Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2024; Vol 23: Issue 1, https://carcinogenesis.com/

Evaluation of Adrenal Insufficiency in Thalassemia Patients – 50 Cases in BSMMU, Dhaka, Bangladesh

Tahmidul Islam[1*], Md. Sunjidul Haque[2], Md. Saiful Islam[3], Khan Md. Shahriar Zaman[4], Rubaiyat-E-Mortaz[5]

[1]Assistant Professor, Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

[2]Assistant Professor (Biochemistry), Khwaja Younus Ali Medical College Hospital, Chauhali, Sirajganj, Bangladesh

[3]Assistant Professor, Department of Laboratory Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

[4]Assistant Professor, Department of Laboratory Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

[5]Assistant Professor, Department of Laboratory Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Corresponding Author: Tahmidul Islam, Assistant Professor, Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, Email ID: tahmidulislam74@gmail.com

ABSTRACT

Background: Thalassemia is a hereditary hemoglobinopathy characterized by chronic hemolytic anemia requiring regular blood transfusions. Repeated transfusions and iron overload may affect endocrine organs, including the adrenal glands, leading to adrenal insufficiency (AI). Limited data exist regarding AI prevalence among thalassemia patients in Bangladesh. This study aimed to evaluate adrenal function in thalassemia patients attending Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. ***Methods:*** This prospective cross-sectional study included 50 patients with transfusion-dependent thalassemia (TDT) aged 5–30 years, attending the Biochemistry and Molecular Biology Department of BSMMU from January 2022 to December 2022. Baseline demographics, clinical history, and transfusion details were collected. Serum cortisol levels were measured at 8:00 AM, and low-dose ACTH stimulation tests (1 µg ACTH) were performed to assess adrenal reserve. Serum ferritin was measured as a marker of iron overload. AI was defined as peak serum cortisol <18 µg/dL after ACTH stimulation. Data were analyzed using SPSS version 26. Continuous variables were expressed as mean ± SD, and categorical variables as percentages. Associations between AI and clinical/biochemical parameters were analyzed using chi-square and t-tests. ***Results:*** Among 50 thalassemia patients, 28 (56%) were male and 22 (44%) females, with a mean age of 16.8 ± 6.2 years. The mean serum ferritin was 2870 ± 1025 ng/mL. Adrenal insufficiency was detected in 12 patients (24%). AI prevalence was higher among patients with serum ferritin >3000 ng/mL (P=0.03) and those with disease duration >15 years (P=0.01). There was no significant association with sex or age. Common clinical features of AI included fatigue (80%), hypotension (50%), and poor growth (30%). ***Conclusion:*** Adrenal insufficiency is a relatively common endocrine complication among transfusion-dependent thalassemia patients in Bangladesh, particularly in those with severe iron overload and longer disease duration. Routine adrenal function assessment and early intervention may improve morbidity and quality of life in this population.

Keywords: Thalassemia, Adrenal Insufficiency, ACTH Stimulation Test, Serum Cortisol, Iron Overload, Bangladesh.

How to Cite: Tahmidul Islam, Sunjidul Haque, Saiful Islam, Khan MS Zaman, Rubaiyat-E-Mortaz, (2024). Evaluation of Adrenal Insufficiency in Thalassemia Patients – 50 Cases in BSMMU, Dhaka, Bangladesh. Journal of Carcinogenesis, Vol.23, No.1, 629-632

Evaluation of Adrenal Insufficiency in Thalassemia Patients – 50 Cases in BSMMU, Dhaka, Bangladesh

1. INTRODUCTION

Thalassemia is an inherited disorder of hemoglobin synthesis characterized by reduced or absent production of one of the globin chains. It is prevalent in South Asia, the Middle East, and the Mediterranean region. In Bangladesh, thalassemia is a major public health problem, with thousands of patients requiring regular blood transfusions for survival [1,2]. Chronic transfusion therapy, while life-saving, predisposes patients to secondary complications, most notably iron overload, which can affect multiple organ systems including the liver, heart, and endocrine glands [3]. Endocrine dysfunctions are well-recognized complications of thalassemia, with hypogonadism, diabetes mellitus, hypothyroidism, and growth retardation commonly reported [4]. Among these, adrenal insufficiency (AI) is an under-recognized but clinically significant complication. The adrenal glands are vulnerable to iron deposition, oxidative stress, and chronic inflammation, leading to impaired cortisol synthesis and adrenal reserve [5,6]. Adrenal insufficiency can present with non-specific symptoms such as fatigue, anorexia, weight loss, hypotension, and poor growth, which may be overlooked in the context of chronic illness [7]. Unrecognized AI may precipitate adrenal crisis, especially during infections or stress, posing a life-threatening risk [8]. Globally, studies report AI prevalence in thalassemia ranging from 10–40%, depending on patient age, transfusion burden, and iron chelation status [9]. However, in Bangladesh, there is limited data on adrenal function in thalassemia patients, particularly using dynamic testing such as the ACTH stimulation test. Given the increasing survival of thalassemia patients due to improved transfusion protocols, understanding the burden of AI is crucial for optimizing long-term management and preventing morbidity. This study aimed to evaluate adrenal function in transfusion-dependent thalassemia patients attending BSMMU, Dhaka, using basal cortisol levels and low-dose ACTH stimulation tests. Additionally, we sought to identify clinical and biochemical predictors of AI, including serum ferritin levels, disease duration, and demographic factors. The findings may provide insight into endocrine surveillance strategies and guide early intervention for adrenal insufficiency in thalassemia patients in Bangladesh.

MATERIALS AND METHODS

Study Design and Participants

A prospective cross-sectional study was conducted at the Biochemistry and Molecular Biology Department of BSMMU from January 2022 to December 2022. Fifty patients with transfusion-dependent thalassemia (TDT), aged 5–30 years, were enrolled after obtaining informed consent. Inclusion criteria were confirmed thalassemia by hemoglobin electrophoresis, history of regular blood transfusions (≥8 transfusions/year), and stable clinical status. Exclusion criteria included acute infection, recent steroid therapy, chronic liver or renal disease, or known adrenal disorders.

Data Collection

Baseline demographic data, transfusion history, chelation therapy, and clinical symptoms suggestive of adrenal insufficiency were recorded. Anthropometric measurements, including height, weight, and blood pressure, were obtained.

Laboratory Investigations

- **Serum Ferritin:** Measured using ELISA as a marker of iron overload.
- **Basal Serum Cortisol:** Collected at 8:00 AM using chemiluminescence immunoassay.
- **ACTH Stimulation Test:** A low-dose (1 μg) ACTH test was performed. Serum cortisol was measured at 0, 30, and 60 minutes. Adrenal insufficiency was defined as peak cortisol <18 μg/dL.
- **Other tests:** CBC, liver function tests, and renal function tests were performed to assess overall health.

Statistical Analysis

Data were analyzed using SPSS v26. Continuous variables were expressed as mean ± SD; categorical variables as percentages. Independent t-tests compared continuous variables between patients with and without AI, and chi-square tests were used for categorical variables. A P-value <0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics

Among 50 patients, 28 (56%) were male and 22 (44%) females. The mean age was 16.8 ± 6.2 years. The mean disease duration was 12.4 ± 5.8 years, and all patients were on regular transfusions. Chelation therapy was used in 80% of patients, mostly deferasirox (60%). Clinical symptoms of AI included fatigue (80%), hypotension (50%), poor growth (30%), and hypoglycemia episodes (10%).

Table 1. Demographic and Clinical Characteristics of Study Participants

Parameter	Value
Number of patients	50
Age (years, mean ± SD)	16.8 ± 6.2
Male/Female	28/22
Disease duration (years)	12.4 ± 5.8
Transfusion frequency/year	10 ± 2.3
Chelation therapy (%)	80%
Clinical features (%)	Fatigue 80%, Hypotension 50%, Poor growth 30%

Biochemical Profile

The mean serum ferritin was 2870 ± 1025 ng/mL. Basal morning cortisol ranged from 4.5–24 µg/dL, with a mean of 15.2 ± 4.8 µg/dL. After ACTH stimulation, peak cortisol ranged from 8–32 µg/dL. Twelve patients (24%) were diagnosed with adrenal insufficiency.

Table 2. Comparison of Biochemical Parameters in Patients With and Without Adrenal Insufficiency

Parameter	AI (n=12)	No AI (n=38)	P-value
Serum ferritin (ng/mL)	3420 ± 980	2650 ± 1020	0.03
Basal cortisol (µg/dL)	9.2 ± 2.1	17.0 ± 3.8	<0.001
Peak cortisol (µg/dL)	13.5 ± 2.2	22.8 ± 3.1	<0.001
Disease duration (yrs)	16.2 ± 4.5	11.0 ± 5.2	0.01

Association Between AI and Clinical/Biochemical Factors

- AI prevalence was significantly higher in patients with ferritin >3000 ng/mL (P=0.03).
- Disease duration >15 years was associated with higher AI prevalence (P=0.01).
- No significant association was found with sex, age, or chelation status.

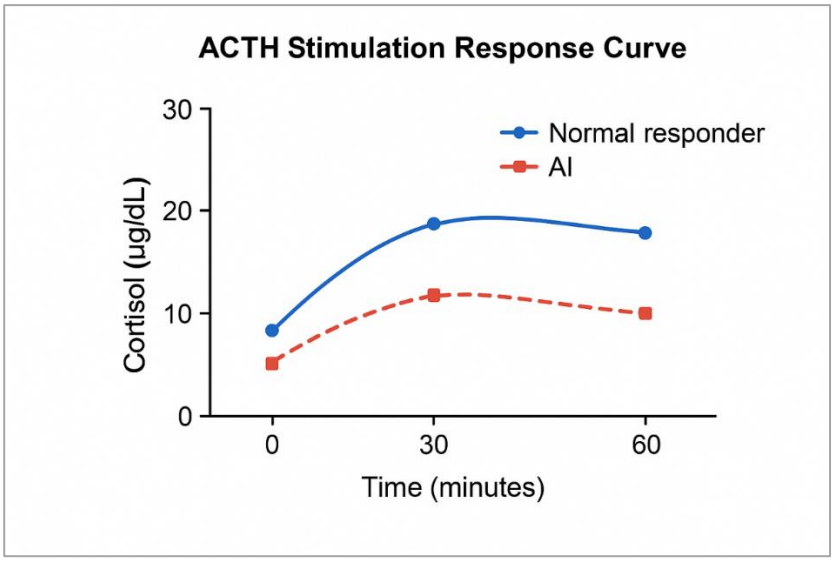

Figure 1. ACTH Stimulation Response Curve in Patients with and Without Adrenal Insufficiency

Peak cortisol response is blunted in AI patients compared to normal responders.

DISCUSSION

This study found that 24% of transfusion-dependent thalassemia patients in BSMMU, Dhaka, had adrenal insufficiency, confirming that AI is a notable endocrine complication in this population. This prevalence aligns with prior reports from India (20–30%) and Iran (22%) [10,11]. The wide variation in prevalence in different studies is likely due to differences in patient age, transfusion burden, chelation adherence, and diagnostic criteria.

Pathophysiology: Chronic transfusions in thalassemia lead to systemic iron overload. Excess iron is deposited in the adrenal cortex, particularly in zona fasciculata and zona reticularis, impairing cortisol synthesis [12]. Oxidative stress and chronic inflammation further exacerbate adrenal dysfunction. The relationship between serum ferritin and AI observed in this study supports this mechanism.

Clinical Implications: AI can be subtle and easily missed. In our cohort, fatigue was the most common symptom, followed by hypotension and poor growth. Early recognition is crucial as adrenal crises may occur during intercurrent illnesses or surgical procedures. Basal morning cortisol measurement alone may not detect partial AI, highlighting the importance of dynamic testing, such as low-dose ACTH stimulation.

Correlation With Iron Overload: Higher ferritin levels were significantly associated with AI. Patients with ferritin >3000 ng/mL had a higher risk of adrenal dysfunction. Similar findings have been reported in previous studies where iron chelation improved endocrine function [13,14]. This emphasizes the importance of stringent iron chelation therapy, particularly in older patients with long-standing disease.

Disease Duration: Longer disease duration (>15 years) was significantly associated with AI, suggesting cumulative iron deposition over time as a critical factor. Sex, age, and chelation status were not significantly associated, though a larger sample size may reveal subtle effects.

Comparison With Other Endocrine Complications: Hypogonadism and hypothyroidism are more commonly studied, with AI often overlooked. Integration of routine adrenal function testing in thalassemia clinics is recommended, especially in patients with high ferritin or prolonged disease duration.

Limitations: The study was limited by a relatively small sample size and single-center design. MRI evaluation of adrenal iron deposition was not performed due to resource constraints. The cross-sectional design precludes causal inference. Future multicenter longitudinal studies with larger cohorts and MRI correlation are recommended.

CONCLUSION

Adrenal insufficiency affects nearly one-fourth of transfusion-dependent thalassemia patients in Bangladesh, predominantly in those with severe iron overload and longer disease duration. Clinical symptoms are non-specific, necessitating proactive screening using basal and ACTH-stimulated cortisol levels. Early diagnosis and timely intervention can prevent adrenal crises and improve growth, metabolic stability, and quality of life. Routine endocrine evaluation, aggressive iron chelation, and patient education are essential components of comprehensive thalassemia care.

REFERENCES

1. Fucharoen S, Weatherall DJ. The hemoglobinopathies. Lancet. 2012; 380: 364–376.
2. Khan WA, et al. Thalassemia in Bangladesh: prevalence and challenges. Bangladesh Med Res Counc Bull. 2020; 46: 123–130.
3. Borgna-Pignatti C, et al. Complications of thalassemia major. Blood Rev. 2013; 27: 115–123.
4. De Sanctis V, et al. Endocrine complications in thalassemia major. Pediatr Endocrinol Rev. 2017; 14: 274–284.
5. Farmakis D, et al. Iron overload and endocrine dysfunction in thalassemia. Ann Hematol. 2015; 94: 1821–1829.
6. Pepe A, et al. Adrenal function in transfusion-dependent thalassemia. Eur J Endocrinol. 2010; 163: 639–645.
7. Donga E, et al. Clinical features of adrenal insufficiency in chronic illness. Clin Endocrinol. 2016; 85: 352–360.
8. Charmandari E, et al. Adrenal insufficiency. Lancet. 2014; 383: 2152–2167.
9. Voskaridou E, et al. Adrenal insufficiency in patients with thalassemia. Blood Cells Mol Dis. 2008; 41: 238–242.
10. Alavi S, et al. Endocrine dysfunctions in thalassemia. Pediatr Hematol Oncol. 2019; 36: 269–278.
11. Agarwal R, et al. Prevalence of adrenal insufficiency in thalassemia. Indian J Endocrinol Metab. 2014; 18: 672–676.
12. De Sanctis V, et al. Adrenal iron overload in thalassemia. Acta Biomed. 2018; 89: 105–112.
13. Pepe A, et al. Iron chelation improves endocrine function. Blood Rev. 2011; 25: 61–66.
14. Borgna-Pignatti C, et al. Long-term complications of thalassemia. Ann N Y Acad Sci. 2005; 1054: 40–47.