



RESEARCH ON CROSS SECTIONAL OBSERVATIONAL STUDY OF ENDOCRINAL DYSFUNCTION IN THALASSEMIA PATIENTS

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ABSTRACT

INTRODUCTION; Thalassemia is most common heterogeneous group of single gene disorders, AIM ;Primary objectives;To study the endocrinal abnormalities in patients of thalassemia major.,To find out correlation between age, sexand serum ferritin levels with endocrinal abnormalities in thalassemia patients.,Secondary Objectives To study growth and development in thalassemia major patients.

MATERIALS AND METHODS: This study was conducted in the Thalassemia Unit of the Department of Pediatrics, Deen Dayal Upadhyay Hospital, New Delhi.Cross sectional observational study (descriptive). It was a hospital based study.,STUDY SITE: Day care thalassemia unit of Deen Dayal Upadhyay hospital, New Delhi. In Thalassemia unit patients are being admitted for regular blood transfusion & investigated routinely.,

STUDY DURATION: 1st October 2013 to 30th June 2014 (9 months)

SAMPLE SIZE: Sample size was calculated using the formula for descriptive study ($Z^2 \times p \times q / d^2$). When the estimated prevalence of endocrinal disorder in Thalassemia major patients (p) = 75%, with the precision error of estimation (d) = 0.12 (or 12%), and $\alpha=0.05$, $\beta=0.02$, a sample size of 50 cases is needed.

DATA COLLECTION: 50 thalassemia patients more than 8 years of age both males & females who were on transfusion therapy attending outdoor or being admitted in Day care Thalassemia unit of Deen Dayal Upadhyay hospital were assessed by history and physical examination (as per proforma) and laboratory investigation taking care of inclusion & exclusion criteria.

STATISTICAL ANALYSIS ; Descriptive statistics will be analyzed

CONCLUSION; The present study was done to find out various endocrinal abnormalities in patients of thalassemia major and to find out correlation between age, sex and serum ferritin level with these endocrinal abnormalities. A total 50 cases of thalassemia major both male and female on regular transfusion were studied. In our study, endocrinal abnormalities like short stature, hypothyroidism , impaired glucose tolerance, delayed puberty & hypogonadism were found to be more frequently associated with patients of thalassemia major although not statistically significant. Osteopenia & Osteoporosis were found to be significantly associated with these patients especially in the higher age groups. Though endocrinopathies were found more in cases having high serum ferritin level (≥ 2000 ng/dl) and higher age groups but correlation between age, sex and serum ferritin levels with endocrinal abnormalities was statistically not significant.

KEYWORDS :

INTRODUCTION

Thalassemia is most common heterogeneous group of single gene disorders, .The carrier rate for -thalassemia gene varies from 1- 3% in southern India to 3% - 15% in northern India. Certain communities in India, such as Sindhis and Punjabis from northern India, Bhanushali's, Kutchis, Lohana's from Gujarat, Mahar's, Neobuddhist's, Koli's and Agri's from Maharashtra, & Gowda's and Lingayat's from Karnataka etc. have a higher carrier rate.^(4,5) The pattern of iron deposition in thalassemia resembles that observed in idiopathic haemochromatosis, a disease associated with multiple endocrine abnormalities.

AIMS AND OBJECTIVES

Primary objectives

- 1 To study the endocrinal abnormalities in patients of thalassemia major.
- 2 To find out correlation between age, sex and serum ferritin levels with endocrinal abnormalities in thalassemia patients.

Secondary Objectives

To study growth and development in thalassemia major patients.

MATERIALS AND METHODS

This study was conducted in the Thalassemia Unit of the Department of Pediatrics, Deen Dayal Upadhyay Hospital, New Delhi

(A) STUDY DESIGN: Cross sectional observational study (descriptive). It was a hospital based study.

(B) STUDY SITE: Day care thalassemia unit of Deen Dayal Upadhyay hospital, New Delhi. In Thalassemia unit patients are being admitted for regular blood transfusion & investigated routinely.

(C) STUDY DURATION: 1st October 2013 to 30th June 2014 (9 months)

(D) SAMPLE SIZE: Sample size was calculated using the formula for descriptive study ($Z^2 \times p \times q / d^2$). When the estimated prevalence of endocrinal disorder in Thalassemia major patients (p) = 75%, with the

precision error of estimation (d) = 0.12 (or 12%), and $\alpha=0.05$, $\beta=0.02$, a sample size of 50 cases is needed.

(E) STUDY SUBJECTS: 50 Cases of Thalassemia major both male & female on regular transfusion therapy.

Inclusion Criteria

1. Children more than 8 years of age.
2. Children on transfusion therapy.
3. Children on regular chelation therapy.

Exclusion Criteria

1. Children less than 8 years of age.
2. Family history of Diabetes/ Thyroid disorder/ Delayed puberty/ short stature.
3. Children having history of chronic liver disease or chronic renal disease.
4. Children not taking chelation therapy regularly.

(F) DATA COLLECTION: 50 thalassemia patients more than 8 years of age both males & females who were on transfusion therapy attending outdoor or being admitted in Day care Thalassemia unit of Deen Dayal Upadhyay hospital were assessed by history and physical examination (as per proforma) and laboratory investigation taking care of inclusion & exclusion criteria.

All investigations were done in laboratory, department of pathology & department of radiology, Deen Dayal Upadhyay Hospital, New Delhi

1) Laboratory Investigation :

- 1) CBC (complete blood count)
- 2) Serum ferritin
- 3) TSH, Free T4, Free T3
- 4) Serum Testosterone
- 5) Glucose Tolerance Test (GTT), Fasting blood Sugar (FBS)
- 6) Bone Density (DEXA)

STATISTICAL ANALYSIS

Descriptive statistics will be analyzed with SPSS version 17.0 software. Continuous variables will be presented as meanSD. Categorical variables will be expressed as frequencies and percentages. Nominal categorical data between the groups will be compared using Chi-squared test or Fisher's exact test as appropriate. A p value less than 0.05 will be taken to indicate a significant difference.

OBSERVATIONS AND RESULTS

This study was conducted at Day care Thalassemia unit of Deen Dayal Upadhyay Hospital, New Delhi with an objective to find out various endocrinal abnormalities in Thalassemia major patient. The observations and results are given below:

Table 1

Table 1 (A)

Distribution of thalassemia patients based on bone mineral density (dexa scan)

Age group	Dexa scan (S.D. Score)			Total	P value
	0.8 to -1	Osteopenia -1.1 to -2.4	Osteoporosis (-2.5)		
8 - 10	5(45.5%)	6(54.5%)	0(0%)	11	<0.001*
10 - 12	8(80%)	2(20%)	0(0%)	10	
12 - 14	1(16.7%)	3(50%)	2(33.3%)	6	
14 - 16	0(0%)	0(0%)	7(100%)	7	
16 - 18	0(0%)	5(31.3%)	11(68.8%)	16	
Total	14	16	20	50	

Fig. 1 (A)

Out of 50 cases, 14 (28%), 16 (32%) and 20 (40%) were diagnosed as normal, osteopenic and osteoporotic respectively. 6 (54.5%) out of 11 patients in 8-10 years age group were osteopenic whereas none had osteoporosis. 2 (20%) out of 10 patients in 10-12 years age group were osteopenic whereas none had osteoporosis. 3 (50%) out of 6 patients in 12-14 years age group were osteopenic whereas 2 (33.3%) had osteoporosis. All the 7 (100%) patients in 14-16 years age group had osteoporosis. 5 (31.3%) out of 16 patients in 16-18 years age group were osteopenic whereas 11 (68.8%) had osteoporosis. There was a highly significant association of occurrence of osteoporosis & osteopenia in thalassemia major patients (p value was 0.001). Furthermore there was significant increase in the chances of osteoporosis in higher age group (14-18 yrs age group).

DISCUSSION

Present study is a hospital based Cross sectional observational study (descriptive) done in Deen Dayal Upadhyay Hospital, New Delhi from 1st October 2013 to 30th June 2014. Total 50 thalassemia cases on regular transfusions were studied, out of which 29 (58%) were males and 21 (42%) were females. There was Male preponderance in our study. Mean age of thalassemia cases was 13.09±3.45 years. All cases were divided into five groups, 8-10 yrs, 10-12 yrs, 12-14 yrs, 14-16 yrs and 16-18 years. There were 11 (22%) cases in 8-10 years age group, 10 (20%) cases in 10-12 years age group, 6 (12%) cases in 12-14 years age group, 7 (14%) cases in 14-16 years age group and 16 (32%) cases in 16-18 years age group. Thus maximum numbers of thalassemia cases, 16 (32%) were in age group 16-18 years.

Out of 50 cases, 43 (86%) were Hindus and 7 (14%) were Muslims. All 50 thalassemia cases were divided into two groups based on their serum ferritin values, 19 (38%) cases were in low ferritin group (<2000ng/dl) & 31 (62%) in high ferritin group (≥2000ng/dl).

Following endocrinal dysfunctions were found in our study.

1) Hypogonadism & delayed puberty

In our study the most common endocrinal disorder was hypogonadism & delayed puberty.

61.5% of males & 90% of females had hypogonadism & delayed puberty. 3 (60%) out of 5 male patients in low ferritin group (<2000) had delayed puberty & hypogonadism whereas 5 (62.5%) out of 8 male patients in high ferritin group (≥2000) had delayed puberty & hypogonadism but this difference was statistically not significant. (p value was 1.000). 3 (75%) out of 4 female patients in low ferritin group (<2000) had delayed puberty & hypogonadism whereas 6 (100%) out of 6 female patients in high ferritin group (≥2000) had delayed puberty & hypogonadism but this difference was also statistically not significant (p value was 0.400).

2) Short stature

In our study second most common endocrinal disorder was short stature. Out of 50 thalassemia cases, 26 (52%) were having short stature. Comparable results were reported by Roth C et al²², Soliman et al²⁴, Wu KH et al²⁵, Najafipour F¹⁹.

Maximum number of short stature cases, 9 (18%) were in 16-18 years age group but maximum affected belonged to 14-16 years age group (85.71%). This can be explained due to low sample size in this age group.

17 out of 29 (58.6%) males & 9 out of 21 (42.8%) females were having short stature but this difference was statistically not significant (p value was 0.271).

8 (42.1%) out of 19 patients in low ferritin group (<2000) had short stature whereas 18 (58.1%) out of 31 patients in high ferritin group (≥2000) had short stature but this difference was statistically not significant (p value was 0.273).

3) Hypothyroidism

In our study prevalence of hypothyroidism was 16.7 (24.1%) out of 29 males were hypothyroid & 1 (4.8%) out of 21 females had hypothyroidism but this difference was statistically not significant (p value is 0.117)

6 (19.4%) out of 31 were in high ferritin group (≥2000) & 2 (10.5%) out of 19 were in low ferritin group (<2000) but this difference was statistically not significant (p value is 0.693).

4) Diabetes

In our study out of 50 thalassemia cases, 2 (4%) were having impaired fasting blood glucose and all these cases belonged to high ferritin (≥2000) group and 16-18 years age group and were equally distributed in both sexes. Out of 50 thalassemia cases, 6% were having impaired glucose tolerance test (IGTT) and all these cases belonged to 16-18 years age group. 2 (6.9%) out of 29 males had IGTT & 1 (4.8%) out of 21 females had IGTT but this difference was statistically not significant (p value is 1.000).

2 (6.5%) out of 31 were in high ferritin group (≥2000) & 1 (5.3%) out of 19 were in low ferritin group but this difference was statistically not significant.

No case of diabetes was detected.

5) Bone mineralization defect

In our study, out of 50 thalassemia cases, 14 (28%), 16 (32%) and 20 (40%) were diagnosed as normal, osteopenic, and osteoporotic respectively. 6 (54.5%) out of 11 patients in 8-10 years age group were osteopenic whereas none had osteoporosis. 2 (20%) out of 10 patients in 10-12 years age group were osteopenic whereas none had osteoporosis. 3 (50%) out of 6 patients in 12-14 years age group were osteopenic whereas 2 (33.3%) had osteoporosis. All the 7 (100%) patients in 14-16 years age group had osteoporosis. 5 (31.3%) out of 16 patients in 16-18 years age group were osteopenic whereas 11 (68.8%) had osteoporosis.

SUMMARY

This study was conducted at Day care thalassemia unit of Deen Dayal Upadhyay hospital, new delhi with an objective to study endocrinal dysfunction in thalassemia major patients and to find out correlation between age, sex & serum ferritin levels with these endocrinal abnormalities. Salient findings are:

- Total 50 thalassemia patients above 8 years of age, on regular blood transfusions and chelation therapy were studied. Out of them 29 (58%) were males and 21 (42%) were females. Though there was a slight male preponderance but it was not statistically significant.
- Maximum numbers of thalassemia cases, 16 (32%) were in 16-18 years of age group.
- Mean age of thalassemia cases was 13.09±3.45 yrs.
- Out of 50 cases, 19 (38%) were having serum ferritin <2000 ng/dl while 31 (62%) were having serum ferritin ≥2000 ng/dl.
- Distribution of endocrinopathies like delayed puberty & hypogonadism, short stature, hypothyroidism, diabetes and bone mineralization defect were studied along with their correlation with age, sex and serum ferritin levels.
- Out of 50 cases, 26 (52%) were short statured, 17 (73.91%) were

having delayed puberty & hypogonadism, 8 (16%) were having hypothyroidism, 36 (72%) were having bone mineralization disorder and 3 (6%) were having prediabetes (impaired glucose tolerance).

- Earliest manifestations of endocrinopathies in thalassemia patients were found to be short stature and bone mineralization defect.

CONCLUSION

The present study was done to find out various endocrinal abnormalities in patients of thalassemia major and to find out correlation between age, sex and serum ferritin level with these endocrinal abnormalities. A total 50 cases of thalassemia major both male and female on regular transfusion were studied.

In our study, endocrinal abnormalities like short stature, hypothyroidism, impaired glucose tolerance, delayed puberty & hypogonadism were found to be more frequently associated with patients of thalassemia major although not statistically significant. Osteopenia & Osteoporosis were found to be significantly associated with these patients especially in the higher age groups. Though endocrinopathies were found more in cases having high serum ferritin level (≥ 2000 ng/dl) and higher age groups but correlation between age, sex and serum ferritin levels with endocrinal abnormalities was statistically not significant.

Early endocrinal evaluation & Regular follow-up of patients with thalassaemia major is needed for early detection and management of associated complications.

RECOMMENDATIONS

- Regular blood transfusions along with proper chelation therapy should be the mainstay of management in thalassemia patients.
- Early endocrinal evaluation is recommended in these patients to detect early endocrinopathies so that appropriate intervention can be started on time.
- Regular follow-up of patients with thalassaemia major is needed for early detection and management of associated complications.
- To optimize Bone Mineral Density in thalassemia major, it is important to ensure adequate iron chelation and adequate intake of calcium and vitamin D.
- Because of small study group further studies are needed to find out any correlation between age, sex and serum ferritin levels with endocrinopathies in thalassemia patients.
- Regular growth monitoring is needed in thalassemia major patient to detect early cases of short stature

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