

AUDIT OF BETA-THALASSEMIA CASES AT SHEIKH ZAYED MEDICAL COLLEGE/ HOSPITAL, RAHIM YAR KHAN

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ABSTRACT

Background: Beta-thalassemia is one of the common genetic disorders in our community. Therefore, it is deemed necessary to study and probe it to encompass all aspects of this disorder. **Objectives:** The objective of the study was to find out the distribution of β -thalassemia in different age groups, prevalence of transfusion related viral infections and serum ferritin levels. **Methodology:** All cases of thalassemia major and thalassemia intermedia registered with the Centre for Thalassemia Care, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, were included in the study. The cases were divided into three different age groups, i.e. 0-5 years, 5.1-10 years, 10.1 years and above. The cases were diagnosed as of β -thalassemia by history & examination, peripheral blood picture, hemoglobin electrophoresis and confirmed by genetic analysis. All cases were screened for HCV, HBV, and HIV. Some of the cases were tested for serum ferritin levels. **Results:** Two hundred and eighty three (63% males and 37% females) registered cases of β -thalassemia were included in the study. Two hundred fifty seven (91%) patients were suffering from thalassemia major and 26 (9%) were having thalassemia intermedia. Out of 283 cases, 196 (69%) were belonging to rural areas and 87 (31%) were residing in urban areas. Fifty-five (19.4%) β -thalassemic patients were found to be positive with anti-HCV antibody and 3(1%) cases were positive for HBV surface antigen. There was a significant difference ($p < 0.05$) between the means of serum ferritin levels in thalassemia major (2775) and thalassemia intermedia cases (1519). **Conclusion:** Majority of thalassemic patients were suffering from β -thalassemia major. Males were predominantly suffering from β -thalassemia major while in thalassemia intermedia sex distribution was almost equal. The overall prevalence of beta-thalassemia in rural areas was comparatively high. Nineteen per cent of β -thalassemia patients were positive for anti-HCV antibody. There was significant difference in means of ferritin levels among the patients of thalassemia major and of thalassemia intermedia.

Key Words: Beta Thalassemia, Thalassemia Major, Thalassemia Intermedia.

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INTRODUCTION

β -Thalassemia major is one of the common genetic disorders of younger population in all communities across the globe. It is estimated that about 70,000 infants per year are born with beta-thalassemia worldwide.¹ In Pakistan, it is estimated that 5000-9000 children with β -thalassemia are born every year.¹ It has been calculated that carrier frequency of β -thalassemia in Pakistan is 4.6%.¹ A study conducted in northern areas of Pakistan, revealed that the prevalence of beta thalassemia in Pathan population was 7.96% and in Punjabis it was 3.26%.² This opens an avenue to analyze some important demographic parameters of β -thalassemic patients in order to make proper planning, preventive measures and management of the disorder. In this study three parameters were focused i.e. blood transfusion related viral infections, urban-rural distribution and serum ferritin levels. The blood transfusion related iron overload has been addressed because it not only

results in adverse effects on liver and endocrine glands but also causes delayed growth and development.³ The objective of the current study was to determine the distribution of Beta-thalassemia in Center for Thalassemia Care, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan according to the age group, prevalence of transfusion related viral infections and serum ferritin levels.

METHODOLOGY

The cross-sectional study was carried out at Centre for Thalassemia Care, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan. The study was conducted on the registered cases of thalassemia in the Centre for Thalassemia Care. They were diagnosed as beta-thalassemia on the basis of history, clinical examination, blood cell morphology, haemoglobin electrophoresis using alkaline cellulose acetate technique and genetic analyses. They were screened for antibodies against HCV, HIV and HBV surface antigen. Anti-HCV and HBsAg testing were carried out by ICT method kits using

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Standard Diagnostics Inc., of Korea make. Screening for HIV was carried out by membrane chromatography method kits of Abon Biopharm Co. of China make. One hundred and thirty nine subjects were also screened for serum ferritin levels using Cobas e 411 Roche, Hitachi kits. The normal values of serum ferritin were taken as (range) 40-350 µgm/L for males and 14-150 µgm/L for females. The cases were divided into three age groups; younger group from zero to 5 years of age, middle group from 5.1 to 10 years of age and older group from 10.1 years and above. Anemia in thalassemia major patients starts developing after 4-6 months of age when fetal haemoglobin F is failed to get converted into adult haemoglobin A.⁴ But the age groups in this study have been included from zero, to keep statistic streamlining. The male of a minimum age of five months and the female of maximum age of 27 years were recorded in the study. Each age group was divided according to the gender subgroups. They were also categorised into urban and rural residents. The data was entered and analyzed by using SPSS version 16.

RESULTS

Total of 283 cases of beta-thalassemia were included in the study. Amongst them 177 (63%) were males and 106 (37%) were females. The majority of the cases were belonging to the younger 0-5 years of age group (55%).

Table I. Age and sex distribution of study subjects

| Age Groups (years) | Gender | | Total |
|--------------------|------------------|------------------|-------------------|
| | Male | Female | |
| 0 – 5 | 95 (61%) | 60 (39%) | 155 (55%) |
| 5.1 – 10 | 62 (67%) | 30 (33%) | 92 (32%) |
| 10.1 above | 20 (56%) | 16 (44%) | 36 (13%) |
| Total | 177 (63%) | 106 (37%) | 283 (100%) |

Out of 283 cases, 257 (91%) were suffering from thalassemia major and 26 (09%) cases had thalassemia intermedia. The ratio of incidence between thalassemia major and thalassemia intermedia was about 10.1. Maximum cases were

recorded in the younger age group (54%) and minimum number of cases were recorded from older age group (13%).

Table II: Distribution according to type of thalassemia

| Age in Years | Thalassemia Major | Thalassemia Intermedia | Total |
|--------------|-------------------|------------------------|------------|
| 0 - 5 | 143 (50%) | 11 (04%) | 154 (54%) |
| 5.1 - 10 | 84 (30%) | 09 (03%) | 093 (33%) |
| 10.1- above | 30 (11%) | 06 (02%) | 036 (13%) |
| Total | 257 (91%) | 26 (09%) | 283 (100%) |

The beta-thalassemia cases were also segregated into urban and rural subgroups. Of the total 283 patients, 87(31%) belonged to the urban areas and 196 (69%) were resident of the rural areas. Therefore, in this study, the rural to urban resident ratio was almost 2:1.

Figure I: Blood transfusion related viral infections

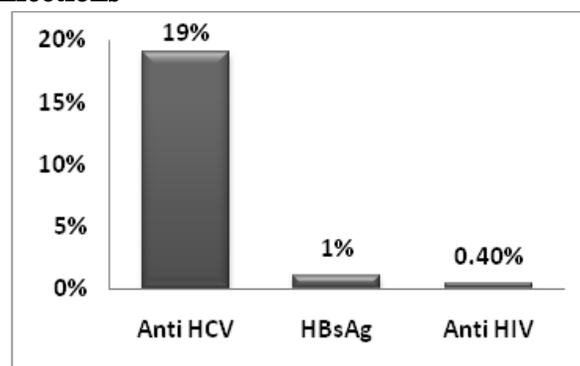


Table III. Serum ferritin levels (µgm/l) in beta-thalassemia cases

| Parameters | Thalssemia Major | Thalassemia Intermedia |
|----------------------------------|------------------|------------------------|
| Mean S. Ferritin (µgm/l) (x) | 2775 | 1519 |
| Number of cases (n) | 125 | 14 |
| Standard deviation (sd) | 2233 | 773 |
| Standard Error of the Mean (SEM) | 200 | 207 |

Fifty five cases (19%) were found to be positive for anti-HCV antibody (12% male and 7% female). Only three males were positive for HBV surface antigen

(1%) and one male was positive for anti-HIV antibody (0.4%). (Figure I)

The results showed very high levels of serum ferritin with high variations in thalassemia major cases as compared to the thalassemia intermedia. The difference of means between the two groups was significant ($p < .05$). (Table IV)

Table IV. Serum ferritin levels ($\mu\text{gm/l}$) according to sex

| Parameters among males | Thalassemia Major | Thalassemia Intermedia |
|----------------------------------|-------------------|------------------------|
| Mean (x) | 3217 | 1751 |
| Number of cases (n) | 82 | 9 |
| Standard Deviation | 2087 | 998 |
| Standard error Of the mean (SEM) | 230 | 353 |
| Parameters among females | Thalassemia Major | Thalassemia Intermedia |
| Mean (x) | 1932 | 1101 |
| Number of Cases (n) | 43 | 5 |
| Standard Deviation | 1099 | 285 |
| Standard error of The mean (SEM) | 168 | 127 |

The table IV shows high mean and standard deviation of serum ferritin levels in male thalassemia major cases as compared to those of thalassemia intermedia cases. The difference between the means of serum ferritin levels in male groups of β -thalassemia major and thalassemia intermedia was statistically significant ($p < 0.05$).

The mean and standard deviation of serum ferritin levels were high in thalassemia major female cases in comparison to those of thalassemia intermedia. However, the difference between means of serum ferritin levels in thalassemia major and intermedia was statistically insignificant.

DISCUSSION

In present study, the ratio between male-to-female thalassemia major cases was almost 1.5:1. This was consistent with a study carried out at Karachi that showed the prevalence ratio of thalassemia major in male-to-female as 1.5:1.⁵ In another study carried out at Isfahan, Iran, the above ratio was exactly the same, i.e. 1.5:1 for thalassemia major.⁶ In current study, 9% cases were registered as of

thalassemia intermedia and 91% as thalassemia major. Thus the prevalence ratio between thalassemia major and thalassemia intermedia was 10:1. These findings are consistent with a study carried out in six cities of India in 2012, in which the prevalence rate of thalassemia intermedia among the thalassemia patients was 9.3%.⁷ The prevalence rate for thalassemia intermedia was found to be 10.38% in Bengal, India.⁸ The male-to-female ratio in thalassemia intermedia patients was 1:1 in the present study. These results were consistent with the findings of Hassan M Yaish et al, that showed incidence of equal sex distribution in thalassemia intermedia.⁹

The rural to urban ratio of thalassemia was 2:1 in the current study. It was most probably due to the more events of cousin marriages in rural areas which is a custom of rural society in Pakistan. Being a genetic disorder, thalassemia runs through the families.⁴ However, ignorance, poor maternity care and illiteracy in rural areas could be the important contributory factors which need immense consideration.

The prevalence rate of HCV infection in β -thalassemia cases in present study was found to be 19% (12% in males and 07% in females cases). While in the study conducted in 2014, the prevalence rate of HCV in healthy subjects was found to be 3.5%.¹⁰ Therefore, it seemed that "corrected" transfusion related HCV infection in thalassemia patients could be about 15.5%, even then the prevalence figure of 15.5% was considerable. However, the prevalence rate in current study was remarkably lower than those of found in other studies in Pakistan. In a study carried out at Lahore in 2014, the prevalence rate of HCV infection in thalassemia patients was 41%.¹¹ A study conducted at Rawalpindi in 2014 showed the rate of HCV infection among thalassemia subjects as 49%.¹² Another study was conducted at the Zoology Department of Government College University, Faisalabad which revealed that anti-HCV activity was 65% in beta thalassemia patients.¹³ The prevalence rate of HCV in β -thalassemia children in current study was comparable to those carried out in other countries. For example, at Gujrat, India in 2015, the prevalence rate of HCV positive in β -thalassemia cases was 6%.¹⁴ In Egypt in 2012, the anti-HCV positivity in β -thalassemia patients was 19.5%.¹⁵ In India in 2014 the anti-HCV activity found to be 20.58% in β -thalassemia patients.¹⁶ For HBV transfusion related infection, the prevalence rate in current study was 1% which is

remarkably low. The HBV prevalence rate in β -thalassemia patients in Rawalpindi in 2014 was 3%.¹² In Indian studies conducted at two different centres, the transfusion related HBV infection in β -thalassemia patients was 9%¹⁴ and 1.47% respectively.¹⁶

In present study, serum ferritin levels were also recorded in (125 out of 257) thalassaemic patients. The levels were remarkably higher in thalassemia major patients with gross variations and are revealed in the standard deviation figures. The higher levels of serum ferritin were recorded in the middle age group (5.1 – 10 years) in both male and female cases. The mean serum ferritin level in thalassemia major cases was 2775 $\mu\text{gm/l}$. The result was comparable with a study conducted at Rawalpindi in 2004 in which mean serum ferritin level was found to be 3390 ng/ml,¹⁷ ($\mu\text{gm/l} = \text{ng/ml}$). In current study, the mean serum ferritin level in male thalassemia major patients was 3217 $\mu\text{gm/l}$ while in female patients it was 1932 $\mu\text{gm/l}$. The difference between two means was significant ($p < 0.05$).

Out of 26 registered thalassemia intermedia cases, serum ferritin levels were carried out in 14 cases. The mean serum ferritin level in these cases was 1519 $\mu\text{gm/l}$. The result is comparable with an Indian study conducted in 2014 which showed the mean serum ferritin level as 486.54 ± 640 $\mu\text{gm/l}$.¹⁸ In present study, the mean serum ferritin level in 9 male patients of thalassemia intermedia was 1751 $\mu\text{gm/L}$ and that of in 5 female cases the mean was 1101 $\mu\text{gm/L}$. The difference between the two means was insignificant ($p > 0.05$).

Concisely, the difference between the means of serum ferritin levels in thalassemia major cases and thalassemia intermedia was significant ($p < .05$). The males of thalassemia major and thalassemia intermedia have statistically significant difference of mean serum ferritin levels ($p < 0.05$). But there is no significant difference in means of serum ferritin levels amongst females in thalassemia major and intermedia ($p > 0.05$). It seems to be because of decreased number of the cases.

CONCLUSION

This study showed that males were suffering from β -thalassemia major disorder in higher number as compared to the females while in thalassemia intermedia it was almost equal involvement in both genders. The ratio between β -thalassemia major

and thalassemia intermedia was 10:1. All these figures are consistent with national and international studies. In present study, the rural-to-urban prevalence ratio for beta-thalassemia was 2:1. This ritual should be discouraged especially in thalassemia families. In this study, significant proportion of cases of β -thalassemia were found to be positive for the anti-HCV antibody.

The conventional methods of screening by ICT method must be replaced by more sensitive ELISA technique. Serum ferritin levels also need attention and iron chelation therapy should be encouraged. Families having thalassaemic child should be educated about the disease. All members of the family should be screened for thalassemia trait and genetic counselling should be done. Moreover, in order to minimise blood transfusions in thalassaemic patients and to cure the disease, free of cost bone marrow transplantation and gene therapy should be provided by the government.

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