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COMPARISON OF FREQUENCY OF CONSANGUINOUS RELATIONSHIP AMONG PARENTS OF BETA THALASSEMIA MAJOR AND NORMAL CONTROLS

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Abstract

Introduction: β Thalassemia is an autosomal recessive disorder, characterized by deletion of both β−chains leading to abnormal production of Hb and excessive destruction of RBCs. Patients present in infancy with poor growth, hepatosplenomegaly and severe microcytic hypochromic anaemia. Any child with β Thalassemia needs frequent blood transfusions throughout life. As the child grows, metabolic complications emerge resulting in death in second decade of life. Present study was conducted to compare the frequency of consanguinity between thalassaemic patients and normal controls.

Materials and methods: This case control study was completed in department of Haematology, The Children's Hospital & the Institute of Child Health Multan from 19th of September 2020 to 19th of March 2021. 182 cases were enrolled after taking informed consent from parents/guardians. Presence or absence of consanguinity including first or second cousin was taken from parents. Final outcome is the mean difference of consanguinity between thalassemic patients and normal controls.

Results: Mean age of patients was 6.9+_1.0 years. Among thalassemic patients, 79% were outcome of consanguineous marriage and 12% were of non-consanguineous. Among controls, 60% were from consanguineous parent and 31% were from non-consanguineous. 112(61%) children were male and 70(38%) were female. 58% were 1st cousin and 18% were second cousin. Mean difference in consanguinity between thalassemic and normal controls was 56.4+_ 43.6(p=0.16) which was not statically significant.

Conclusion: Mean difference of consanguinity between patients and normal controls was noted to be 56.4+_43.6% (p=0.16) showing role of consanguinity in thalassemia.

Keywords: Consanguinity, microcytic hypochromic anaemia, thalassemia

Introduction

β –Thalassemia is one of the commonest genetically transmitted disorders throughout the world. β Thalassemia is an autosomal recessive disorder, characterized by deletion of both β−chains leading to abnormal production of Hb and excessive destruction of RBCs[1]. More than 200 mutations causing β thalassemia have been described.[2] The majority of infants with β-thalassemia mostly present during

first year of life but not during first few months of life .Initially they develop progressive pallor, low grade fever, feeding problems and abdominal enlargement due to hepatosplenomegaly.[3] Haemoglobin electrophoresis is the standard method of diagnosis and gene analysis may be used for specific genetic mutation analysis[4]. Beta thalassemia major is the most severe form of beta thalassemia, requiring regular blood transfusions and extensive ongoing medical care. These lifelong blood transfusions can lead to iron overload that causes visceromegaly, endocrinopathies and cardiac failure[5]. Blood transfusion and iron chelation are the mainstay of treatment. [6, 7]

The World Health Organization (WHO) has identified control of haemoglobinopathy, particularly β-thalassemia, in developing world, as a priority.[8] An estimated 5000-9000 children with β-thalassemia are born per year, although no documentary registry is available in Pakistan. The estimated carrier rate is 5-7%, with 9.8 million carriers in the total population [8].The likely number of children suffering from thalassemia major in total 120 million population of Pakistan would stand at approximately 36000[9]. Consanguineous marriages play an important role in β-thalassemia. The risk is approximately doubled in a first cousin marriage.[11]

So we should pay attention on the consanguinity and particularly screening of families should be done who have thalassaemic patients. By applying this approach we can decrease the rate of thalassemia in Pakistan and can decrease the burden on families. So studies should be done to favour this approach.

A study conducted on this topic in SHIRAZ CITY IRAN showed the results that 49.4% of cases were outcome of first or second cousin marriages whereas in control group 22.4% were outcome of 1st cousin and 8.6% were outcome of 2nd cousin marriages ($p<0.00001$).[12] As no or fewer studies conducted on this topic and vary from province to province and caste to caste. In this study we wanted to know the risk of thalassemia between consanguineous and non-consanguineous marriages.

Materials and methods

This Case control study was carried out in Thalassemia centre at The Children hospital & Institute of Child health Multan (CH& ICH) from 19th September 2020 to 19th March 2021. Non-probability consecutive sampling was used. The calculated sample size was 182 with 91 children in each group with power of study 80% and 95 % confidence level taking expected percentage of consanguinity 49% in cases and 31% in controls as reported by ASADI AL POYA[11]. So a total of 182 children were enrolled after taking informed consent from guardians/parents according to following criteria: cases include Thalassemia patients, age 1 to 12 years including both male and female gender and controls include normal children visiting our general outdoor for minor complaints, not suffering from any haemolytic anaemia, no anaemia or splenomegaly detected on physical examination, age 1 to 12 years including both male and female gender. Details regarding consanguinity or non-consanguinity and first or second cousin were taken from parents/guardians. Patients were excluded according to following criteria: patients with haemolytic anaemia other than thalassemia, exact relationship of parents not known.

Controls were taken from normal population attending general OPD for minor illnesses. Their details regarding consanguinity were also taken during visit. All information were collected on specifically designed Performa for study.The final outcome is presence or absence of consanguinity in thalassaemic and non thalassaemic patients.

All the data was entered using computer software SPSS version 10. Descriptive statistics was applied. Mean and standard deviation was determined for quantitative factors like age of the children. Frequencies and percentages were determined for qualitative variables like gender, presence of consanguinity or non-consanguinity, and 1st or 2nd cousin in cases and controls. Outcome variable is frequency of consanguinity was compared among cases and controls. Chi Square test was applied

Effect modifiers like age and sex were controlled by stratification of information. . Chi square test was applied to compare the frequency of consanguinity in both groups (cases and controls) and p value ≤ 0.05 was considered significant.

This study was affirmed by the institutional Ethical committee of the Children hospital and the institute of child health, Multan.

Results

Table I shows descriptive statistics. Age range was 1-12 years. Mean age of the population was 6.98 ± 1.307 years.

Table II shows distribution of population. Out of 182 children included in the study, 112 (61.5%) were male and 70(38.5%) were female. 140(76.9%) Children were outcome of consanguineous and 42(23.1%) were of non-consanguineous marriage. Among the total consanguineous 107(58.8%) were outcome of first cousin and 33(18.1%) were second cousin.

Table III shows stratification of data according to age and gender. The stratification of age showed that 73 patients had age 1-3 years, 65 had 3-6 years, 19 had 6-9 years and 26 had 9-12. According to age group in consanguineous marriages 53 were in age group 1-3yrs, 54 from 3-6yrs, 13 from 6-9 years and 20 from 9-12 yrs. while in non-consanguineous marriages 20 were from age group 0-3 yrs,11 from 3-6yrs,5 from 6-9 years and 6 from 9-12 yrs.

Among consanguious marriages 90 were male and 50 were female whereas in non-consanguious marriages 22 were male and 20 were female in both cases and controls.

After stratification of age groups Chi-Square test value was noted to be 2.37. Odd ratio was noted to be 3.23 which was 1.9 for thalassemic patients and 0.6 for non-thalassemic patients. Mean difference in consanguinity between thalassemic patients and normal controls was 56.4+_43.6 (p=0.16) which was not statically significant Frequency of consanguinity noted among cases (Thalassemic) were 79(56.4%) and 12(28.6%) were non-consanguineous. Whereas among non-thalassemic (control) patients 61(43.6%) were outcome of consanguineous and 30(71.4%) were of non-consanguineous.

Table I: Descriptive statistics of the population n=182

N=182	Age (years)
Mean	6.98
St. deviation	1.307
Range	1-2 years

Table II: Distribution of the population n=84

N=182		**Frequency**	**Percentage**
Gender	Male	112.0	61.5%
	Female	70.0	38.5%
Consanguinity	consanguineous	140.0	76.9%
	Non-consanguineous	42.0	23.1%
1^{st} or 2^{nd} cousin	1^{st}	107.0	58.8%
	2^{nd}	33.0	18.1%

Table III: Stratification of data according to age and gender

N=182		Consanguinity			P Value*
		yes	No	total	
Age(years)	1-3	53	20	73	0.49
	3-6	54	11	65	
	6-9	13	6	19	
	9-12	20	6	26	
Gender	Male	90	22	112	0.16
	Female	50	20	70	
Total		140	42	182	

*Chi-square test of significance

Table IV: Frequency of consanguinity

Total(N= 182)	consanguinity	Non-consanguinity	p- value
Cases (91)	56.4%(79)	28.6%(12)	0.16
Control (91)	43.6%(61)	71.4%(30)	
Total%	100%	100%	

Discussion

Thalassemia is an Autosomal recessive disorder. This familial disease presents with anaemia in first year of life and child needs frequent blood transfusions throughout his/ her life. As the child grows, iron overload and metabolic complications emerge resulting in death in second decade of life even in adequately transfused patients. The cost of treatment is prohibitive and the social burden for the family is enormous. [1]

In a study conducted in abu dubai determining consanguity as a risk factor in prevalence of beta thalassemia it showsTribalism and consanguineous marriages are common in parts of the world with a high prevalence of the β-thalassemia (β-thal) mutations, and increase the risks of homozygosity for this and other recessive disorders. [13]

A cross-sectional study was conducted in Iran on 648 beta-thalassemia patients who were referred to Cooley's clinic for blood transfusion in Spring 2003. The mean age of the patient was11.8 ± 5 years. Out of the 648 patients, 347 (53.5%) were male and 301 (46.5%) were female. A non-statistically significant difference was observed between number of male and female thalassemia patients (p= 0.07). It was noticed that in approximately 49.5% of cases, the patients were outcomes of first-or second-cousin marriages. The total number of first-cousin and second- cousin marriages (studied in 6004 families) was noted to be 22.4% and 8.6% of total marriages, respectively .The comparison of consanguinity between parents in thalassaemic families and general population in the same area revealed a highly significant difference (p< 0.00001). [12]

In one study conducted at The Thalassemia Centre, Sir Ganga Ram Hospital, Lahore, from July to September 2009 which showed 81.7% couples had consanguineous marriage; of them 65.3% were first cousins and remaining 18.3% were non-consanguineous. [14]

In another study conducted in India on 122 β-thalassemia children from 104. Of the total affected children, 74 (60.66%) were males, while 48 (39.34%) were females. The β-thalassemia children born to consanguineous parents were 84 (68.58%) and remaining 38 (31.15%) were born to non-consanguineous parents. In the consanguineous marriages 21 (25.00%) were born to uncle niece parents, 45 (53.57%) were born to I cousins, 12 (14.29%) were born to II cousins and 6 (7.14%) were born to III cousins. [15]

A study was conducted to screen extended families for genetic haemoglobin disorder like beta thalassemia in Pakistan where consanguious marriages were common. Fifteen large Pakistani families, 10 with a history of a haemoglobin disorder and 5 without any such history (controls), were screened for beta-thalassemia and abnormal haemoglobins. All carriers and married couples consisting of two carriers received counselling, and eight families have been followed for two years. All carriers reported that they have used the information provided in the testing and counselling process: carriers married to carriers with two or more healthy children have avoided further pregnancy, and most such couples with one or no healthy children have used prenatal diagnosis.[16]

Conclusion

Mean difference of consanguinity between patients and normal controls was noted to be 56.4+_43.6% (p=0.16) showing role of consanguinity in thalassemia.

CONFLICT OF INTEREST / DISCLOSURE

All the authors who have contributed to the manuscript certify that they have NO affiliations any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

REFERENCES

1. Iqbal I. Prevention of Thalassemia In Pakistan. Nishtar Medical Journal 2009; 1:1-3.
2. Steinberg MH, Forget BG, Higgs DR, Nagel RL, eds. Disorders of Hemoglobin: Genetics, Pathophysiology, and Clinical Management. Cambridge, UK:Cambridge University Press; 2001:252-276.
3. McDonag KT,Neinhuis AW.The thalassemia in haematology of infancy and childhood.Nathan and Osaki;1993;4(1).
4. Hilman RS, Ault KA, Rinder HM. Thalassemia. IN: Robert RS, Hillman MD, Kenneth A, Ault MD, Menry M, Rinder MD. Hematology in clinical practise. London: mcgrow Hill, 2005.P. 73-9
5. Micheal R, DBaun,Vichincity E.Heomoglobinopathies;Thalessemia syndromes. In:Kliegman RM, Behrman RE, Henson HB, Stanton BF,editors.Nelson textbook of paediatrics Philadelphia:Elsevier;2008.p.2034-5
6. Modell B. Total management of thalassemia major.Archieves of diseases of childhood 1997; 52:485-500.
7. Cohen A.Markenson AL,Schwarz E.Transfusion requirements and splenectomy in thalassemia major.J Paeds 1980;97:100-2
8. Angastiniotis M, Modell B. Global epidemiology of hemoglobin disorders. Ann NY Acad Sci. 1998; 850:251–69.
9. Ahmed S, Saleem M, Modell B, Petrou M. Screening extended families for genetic hemoglobin disorders in Pakistan. N Engl J Med. 2010; 347:1162–68.
10. George WF.circulating body fluids.In review of medical physiology.appleton and Lange.Standford,Connecticut.18th ed.1997

11. George WF.circulating body fluids.In review of medical physiology.appleton and Lange. Standford, Connecticut.18th ed.1997.
12. Asadi-Pooya AA, Doroudchi M. Thalassemia major and consanguinity in Shiraz city, Iran.Turk J Haematol 2004; 21 (3):127-130.
13. Denic S1, Aden B, Nagelkerke N, Essa AA, β-Thalassemia in Abu Dhabi: consanguinity and tribal stratification are major factors explaining the high prevalence of the disease.Epub.2013 22 Apr;37(4):351-8.
14. Fouzia Ishaq, Hasnain Abid, Farkhanda Kokab, Adil Akhtar and Shahid Mahmood Awareness among parents of b-thalassemia major patients, regarding prenatal diagnosis and premarital screening JCPSP- Apr 2012;22(4):218-21. Sir Ganga Ram Hospital, Lahore.
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