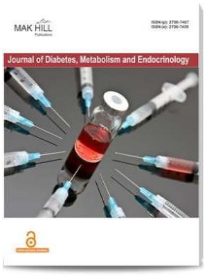

ISSN Print: 1813-176x
ISSN Online: 1994-4624

International Journal of Molecular Medicine and Advance Sciences
https://ijmmas.com/

Research Article

Prevalence of Diabetes Mellitus and other Endocrine Disorders in Transfusion Dependent Thalassemia children of a tertiary care hospital in central India : Case-Control Study.

Anurag Udhwani[1], Priyanka Shukla[1], Gaurav Tripathi[1]*, Naresh Bajaj[1].
[1]Department of Pediatrics, Shyam Shah Medical College, Rewa, Madhya Pradesh, India.

Correspondence:
Gaurav Tripathi.

Email: drgtripathi@gmail.com

Received: 24-08-2026
Revised: 03-09-2026
Accepted: 18-09-2026
Published: 29-09-2026

DOI: 10.61336/ijmmas.22-03-11

Abstract: Background: Children with Transfusion dependent Thalassemia (TDT) are at risk of iron overload-induced endocrine dysfunctions. To improve the life quality of children with TDT, the burden of endocrine issues and their connection to iron overload at a young age must be recognised as soon as possible. There is limited data on such complications from central India. This study evaluates the prevalence of diabetes mellitus (DM) and other endocrinopathies in children with TDT of a tertiary care hospital in central India. ***Objective:*** To assess the prevalence of endocrine disorders in children with TDT and their association with serum ferritin levels. ***Methods:*** A case-control study was conducted on 100 children with TDT and 100 age- and sex-matched controls. Fasting blood glucose (FBG), HbA1c, impaired glucose tolerance (IGT), thyroid profile, serum ferritin, calcium, phosphate, and vitamin D were assessed. Endocrinopathies were diagnosed as per standard criteria and cutoff values. ***Results:*** DM, impaired FBG , and impaired glucose tolerance were present in 19%, 11%, and 7% of TDT cases, respectively, versus 0%, 10%, and 2% in controls ($p<0.0001$). Hypothyroidism was seen in 4% of cases. Short stature occurred in 55% of children with TDT . Vitamin D deficiency and insufficiency were found in 19% and 64% of children with TDT. Serum ferritin correlated positively with FBG ($r=0.097$, $p<0.0001$) and TSH ($r=0.282$, $p<0.0001$), and negatively with serum calcium ($r=-0.075$, $p<0.0001$). ***Conclusion:*** Endocrinopathies are prevalent in children with TDT, correlating with iron overload. Routine endocrine evaluation is warranted.

Keywords: Transfusion dependent Thalassemia, endocrine dysfunction, diabetes mellitus, hypothyroidism, short stature, serum ferritin.

INTRODUCTION

Beta-thalassemia major (TDT) is a hereditary anemia necessitating lifelong transfusions. Resultant iron overload contributes to organ dysfunction, particularly affecting endocrine glands. Long-term extravascular hemolysis caused by TDT enhances the digestive tract's ability to absorb iron. This, combined with repeated blood transfusions (BT), might result in iron toxicity & iron deposition in the tissues. It can induce gradual tissue injury in the liver, heart, endocrine glands as well as other organs by producing free radicals and oxidative damage [1,2,3].

The frequency of impaired glucose homeostasis in TDT has steadily risen in recent years, possibly due to patients' longer life expectancies and rising concerns about the coexistence of thalassemia and diabetes. By destroying membrane lipids and other macromolecules, free iron facilitates the creation of reactive oxygen species, which induce cell death and eventually organ failure. Iron buildup ismeasured using serum ferritin, serumiron,and transferrin levels, and the iron saturation % is calculated.

Although iron excess contributes to the emergence of endocrine problems, the severity of clinical symptoms is mostly controlled by the type of underlying globin gene alteration, which are typically mutations or gene deletions. The majority of individuals will require regular transfusions to live.

Mutations in the β-globin gene (HBB) cause TDT, but mutations and genetic modifiers affecting fetal γ-globin expression primarily dictate how severe the disease becomes. [4]. Co inheritance of α-thalassemia also reduces the severity of TDT. Furthermore, chronic liver illness caused by iron overload and hepatic viral infections, primarily hepatitis C virus, caused by multiple transfusions play a substantial influence in TDT patients' endocrinopathies, particularly the development of diabetes mellitus.

This study aims to determine the prevalence of diabetes mellitus and other endocrine disorders in children with TDT and assess their correlation with iron overload about which there is very limited data from central India particularly from Vindhya region and Madhya Pradesh.

MATERIALS AND METHODS

A case-control study was conducted on 100 children with TDT (aged 2–18 years) receiving regular transfusions at Shyam Shah Medical College, Rewa, and 100 healthy controls. Informed consent and ethical clearance were obtained.

Inclusion of cases and controls :

- Cases : All children with TDT (Aged 2-18years) diagnosed by HPLC and/or screening of parents wherever required on regular transfusion protocols of leucoreduced PRBC transfusion every 2-3 weekly as per requirements to maintain a pre transfusion hemoglobin between 9.5-11 g/dl and were on regular chelation therapy started once serum ferritin reaches more than 1000 ng/ml with regular monitoring and investigations as per TIF (Thalassemia international federation) guidelines [5].
- Controls : healthy controls of same age group attending our department OPD for consultations of routine pediatric disorders excluding anemia or thalassemia .

Measurements: Anthropometry, Tanner staging, fasting and post-load glucose, HbA1c, serum ferritin, TSH, T3, T4, calcium, phosphate, and vitamin D levels were recorded.

Definitions:

- Diabetes : FBG ≥126 mg/dL, 2-hr IGT ≥200 mg/dL, or HbA1c ≥6.5%
- Hypothyroidism: TSH >5.4 mIU/L
- Short stature: Height <-2 SD for age and sex was considered as short stature. Mid parental height (MPH) as well as target height were also calculated to rule out other causes of short stature like constitutional and familial short stature
- Delayed puberty: Detailed menstrual history was obtained. Tanner's staging was done on all males older than 14 years and females older than 13 years of age. Delayed puberty was described in girls as the age of more than 13 years & not having attained the tanner B2 stage or age of more than 15 years with primary amenorrhea. In males, it was defined as the age of more than 14years and not having achieved tanner stage G2 or on hormonal replacement therapy.
- Lab Investigations: Venous blood samples were taken from all patients and divided into two tubes: 2 ml blood in an EDTA vials for complete blood count (CBC) and glycosylated haemoglobin (HbA1C) and 6 ml blood in 2 red coloured serum vials for ferritin level, TSH, triiodothyronine(T3), thyroxine(T4), serum calcium , phosphate & vitamin D levels.
- Statistical Analysis: SPSS software version 28.0 was used ; t-test, Chi-square, Pearson's correlation. Significance at $p<0.05$..

RESULTS

Table 1: Demographics and Anthropometry

Parameter	TDT (n=100)	Controls (n=100)	p-value
Mean age (years)	7.5 ± 4.1	6.3 ± 3.1	0.045
Male (%)	55	48	0.31
Height (cm)	109.6 ± 27.9	117.6 ± 23.9	0.0306
BMI (kg/m2)	16.87 ± 5.12	17.55 ± 5.97	0.388

Table 2: Endocrine Complications

Parameter	TDT (%)	Controls (%)	p-value
Diabetes mellitus	19	0	<0.0001
Impaired fasting glucose	11	10	0.04
Hypothyroidism	4	1	0.048
Short stature	55	9	<0.0001
Vitamin D deficiency (<20 ng/mL)	19	8	<0.0001

Table 3 : Correlation between Serum ferritin with Blood glucose level (FBS)

Serum ferritin	Bloodglucoselevel (FBG)	r	Correlation	PValue	Results
1737.91± 935.85	105.31±20.29mg/dl	0.0969	MildPositive correlation	<0.0001	Significant

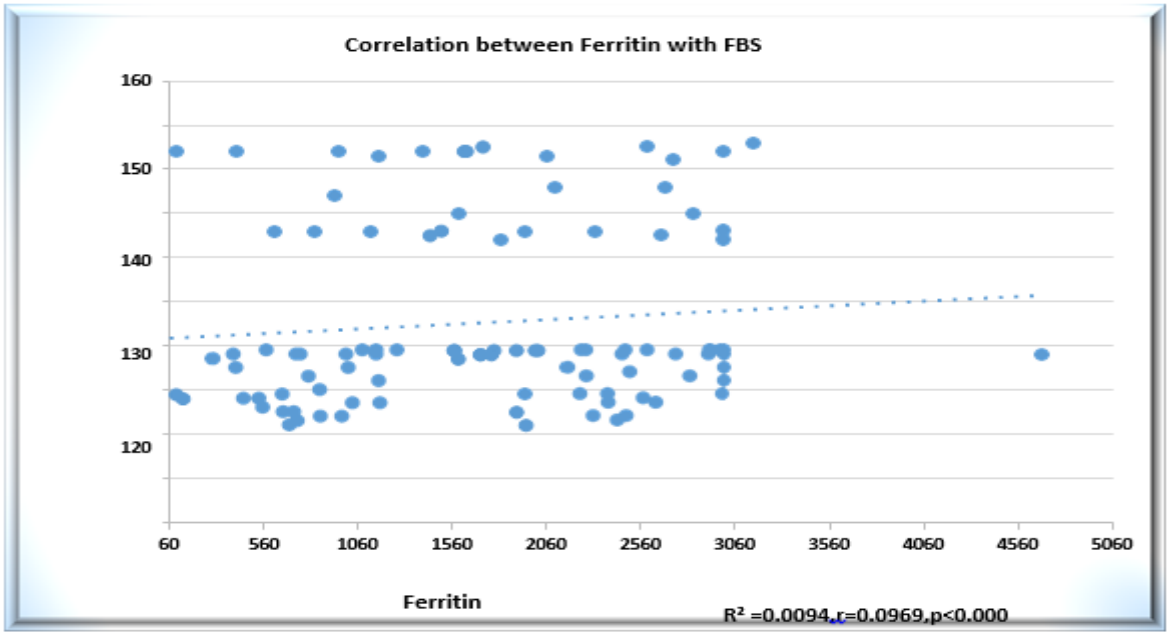

Figure 1: It shows a statistically significant correlation between mean Serum ferritin with Blood glucose level (FBG) with p value {p<0.0001}.

Table 4: Correlation Analysis (Pearson's r) shows statistically significant correlation of serum ferritin with blood glucose (FBG) and hypothyroidism and negative correlation with serum calcium levels.

Parameters	r	p-value
Ferritin and FBG	0.097	<0.0001
Ferritin and TSH	0.282	<0.0001
Ferritin and Calcium	-0.075	<0.0001

Table 5 study population according to mean Height between two groups

Height(in metre)	Case (with TDT)	Controls	$\|t\|_{cal}$	P Value	Results
Mean± s.d	1.096±0.279m	1.176±0.239m	2.178	0.0306	Significant

There was statistically significant difference in comparison of height (m) between two groups, with p-value {p<0.05}. In Children with TDT mean height was less than in normal children.

DISCUSSION

Our study revealed a high prevalence of DM and other endocrine abnormalities in TDT children, consistent with prior studies. In the current study, the overall percentage of endocrinal anomalies was 80%, that is greater than that reported by previous studies done. Significant correlations between serum ferritin and glycemic parameters and TSH underscore the role of iron overload. No significant association was observed between Tanner staging and ferritin, though the sample size was less . In accordance with earlier studies [6] the presence of endocrine problems was not significantly related with risk variables such as hemoglobin concentration prior to transfusion or splenectomy history which was in eight percent (8%) children with TDT in our examined group.

This study showed a 4% frequency of hypothyroidism in children with TDT and 1% in controls , which is lower than the results of Sharma et al. (8.9%)[7], Fung et al. (10%) [8], and Najafipour et al. (16%) [9], although Baul et al. [10] discovered a significantly higher percentage. Diabetes, IFG, and IGT were found to be 19%, 11%, and 7% prevalent in cases, and 0%, 10%, and 2% prevalent in controls , respectively in our study.

Serum ferritin and serum calcium exhibited a statically meaningful mild negative association in our investigation (table 4). Many studies, on the other hand, found no link among serum ferritin and the occurrence of endocrinopathy .\

Tanner staging was employed in only 10 cases in the case group and 5 cases in the control group, with 20% (n=2/10) of the case group experiencing delayed puberty, which was lower than in previous research. No delay in puberty was found in control group. Delayed Puberty didn't show any statistically meaningful association with serum ferritin as contrary to the studies like

Dixit etal & Sutay etal. A meta-analysis [11] of 44studies from around the world revealed that the percentage of diabetic mellitus, impaired fasting glucose, and impaired glucose tolerances in children with TDT were 6.54%, 17.21%, and 12.46%, correspondingly. In terms of the age difference between the first transfusion and the start of chelation, TDT patients with diabetes differed significantly from those without diabetes, as observed in the Gamberini et al. study [12]

Limitations:

1.Lack of MRI-based iron quantification and hormonal assays for gonadal and adrenal function.
2. Number of patients assessed for puberty is small in this study.
3. Serum ferritin may not fully reflect iron overload in TDT patients
4. Larger studies with more number of cases might help in deriving stronger correlations.

CONCLUSION

Endocrine dysfunctions, particularly diabetes and growth disorders, are common in children with TDT, though clinically less significant, correlating with iron overload. Routine endocrine monitoring and timely intervention are crucial. In the current scenario, holistic management with effective transfusion/regular chelation, regular surveillance for signs and symptoms of endocrine dysfunctions by pediatricians/physicians, and timely referral to endocrinologist and hemoglobinopathy clinic is the key to reducing comorbidities, and further analyses can be done to see the consequences of early lifestyle modifications and dietary modifications on endocrine complications in thalassemia children.

Funding: None

Conflict of Interest: None declared

Acknowledgments: We acknowledge the staff of Shyam Shah Medical College, Rewa, and the participating children and their families. It was done as a part of PG thesis of Dr. Anurag Udhwani in Shyam Shah Medical College, Rewa and not yet published.

Declaration of data availability : the data of above mentioned study is available with the corresponding author and can be accessed at drgtripathi@gmail.com

Contribution of authors : AU- conduct of study and data collection , PS- conduct and statistical analysis , GT- study design and writing manuscript , NB- concept of study.

REFERENCES

1. Viprakasit V, Lee-Lee C, Chong QT, Lin KH, Khuhapinant A. Ironchelation therapy in the management of thalassemia: the Asian perspectives. Int J Hematol. 2009 Nov;90(4):435–45.
2. Porter JB. Monitoring and treatment of iron overload: State of the art and new approaches. Semin Hematol. 2005 Apr;42(2):S14–8.
3. Gomber S, Dabas A, Bagmar S, Madhu SV. Glucose Homeostasis andEffect of Chelation on β Cell Function in Children With β-Thalassemia Major. J Pediatr Hematol Oncol. 2018 Jan;40(1):56–9.
4. Nibedita Mitra etal. Multiomics analysis of red blood cells reveals thalassemia severity beyond globin gene mutations , Blood advances, volume 10, issue 10. 2026 May 26: 3690-3704
5. Cappellini, M.D., Farmakis, D., Porter, J. Taher, A. et al.Guidelines for management of Transfusion- Dependent Thalassemia (4th Edition/ Version 2.0), prepared by Thalassemia International Federation: 2021
6. Mahmoud RA,KhodearyA,Farhan MS.Detectionof endocrinedisorders in young children with multi-transfused thalassemia major. Ital J Pediatr. 2021 Dec;47(1):165.
7. Sharma R, Seth A, Chandra J, Gohain S, Kapoor S, Singh P, et al. Endocrinopathies in adolescents with thalassaemia major receiving oral iron chelation therapy. Paediatr Int Child Health. 2016;36(1):22-7.
8. Fung EB, Harmatz PR, Lee PDK, Milet M, Bellevue R, Jeng MR, et al. Increased prevalence of iron-overload associated endocrinopathy in thalassaemia versus sickle-cell disease. Br J Haematol. 2006;135(4):574-82.
9. Najafipour F, Aliasgarzadeh A, Aghamohamadzadeh N, Bahrami A,Mobasri M, Niafar M, et al. A cross-sectional study of metabolic and endocrine complications in beta-thalassemia major. Ann Saudi Med. 2008 Sep;28(5):361–6.
10. Baul S, Dolai T, Sahana P, De R, Mandal P, Chakrabarti P. Does thyroid dysfunction correlate with iron overload in E-β thalassemia patients? A study from a tertiary care thalassemia center in India. Arch Med Health Sci. 2019;7(2):206.
11. He LN, Chen W, Yang Y, Xie YJ, Xiong ZY, Chen DY, et al. Elevated prevalence of abnormal glucose metabolism and other endocrine disorders in patients with β-thalassemia major: a meta-analysis. Biomed Res Int. 2019;2019:1-13.
12. Gamberini MR, Fortini M, De Sanctis V, Gilli G, Testa MR. Diabetes mellitus and impaired glucose tolerance in thalassaemia major: incidence, prevalence, risk factors and survival in patients followed in the Ferrara Center. Pediatr Endocrinol Rev. 2004;2(Suppl 2):285-91.