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Association of Consanguinity and ABO Blood Groups with β-thalassemia major in District Dadu and Hyderabad, Pakistan

Z. A. LAGHARI, T. R. CHARAN**, N. M. BAIG, M. R. QAMBARANI* J. WARSI

Department of Physiology, University of Sindh, Jamshoro, Sindh, Pakistan

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Abstract: Consanguineous marriages are the deeply rooted social trend in Pakistan, which lead to the high prevalence of inherited diseases. Thalassemia is an inherited disorder characterized by the abnormal synthesis of hemoglobin leading to anemia. β-thalassemia is the most common inherited disorder in Pakistan particularly in Sindh. The patients of β-thalassemia need repeated transfusion, which might cause complications causing the high rate of mortality in blood transfusion dependent β-thalassemia patients. Several studies have previously reported the high prevalence of β-thalassemia in Pakistan, however, the prevalence of β-thalassemia in the siblings borne from β-thalassemia carrier parents and association of ABO blood group with β-thalassemia have not been extensively studied. The purpose of this study was to find out the prevalence of β-thalassemia in the siblings of β-thalassemia carriers parents. This study was also set to find out the association of β-thalassemia with ABO blood groups. This was a cross sectional study carried out from August 2016 to July 2017 in the Thalassemia centers of district Dadu and district Hyderabad. In this study, 168 children from 50 families were selected for the study. The results indicate that almost half of the births 44.64% from β-thalassemia carriers are the β-thalassemia patients. B blood group was found to be higher in both in male and female β-thalassemia patients. Male had higher prevalence of β-thalassemia than female children. The pattern of ABO blood group distribution was B > O > A > AB, and for the RH factor it was RH + ve > Rh –ve. Conclusively, this study indicates the higher prevalence of β-thalassemia in siblings borne from β-thalassemia carrier's parents. β-thalassemia was higher in male children and B blood group was higher than other blood groups.

Keywords: β-thalassemia, ABO Blood Groups, Consanguinity.

1. INTRODUCTION

Thalassemia is an inherited disorder characterized by abnormal hemoglobin production due to mutation in alpha globin gene or beta globin gene (Vichinsky *et al*. 2005; Weatherall *et al*. 2010). There are about 80 to 90 million carriers of β-thalassemia gene around the globe, particularly in the countries with high consanguineous marriages (Qurat-ul-Ain, *et al.* 2011). β-thalassemia is prevalent in 60 countries; the high prevalence of β-thalassemia has been reported from the countries where consanguineous marriages are common (Vichinsky *et al.* 2005). The majority of these countries are in the Middle East and North Africa and South Asia particularly India and Pakistan (Zahed *et al.* 2001; Lahiry, Al-Attar *et al.* 2008; Haj *et al*. 2010; Qurat-ul-Ain, *et al.* 2011).

Pakistan has 8 million carriers giving birth to 4000 or 5000 β-thalassemia children in each year (Ahmed, *et al.* 2002). In Pakistan, currently, 80000 β-thalassemia patients are suffering from β-thalassemia, this number is increasing annually due to high rate of consanguineous marriages (Qurat-ul-Ain, *et al.* 2011; Ahmed *et al.* 2015; Shahzad, *et al.* 2017). The poverty, the lower literacy rate, high birth rates and lack of awareness about β-thalassemia and risk associated with consanguineous marriages are the factors for the increase in β-thalassemia patients in Pakistan (Baig, *et al*. 2006; Arif, Fayyaz *et al.* 2008; Ishaq, Hasnain *et al.* 2012; Shahzad, *et al*. 2017).

Thalassemia affects both male and female gender, however, the number of reports published till date suggest the comparatively higher prevalence in male gender (Asadi-Pooya and *et al.* 2004; Qurat-ul-Ain, *et al.* 2011; Bejaoui and Guirat *et al.* 2013; Khan, Ahmed *et al.* 2015; Laghari, *et al.* 2018). The reason for the higher prevalence in male gender has not been fully investigated. Some studies suggest the higher number of male gender registered in thalassemia centers is due to gender bias, where male children are preferred over female children, however, the subject has still been understudied.

Several studies have reported the association of ABO blood groups with various diseases (Franchini and Lippi *et al.* 2015). In these studies, the distribution of ABO blood groups was observed in patients and normal population. The higher frequency of either blood group on any disease is suggestive of a possible link between the blood group and diseases. Increasing evidence suggest the association ABO blood groups with number of diseases. The exact mechanism of higher frequency of particular blood group in some diseases has not been

++Corresponding Author's E-mail: zulfiqar.laghari@usindh.edu.pk
*University of Sindh, Jamshoro
**Department of Zoology , University of Sindh, Jamshoro

unraveled. The association of ABO blood groups with β-thalassemia has been previously reported in some studies (Zahed *et al.* 2001; Mohssin, Mahmood *et al*. 2015; Laghari, *et al.* 2018; Marbut, *et al.* 2018), where these suggest the higher distribution of blood group O in β-thalassemia patients, however, some studies also reported the higher prevalence of blood group B. Majority of these studies were mainly hospital based and distribution of ABO was observed in β-thalassemia patients.

According to the literature review available, no extensive study has been conducted to observe the distribution of ABO blood groups on total births from consanguineous marriages of β-thalassemia carriers' parents. Therefore, the purpose of this study was to evaluate the frequency of ABO blood group in the normal children and blood transfusion dependent β-thalassemia patients from the consanguineous marriages living in the urban and rural areas of district Hyderabad and Dadu. The population of Hyderabad is 2.2 million and the population of district Dadu is 1.5 millions. According to the 2017 census, both districts represent the major ethnic groups living in the urban and rural areas.

2. MATERIALS AND METHODS

Data collection

This was a cross sectional study carried out from August 2016 to July 2017. The data was collected through interview based structured questionnaire; the questionnaire was divided into various sections, which were further divided into different elements. The data was collected from the participants living in district Hyderabad and district Dadu, Sindh Pakistan. Total 82 families were approached for the collection of data from Aliza Center of thalassemia and Shifa Pathology Laboratory and blood bank from district Dadu and Zainabia Blood bank & thalassemia center Hyderabad, Sindh, Pakistan. Out of 82 families, only 50 families gave the consent for ABO blood typing test and provided the complete data. Out of 14 families from the district Dadu 8 families agreed to participate in the study and from district Hyderabad 42 out of 68 families agreed to participate in the study.

ABO blood groups and Rhesus factor (D) detection

Venous blood was drawn from β-thalassemia patient and their siblings and their parents for observing the blood group using the standard hemagglutination reaction. The drop of blood was mixed with either anti sera A, B and D to observe the hemagglutination reaction.

Ethical approval and Statistical analysis

Ethical approval was obtained from the Departmental Ethical Committee; the verbal consent was sought from the parents of the patients before collecting the data. Statistical analysis was carried out using SPSS 18. Frequencies and percentages were calculated for categorical study variables like gender, distribution of ABO blood groups and Rh Factor, living area and the history of consanguineous marriages.

3. RESULTS

Total 82 families were approached for the study, out of 82 only 50 families agreed to participate giving the response rate of (60.97%). These carriers had 168 children, out of 168 children, 75 were β-thalassemia patients (44.64%) and 93 (55.36%) were normal children. Higher prevalence of β-thalassemia was found in male children 46.74% than in female children 42.11% **(Table 1).**

Table 1. β-thalassemia Patients and normal siblings borne from β-thalassemia carrier Parents

Variables	Male children		Female children		Total	
	n=92	%	n=76	%	n=168	%
Patients	43	46.74	32	42.11	75	44.64
Normal	49	53.26	44	57.89	93	55.36

(Table 2) shows the frequency of ABO blood groups in the mother and father of β-thalassemia patients. In both parents, the blood group B was higher than other blood groups. In mother, the frequency of blood group B was highest 48%, followed by blood group O, 28%, and then A, 22% and AB, 2%. The overall pattern was B > O > A > AB. Similarly, the father also had higher distribution of blood group B 50%, followed by O, 30%, and then A, 16% and then AB, 4%. The distribution of Rh factor in both parents was found at 2% **(Table 2).**

Table 2. Distribution of ABO blood groups and Rh factor in β-thalassemia carrier parents

ABO blood groups	Mother		Father	
	(n=50)	%	(n=50)	%
A	11	22	8	16
B	24	48	25	50
AB	1	2	2	4
O	14	28	15	30
Rh Typing				
Rh +ve	49	98	49	98
Rh –ve	1	2	1	2

According to the Table 3, the distribution B blood group was found higher in female β-thalassemia patients 53.12% than in male β-thalassemia patients 39.53%. Distribution of blood group A and O was higher in male β-thalassemia patients than female β-thalassemia patients table 3. The female β-thalassemia patients, however, had higher distribution of Rh negative than male β-thalassemia patients. Overall, the pattern in male and female β-thalassemia patients was B > O > A > AB. The distribution pattern in normal sibling of β-thalassemia patients was same B > O > A > AB, however, the pattern in normal children female was quite different, which was O > B > A > AB **(Table 3).**

Table 3. The Distribution of ABO blood groups and Rh factor in β-thalassemia patients and Their Siblings.

ABO Blood groups	Male children (n=92)				Female children (n=76)			
	Normal (n=49)		Patients (n=43)		Normal (n= 44)		Patients (n= 32)	
	(n)	%	(n)	%	(n)	%		
A	9	18.37	9	20.93	9	20.45	5	15.63
B	24	48.98	17	39.53	11	25	17	53.12
AB	5	10.20	1	2.33	1	2.27	1	3.13
O	11	22.45	16	37.21	23	52.28	9	28.12
Rh factor								
Rh +ve	46	93.88	43	100	42	95.46	29	90.62
Rh –ve	03	6.12	00	00	2	4.54	3	9.38

4. DISCUSSION

Several studies have previously reported the outcome of β-thalassemia patients from consanguineous marriages, this outcome from consanguineous marriages ranges from 65.4 to 76.15% (Hafeez, *et al.* 2007; Qurat-ul-Ain, *et al.* 2011; Khan, *et al*. 2015; Shahzad, *et al.* 2017), these studies suggest consanguinity is the major cause of high prevalence of β-thalassemia. The data, we have collected indicate the higher prevalence 44.64% of β-thalassemia in siblings of β-thalassemia carrier parents having the consanguineous marriages. Previously, the incidence of β-thalassemia trait was found in the siblings was at 58% (Khattak and Khan *et al.* 2004), in another study conducted in Lahore on the relatives of β-thalassemia major patients, the prevalence of β-thalassemia trait was 51.92% (Majeed, *et al.* 2013). The higher prevalence of β-thalassemia trait in these studies is due to the fact that these studies were directed towards finding out the thalassemia traits, whereas we selected the families and observed the proportion β-thalassemia patients from the total siblings borne from β-thalassemia carriers' parents.

In this study, we have shown that male patients are higher in number than female patients, we have previously reported the higher prevalence of male patients (Laghari, *et al.* 2018), however, the previous study was the hospital based study and this study is conducted in all siblings of the selected families having major β-thalassemia patients. In several studies, β-thalassemia has previously been reported higher in male gender (Asadi-Pooya *et al.* 2004; Qurat-ul-Ain, *et al.* 2011; Bejaoui and Guirat *et al.* 2013; Khan, *et al.* 2015). Collectively, these studies suggest that male β-thalassemia patients are higher; the reason why male patients are higher has not been fully understood and needs to be investigated.

In this study, the frequency of ABO blood group was observed in the siblings of β-thalassemia major patients, we report here the higher frequency of blood group B followed by O, then B and finally AB. Our study is different from previous studies where they have shown the blood group O as the highly frequent blood group (Zamani, *et al.* 2018), similar results were found in some other studies (Sinha, *et al.* 2017). Quite recently, the study conducted in Iraq also showed the O positive being the highest, we also previously reported O positive as the highest prevalent group (Mohssin, *et al.* 2015; Marbut, *et al.* 2018). The reason why B blood group was higher in our study is due to the fact that parents of these β-thalassemia patients also had higher prevalence of B blood group. In this study, we report higher prevalence of Rh factor in female patients, which is consistent with previous reports.

5. CONCLUSION

We conclude here that almost half of the sibling borne from β-thalassemia carriers are β-thalassemia patients, further the male had higher prevalence of β-thalassemia, where as the blood B blood group was found higher in beta β-thalassemia patients.

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