B-THALASSAEMIA MAJOR, A CASE OF CONCERN: STATISTICAL STUDY IN KHYBER PAKHTOONKHAWA OF PAKISTAN

Qamruz Zaman[1], Muhammad Iqbal[1], Habib Nawaz[2] & Siraj ud Din[3]
1Department of Statistics, University of Peshawar.
[2]Institute of Management Sciences, Bannu University.
[3]Department of Business Administration, Gomal University, Dera Ismail Khan

ABSTRACT
Aim: β-thalassaemia major cases need proper attention and timely blood transfusions. The present study comprising 320 patients was conducted to assess the effects of risk factors and their relationship related directly or indirectly to the disease of β-thalassaemia major at Peshawar, Pakistan.
Results: There were 191 male and 129 female patients in the study. Mean age of overall, males and females was 124.68± 54.52, 124.43± 55.20, and 125.05± 53.71 respectively. The mean transfusion age was 97.55± 38.72, 96.25± 38.75, and 99.47± 38.72 for overall, males and females respectively. It is found that 4 (included patient) out of 11 children of a family were affected with the disease (i.e. 36% of the family). The number of transfusions and the age of transfusions were significantly correlated ($p < 0.05$), to consider both the males and females patients together (overall) or separately. Similar results we obtained for considering the correlation between the height and weight of patients at the start of first and before the last treatments. Wilcoxon Signed Ranks Test also showed significant difference ($p < 0.05$) between the paired studied characters.
Conclusion: It was found that the disease was common in both the males and females patients. The number of transfusion showed a significant ($p < 0.05$) positive correlation with the age. Awareness about family planning and the test during pregnancy test plays a pivotal role in controlling the disease. Similarly reduction in the percentage of interfamily marriages and need of education for parents and people about the disease is also necessary.
Keywords: β-thalassaemia major, Risk factors, Wilcoxon Signed Rank Test.

INTRODUCTION

Thalassaemia is an inherited blood disease and is considered to be more common in genetic diseases (Hong, 2000). Thalassaemia is broadly divided in to α-thalassaemia and β-thalassaemia. The former group of thalassaemia is the result of insufficient production of α protein and more common in Africa, Middle East, occasionally Mediterranean regions. Similarly β-thalassaemia is the result of lack of production of beta protein and prevailed in countries like Iran, Pakistan, and Southeast Asia etc (Zaman and Strasak, 2006). β-thalassaemia is further divided into minor, intermediate and major thalassaemia, based on the severity of disease and the number of transfusions required for patients (Salahuddin and Zaman, 2005).

Pakistan is one of the developing countries where β-thalassaemia is very common (Thalassaemia Society, 1995). For the healthy survivors, β-thalassaemia patients need regular and lifelong treatment of blood transfusion (Rino et al., 1995). This indicates that a blood group is significantly correlated with the disease (Gajalakshmi and Viswanathan, 1984). Severity of the disease has serious effects on the social and other aspects of Patients life e.g. education. Zaman and Salahuddin (2005) has reported that the thalassaemic patients have the thirst of getting education but with the passage of time: they are not able to continue it because of its severity.

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Constantoulakis et. al. (1975) determined that the disease affect the height of the patients by studying 229 Greek patients. They showed that a high percentage of Greek children with homozygous β-thalassaemia were short and had a lag in growth, though some severely affected attained normal height.

Many studies have been conducted to asses various risk factors and their possible reasons on the subject-matter (Amrolia et al., 2001, Anichini et al., 1983, Logothetis et al., 1972, Politis et al., 1991, Ahmed et al., 1994), but still there exists some of the aspects which need special attention. This article which is a part of (Zaman and Salahuddin, 2005) research, is based on the aim to highlight some facts related to correlation between different factors, the facts about the brothers and sisters of patients. Although these are simple and easily ignorable, still they are very important and need attention. As with some precautionary measures, one can easily protect the new/ coming generation from this disease.

METHODS

The study comprising of 320 β-thalassaemia major patients was conducted during November 2002 to April 2003 in Fatimid Foundation, Peshawar (Politis et al., 1991), Pakistan. Fatimid Foundation is the pioneer of providing voluntarily blood transfusion services in Pakistan and deals with the cases of thalassaemia as well as other blood diseases.

A predefined questionnaire was designed with the help of concerned medical doctors, field experts and consulting the recent literature available on the subject, to collect information on different aspects of the disease. The information was collected from their records (from 1988 to April 2003) with the guidance of medical doctors. For interview of lived patients, the time of data collection was not fixed in order to collect every kind of information from the patients of different status. As the employed parents like to visit the foundation in afternoon, while the other reached the centre early morning. During the whole data collection process, we tried to avoid overlapping e.g. if there is more than one patient in the family, we just considered one.

The questionnaire sheltered almost all the questions related to the possible risk factors and aspects of the disease. The basic factors, which are the main theme of this Article were:

1. sex
2. Age (in months) at the time of first transfusion
3. Age (in months) at the time of last transfusion
4. Age of transfusion (3-2)
5. Weight at the time of first transfusion
6. Weight at the time of last transfusion
7. Height at the time of first transfusion
8. Height at the time of last transfusion
9. Family size (including parents)
10. Number of brothers and sisters
11. Number of brothers and sisters suffering from minor/ major thalassaemia
12. Number of transfusions

STATISTICAL ANALYSIS

Continuous data normally distributed is expressed as mean ± SD, otherwise medians and ranges are indicated. A non-parametric Wilcoxon Signed Rank Test is was applied to test the significance between the averages of various mentioned factors due to non-normally assumptions of the observed data. Strength of correlation between two different factors is tested by Spearman's rank correlation analysis. 2-sided p-values equal to 0.05 or less are considered to indicate statistical significance. Responses to structured questions are entered and analysed using SPSS, version 11.5 (SPSS Chicago, 2004).

RESULTS

Response rate was 100%, as all the questionnaires were completed and collected carefully. Out of 320 patients, 191 (60%) were male and 129 (40%) were female. Furthermore, 85 male patients and 57 female patients died (Fig. 1).

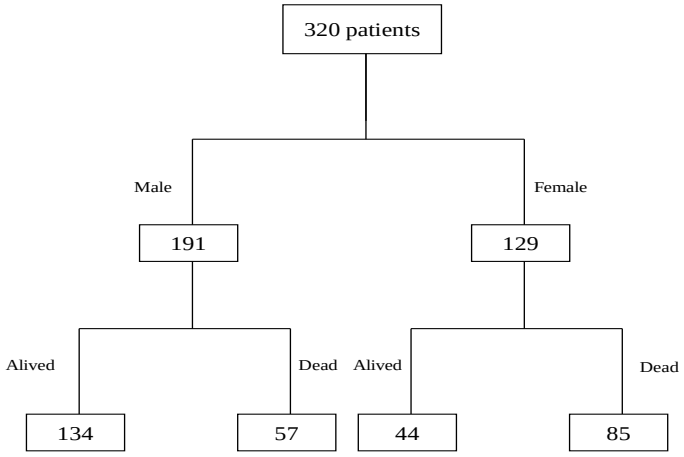

Figure 1. Distribution of 320 β-thalassaemia major patients

The descriptive statistics about the mean age ± standard deviation of patients and mean age ± standard deviation of transfusions (overall) was 124.68 ± 54.52 and 97.55 ± 38.72 months, respectively (Table I).

Table I. Descriptive measures for the age and time of transfusion (months) β-thalassaemia patients

Age of Patients		
Age in months	Mean ± SD	124.68 ± 54.52
	Median/ range	116.50 (375)
Age in months (Males)	Mean ± SD	124.43 ± 55.20
	Median/ range	116 (364)
Age in months (Females)	Mean ± SD	125.05 ± 53.71
	Median/ range	120 (328
Age of Transfusion		
Age in months	Mean ± SD	97.55±38.72
	Median/ range	94 (210)
Age in months (Males)	Mean ± SD	96.25±38.75
	Median/ range	93 (209)
Age in months (Females)	Mean ± SD	99.47±38.72
	Median/ range	95 (174)

The range of family size (3 to 13), includes parents. 15% of these families contained only one child affected with the disease (Table II). It also showed that more than 40% of the children had no symptoms of disease. 18% of the more cases of thalassaemia were found of the family of size 6. Furthermore, 4 (included patient) out of 11 children of a family of size 13 were affected with the disease (i.e. 36% of the family). Similarly, thalassaemia major families were not saved from thalassaemia minor. Unlike the western society; the family size in this part is much larger, which also increases the chances of thalassaemia among the children.

In some fields or areas, it is difficult to find high statistical correlation, for example the correlation between Law School Admission Test (LSAT) scores and the first year grades in law school of admitted applications is only r= 0.36 and they considered the correlation exists (David, 1980).

Table II.Distribution of the affected families (no. of thalassaemia major and minor cases)

Family size	No. of brothers and sisters	Frequency	Total children	No. of symptoms of disease	Thalassaemia minor	Thalassaemia major
3	0	47	0	0	0	0
4	1	59	59	23	23	13
5	2	57	114	54	42	18
6	3	53	159	84	46	29
7	4	52	208	91	71	46
8	5	24	120	63	42	15
9	6	9	54	30	16	8
10	7	9	63	28	17	18
11	8	6	48	27	9	12
12	9	3	27	15	8	4
13	10	1	10	5	2	3

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As compared to (LSAT), the correlations between the appropriate covariates in our study were much stronger e.g. the correlations between the number of transfusions and age of transfusions were 0.735, 0.762 and 0.687 for overall, males and females patients respectively (Table III).

Table .III Spearman's rank correlation analyses for the studied factors of β-thalassaemia patients

Variables	Results of Spearman correlation coefficient			p-value
	Overall	Male	Female	
Age of transfusion and Number of transfusion	0.735	0.762	0.687	≥ 0.000
Weight and Height (At the start of treatment)	0.921	0.925	0.925	≥ 0.000
Weight and Height (At last treatment)	0.974	0.976	0.976	≥ 0.000

This revealed that the age of transfusion and the number of transfusions have strong effects. Similarly, non-parametric test for paired data (age at the start and at last treatment, weight at the start and at last treatment, height at the start and at last treatment) gave the significant results (Table IV).

Table .IV Wilcoxon Signed Ranks Test of β-thalassaemia patients

Variables	Results of Wilcoxon Signed Rank test			p-value
	Overall	Male	Female	
Age (at first and at last treatment)	15.504	11.985	9.855	≥ 0.000
Weight (at first and at last treatment)	14.022	10.692	9.091	≥ 0.000
Height (at first and at last treatment)	13.844	10.497	9.043	≥ 0.000

DISCUSSION

β-thalassaemia major is the inherited blood disease in Pakistan, in which patients need blood transfusion every month. Fatimid foundation is one of the organizations in Pakistan, which hold the responsibility of the treatment of patients. Organization managed the blood and medicine for them.

The present study was conducted to find the correlations of different factors and on the basis of this study; we reached to the conclusion that, number of transfusions is highly and positively correlated with the age of transfusion. This may be due to the fact that as age increases, the severity of the disease increases and for curing the disease, the number of transfusions increases.

Similarly, the height and weight before the start and the last recorded treatments are also correlated, which is contrary to a general concept that the height of thalassaemic patient is affected by the disease. This study shows that the height, weight and both have the same tendency in the same direction. As the treatment is life long affective process, as paired tests results showed. More children in the family gave more cases of the disease.

This is the first such type of report in Pakistan, we are aware of, based on different statistical techniques, unlike the previous work by Ahmed et. al. (1994). It has been found that thalassaemia is a

blood disease and is common in both sex.

Based on the results obtained from the present study, the following suggestions are forwarded for effective treatment and control of the disease.

One of the easy ways of controlling the disease in Pakistan is the awareness of family planning and reduction in interfamily marriages. As there is a joint family system and parents are responsible for the marriages of their children. They usually select the girl/boy for their son/ daughter from their own family and this opens the gateway for thalassaemia as well as for other family diseases.

This is not only the responsibility of foundation and government to control the disease, but it is also the responsibility of every carrier and especially, it is the duty of carrier married women to visit the doctors regularly during pregnancy.

Couples should go for a blood test to test their DNA build up before planning to start a family. In this way, they will be aware of the possible genetic diseases that their children may acquire. Genetic counselling will then be able to advise and present the options for the couple to decide on the family they want. Prenatal diagnosis will also be able to detect any deformities or genetic disease of the child. Therefore, knowing that the child has thalassaemia major genes before it is born will help decrease the cases in Pakistan (it all still depends on the decisions of couples).

Most of the parents are illiterate and have little knowledge about disease, which is one of the main reasons of spreading the disease. Without proper health education it is impossible for them to know the exact nature of this deadly disease.

REFERENCES

Ahmed S, Saleem M, Rashid Y (1994). First prenatal diagnosis of thalassaemia in Pakistan: a case report. *Pakistan J Pathol*. 7:69-71.

Amrolia PJ, Vulliamy T, Vassiliou G, Lawson S, Bryon J, Kaeda J, Dokal I, Johnston R, Veys P, Darbyshire P, Roberts IA (2001). Analysis of chimaerism in thalassaemic children undergoing stem cell transplantation.*Br-J-Haematol*, 114(1); 219-25.

Anichini P, Reynaudo G, Pacini G (1983). Predictive value of a new Osmotic test in the screening of heterozygous beta-Thalassaemia. *Scand-J-Clin-Lab-Invest*. 43(2); 171- 73.

Constantoulakis M, Panagopoulos G, Augoustaki O (1975). Stature and longitudinal growth in Thalassaemia major. A study of 229 Greek patients. Clin pediatr (Phila). 14(4): 355-7/362-8.

David K (1980).The information on the LSAT, along with much useful information about the alleged cultural bias of such tests, is found in David Kaye, "Searching for the Truth about testing", *The Yale Law Journal*. 90: 431-457.

Fatimid Foundation A symbol of hope Pakistan established (1981). www.thalassemia.com.pk

Gajalakshmi BS, Viswanathan V. (1984). Correlation of blood groups with congenital disorders and gastro intestinal diseases. *Indian J of Physiol Pharmacol*. 28 (1): 42-46.

Logothetis J, Constantioulakis M, Economidou J. (1972). Thalassemia major (homozygous beta-thalassemia). A survey of 138 cases with emphasis on neurologic and muscular aspects. Neurology. 22; 294-304.

Politis C, Richardson C, Yfantopoulos JG.(1991). Public knowledge of Thalassaemia in Greece and current concepts of the social status of the thalassaemic patients. Social Sci in Med. 32 (1); 59-64.

Rino V, Bernadette M, Evgentia. G.(1995). What is Thalassaemia, 2nd ed. Thalassaemia International Federation.

SPSS Corporation. SPSS 11.5 for windows. Chicago, 2004

Salahuddin, Zaman Q.(2005). Analysis of β-thalassaemia by using the Survival Analysis Techniques. AIM. 13(4): 192-7.

Thalassaemia Society of Pakistan Established 1995.www.thalassaemia.org.pk

Zaman Q, Strasak AM (2006). World of Thalassaemia. Materia Socio Medica. 18(1): 35-7.

Zaman Q, Salahuddin (2005). *Correlation between the education and Thalassaemia*: A Statistical Study. Presented in the ICCS-VIII conference December 19-22.