the study from India in which 63.55% participants reported that genetic counseling can prevent thalassemia. This lack of knowledge regarding pre conception genetic counseling is strong contributory factor responsible for high prevalence of thalassemia among consanguineous marriage.<sup>21</sup> About 63.55% agreed that premarital screening can prevent thalassemia which was similar to studies by Ishaq et al<sup>26</sup> and Hajeri et al.<sup>27</sup> Screening can be effective strategy in early carrier detection and reduction in number of marriages between carriers. It should be done on voluntary basis after taking informed consent followed by counseling.<sup>21</sup>

These results suggest that participants have limited knowledge (24%) regarding premarital carrier screening (PMCS) however majority 63.5% value its usefulness of thalassemia trait screening before marriage can prevent transmission of hereditary diseases to next generation. These finding support that majority of participants were in favor premarital carrier screening (PMCS) after getting information during data collection. Many countries like Jordan and Saudi Arabia had implemented mandatory pre-marital screening and genetic counseling for prevention of thalassemia since these countries have high prevalence of thalassemia. Carrier detection is still non-existent at population level in Pakistan although Government has currently working on implementation of legislation for mandatory premarital thalassemia screening. This approach is cost effective and easier to reduce the burden of disease. Such measures should be adapted on urgent basis in our country in order to avoid genetic transmission of this disease.<sup>28</sup>

In our study only 17% of participant had knowledge regarding pre natal diagnosis of thalassemia. In Pakistan prenatal diagnosis of thalassemia started in 1994. However vast majority of population remained unaware of its availability due lack of public awareness, poor accessibility and increase cost of service. Baig et al stated that in 16 years from 1994 to 2010

only 3000 pre natal diagnosis were performed while around 5000 to 7000 thalassemia major children are born every year.<sup>29</sup> Considering the scenario, Punjab Government started the Punjab Thalassemia Prevention Program in 2010 to offer genetic counseling, prenatal diagnosis and carrier screening and termination of pregnancy in high risk couples.<sup>30</sup>

On inquiring about their opinion about cousin marriages 52% were still in favor of cousin marriages and 48% were against it. Previous study reported that 40% couples were against cousin marriages in future.<sup>31</sup> This issue must be addressed as lack of information about its association with cousin marriage is the reason for increase in burden of disease.

## CONCLUSION

Our study suggests that lack of knowledge and trends consanguineous marriages are strong contributory factor of this disease. Results of our study suggested that thalassemia is most prevalent among first degree familial relatives. Since in our socio cultural set up the trends of cousin marriages is very high; this is the reason behind continuous increase in prevalence of this disorder. Moreover low level of knowledge regarding the disease also contributes towards increasing burden. Study also revealed that males were affected more as compared to females.

## RECOMMENDATION

Low level of knowledge and trend of consanguineous marriages highlights the urgency of implementing effective public health interventions. These findings also strongly necessitate the importance of implementing public health education programs and the importance of holistic approach to implement the health promotional activities according to socio cultural and religious beliefs of our society. Prospective prevention programs including premarital genetic counseling, mass screening for carrier detection should be implemented by government to tackle with this public health issue. Population based education programs based on health belief models should be initiated with focus on addressing socio cultural beliefs

and increasing knowledge can prove to be cost effective strategies in prevention of thalassemia on long term basis. Most important challenge is establishment of National preventive program with joint effort of Government, legislation, non-government organizations (NGO's) and thalassemia societies as most of children in our country die even before the diagnosis.

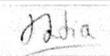
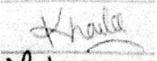
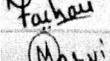
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