Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 1155-1160 | ISSN:2251-6727

Estimation of Thiamine Levels in Children with Type-1 Diabetes Mellitus

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(Received: 16 March 2025 Revised: 20 April 2025 Accepted: 01 May2025)

KEYWORDS

Thiamine deficiency, Type 1 Diabetes Mellitus, Diabetic ketoacidosis, Glycemic control, Pediatric endocrinology

ABSTRACT:

Background

Thiamine (vitamin B1) plays a vital role in glucose metabolism, yet its status in children with Type 1 Diabetes Mellitus (T1DM), particularly during diabetic ketoacidosis (DKA), remains under-investigated. This study aimed to assess the prevalence of thiamine deficiency and its association with glycemic control in pediatric T1DM.

Methods: A cross-sectional study was conducted in 35 children with T1DM aged 1–18 years. Participants were categorized as newly diagnosed (DKA) or previously diagnosed. Serum thiamine levels were measured using high-performance liquid chromatography. Glycemic status was evaluated via HbA1c, insulin dose, and random blood sugar. Statistical comparisons and correlation analyses were performed.

Results: Thiamine deficiency was present in 60% of the cohort. The prevalence was higher in newly diagnosed children (72.7%) compared to previously diagnosed cases (54.2%). Mean HbA1c was significantly higher in the DKA group (13.03 ± 1.68%) versus previously diagnosed patients (7.33 ± 2.29%, $p < 0.05$). Thiamine levels were lower in children with HbA1c > 9%, but the difference was not statistically significant. No significant correlation was found between thiamine levels and HbA1c, insulin dose, RBS, or disease duration. However, a significant negative correlation was observed between HbA1c and daily insulin dose ($r = –0.412$, $p < 0.05$).

Conclusions: Thiamine deficiency is common in children with T1DM, particularly during initial presentation with DKA. While not directly correlated with glycemic markers, its high prevalence may have clinical implications. Routine screening and consideration of supplementation warrant further investigation.

Introduction

Type 1 Diabetes Mellitus (T1DM) is an autoimmune disorder of the pancreatic β-cells, leading to absolute insulin deficiency and lifelong dependence on exogenous insulin. The global incidence of T1DM has been rising steadily, increasing by approximately 3–5% annually, with India ranking among the top three countries in terms of total disease burden [1].

While glycemic control remains the cornerstone of diabetes management, micronutrient deficiencies—particularly of thiamine (vitamin B1)—have emerged as under-recognized contributors to both the onset and complications of diabetes. Thiamine acts as a coenzyme for transketolase and other key enzymes in the Krebs cycle, playing an essential role in glucose oxidation, ATP generation, and reduction of oxidative stress [2,3]. Deficiency of thiamine impairs glucose metabolism,

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exacerbates lactic acidosis, and contributes to endothelial dysfunction and vascular injury—mechanisms implicated in both acute and chronic diabetic complications [4].

Numerous studies have shown that diabetic individuals are at increased risk of thiamine deficiency due to excessive urinary excretion, reduced gastrointestinal absorption, and increased metabolic demand [5,6]. This is particularly relevant in pediatric patients, especially those with diabetic ketoacidosis (DKA), where heightened oxidative and metabolic stress may accelerate thiamine depletion [7]. A study by Rosner et al. demonstrated significantly lower thiamine levels in children with DKA compared to healthy controls [8].

Furthermore, elevated HbA1c levels have been associated with increased oxidative stress and activation of harmful metabolic pathways such as the polyol and hexosamine pathways. Thiamine and its synthetic derivative, benfotiamine, have been shown to block these pathways and attenuate complications like neuropathy, retinopathy, and nephropathy in experimental models [9,10].

Despite mounting evidence, thiamine deficiency is seldom evaluated in routine diabetes care, particularly in the pediatric population. In India, where nutritional deficiencies remain common and diabetes incidence is rapidly rising, assessing thiamine status in children with T1DM may offer new insights into comprehensive diabetes care.

This study was conducted to estimate serum thiamine levels in children with T1DM and to assess the prevalence of thiamine deficiency. Secondary objectives included evaluating the association of thiamine status with glycemic markers (HbA1c), insulin usage, disease duration, and clinical presentation.

Materials and Methods

Study Design and Setting

This was a hospital-based cross-sectional observational study conducted in the Department of Paediatrics at JSS Hospital, Mysuru. The study was carried out over an 18-month period between January 2021 and June 2022 following approval by the Institutional Ethics Committee. Written informed consent was obtained from parents or legal guardians of all participants.

Study Population

A total of 35 children aged 1 to 18 years with a confirmed diagnosis of Type 1 Diabetes Mellitus (T1DM) were enrolled. Patients were recruited from both outpatient and inpatient services and were divided into two groups:

- **Group A**: Newly diagnosed children presenting with diabetic ketoacidosis (DKA)
- **Group B**: Children with previously diagnosed T1DM on insulin therapy

Inclusion Criteria

- Children aged 1–18 years with a diagnosis of T1DM
- Either newly diagnosed or on established insulin therapy
- Consent obtained from parents or guardians

Exclusion Criteria

- Children with Type 2 Diabetes Mellitus
- Children with known chronic systemic illness (e.g., renal failure, liver disease)
- Children on vitamin supplementation in the past 30 days

Data Collection and Clinical Evaluation

A structured data collection form was used to record demographic details, clinical history (including disease duration), insulin dosage, and presenting symptoms. Anthropometric measurements and vital signs were obtained on admission. Relevant biochemical investigations, including random blood glucose (RBS), HbA1c, blood pH (for DKA confirmation), and serum thiamine levels, were measured.

Thiamine Estimation

Serum thiamine levels were measured using a high-performance liquid chromatography (HPLC) method. Thiamine deficiency was defined as serum levels below the laboratory-specific cutoff of 48 nmol/L. Samples were collected under fasting conditions and processed at the central laboratory using standardized protocols.

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Outcome Measures

The primary outcome was the prevalence of thiamine deficiency in children with T1DM. Secondary outcomes included:

- Association between thiamine levels and HbA1c
- Comparison of thiamine status in newly diagnosed (DKA) vs previously diagnosed patients
- Correlation of thiamine levels with insulin requirement, disease duration, and RBS

Statistical Analysis

All data were entered and analyzed using SPSS version 22.0. Descriptive statistics were presented as mean ± standard deviation for continuous variables and percentages for categorical variables. Intergroup comparisons were made using the Student's*t*-test or Mann–Whitney U test for continuous variables and chi-square test for categorical variables. Correlations were assessed using Pearson or Spearman correlation coefficients depending on data distribution. A p-value < 0.05 was considered statistically significant.

1. Study Population and Baseline Characteristics

A total of 35 children diagnosed with Type 1 Diabetes Mellitus (T1DM) were enrolled in the study. The mean age of participants was 10.9 ± 3.8 years, with a near-equal distribution of genders: 18 males (51.4%) and 17 females (48.6%). Based on clinical presentation, 11 patients (31.4%) were newly diagnosed with T1DM and presented in diabetic ketoacidosis (DKA), while 24 children (68.6%) had been previously diagnosed and were on regular insulin therapy.

This distribution provided a comparative framework to evaluate thiamine status across different phases of disease progression, from acute onset to chronic management. Baseline characteristics of the study cohort are summarized in Table 1.

Table 1: Baseline Characteristics of Study Participants

Parameter	Value
Total Participants	35
Age (mean ± SD)	10.9 ± 3.8 years
Gender - Male	18 (51.4%)
Gender - Female	17 (48.6%)
Newly Diagnosed (DKA)	11 (31.4%)
Previously Diagnosed T1DM	24 (68.6%)

2. Prevalence of Thiamine Deficiency

Among the 35 children with Type 1 Diabetes Mellitus enrolled in the study, thiamine deficiency was observed in 21 patients (60%), indicating a high prevalence in this population. When stratified by diagnosis status, 8 out of 11 children (72.7%) who were newly diagnosed and presented with diabetic ketoacidosis (DKA) were thiamine deficient. In contrast, among the 24 children with previously diagnosed T1DM, 13 (54.2%) exhibited thiamine deficiency.

Although the prevalence appeared higher in the newly diagnosed group, the difference between the two groups did not reach statistical significance ($p > 0.05$). These findings suggest that thiamine deficiency is common in both new-onset and long-standing T1DM and may not be limited to acute metabolic decompensation.

Table 2: Thiamine Status by Diagnosis Group

Group	Thiamine Deficient n (%)	Total n
Newly Diagnosed (DKA)	8 (72.7%)	11
Previously Diagnosed T1DM	13 (54.2%)	24
Total	21 (60%)	35

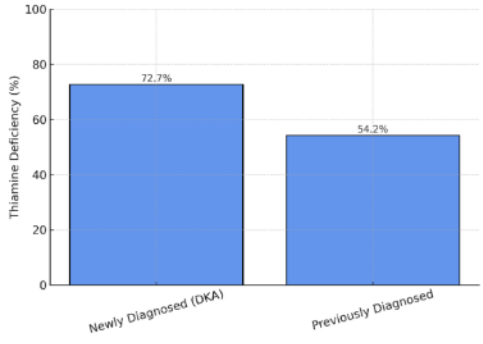

Figure 1. Thiamine Deficiency Prevalence by Group.

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Bar chart comparing the percentage of thiamine-deficient patients between newly diagnosed (DKA) and previously diagnosed T1DM groups.

3. Comparison of HbA1c Levels Between Groups

A significant difference in glycemic control was observed between the newly diagnosed and previously diagnosed groups. Children who presented with new-onset Type 1 Diabetes Mellitus and diabetic ketoacidosis (DKA) had markedly elevated HbA1c levels, with a mean of 13.03 ± 1.68%. In contrast, those with previously diagnosed T1DM had a mean HbA1c of 7.33 ± 2.29%.

The difference in mean HbA1c levels between the two groups was statistically significant ($p < 0.05$), highlighting the poor glycemic control at initial presentation compared to those who were already receiving insulin therapy and ongoing management.

Table 3: HbA1c Comparison Between Newly and Previously Diagnosed Patients

Group	Mean HbA1c (%)	p-value
Newly Diagnosed (DKA)	13.03 ± 1.68	< 0.05
Previously Diagnosed T1DM	7.33 ± 2.29	

4. Association Between Thiamine Levels and Glycemic Control

To assess whether thiamine levels were associated with long-term glycemic control, participants were stratified based on HbA1c levels using a threshold of 9%. Children with HbA1c values greater than 9% had a mean serum thiamine level of 41.32 ± 26.76 nmol/L, while those with HbA1c below 9% had a mean level of 53.54 ± 29.2 nmol/L. Although thiamine levels appeared lower in patients with poorer glycemic control, the difference was not statistically significant ($p > 0.05$).

These results suggest that while thiamine deficiency is common in T1DM, it may not directly correlate with glycemic control as measured by HbA1c alone.

Table 4: Mean Thiamine Levels by HbA1c Group

HbA1c Group	Mean Thiamine (nmol/L)	p-value
HbA1c > 9%	41.32 ± 26.76	> 0.05
HbA1c < 9%	53.54 ± 29.2	

5. Correlation Analysis of Thiamine Levels with Clinical Parameters

Correlation analyses were performed to assess the relationship between serum thiamine levels and key clinical parameters, including random blood sugar (RBS), daily insulin dose, and duration of illness. There was no statistically significant correlation between thiamine levels and RBS or duration of illness. Additionally, no significant correlation was found between thiamine levels and daily insulin dose.

Interestingly, a statistically significant negative correlation was observed between HbA1c and daily insulin dose ($r = -0.412$, $p < 0.05$)as shown infigure2, suggesting that better glycemic control may be associated with higher insulin sensitivity or adherence.

Table 5: Correlation of Thiamine with Clinical Variables

Variable	Correlation Coefficient (r)	p-value
Random Blood Sugar	-0.064	> 0.05
Duration of Illness	-0.021	> 0.05
Daily Insulin Dose	-0.102	> 0.05
HbA1c vs Insulin Dose	-0.412	< 0.05

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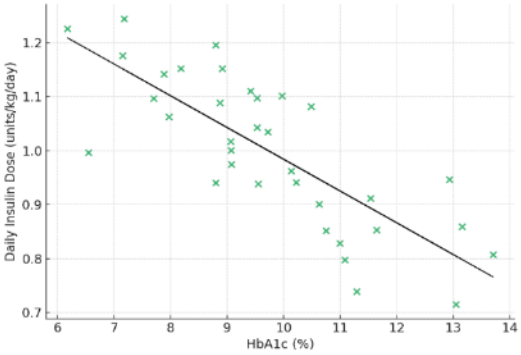

Figure 2. Correlation Between HbA1c and Daily Insulin Dose.

Scatter plot illustrating a significant negative correlation between HbA1c levels and insulin dosage ($r = -0.412$, $p < 0.05$), indicating poorer glycemic control in children receiving lower insulin doses.

Discussion

This study demonstrated a high prevalence of thiamine deficiency among children with Type 1 Diabetes Mellitus (T1DM), with 60% of the participants exhibiting subnormal serum thiamine levels. Notably, the prevalence was even higher (72.7%) among children who presented with diabetic ketoacidosis (DKA). These findings reinforce earlier reports suggesting that thiamine deficiency is both common and underrecognized in the pediatric diabetic population [11,12].

The mechanisms underlying thiamine depletion in diabetes are multifactorial. Insulin deficiency impairs gastrointestinal absorption of thiamine, while polyuria—frequently observed in poorly controlled diabetes—increases renal loss [13]. Additionally, metabolic stress during DKA raises the demand for thiamine as it serves as a coenzyme for enzymes involved in aerobic glucose metabolism. The resultant deficiency may exacerbate lactic acidosis and further compromise metabolic homeostasis [14].

Despite the overall high prevalence, our study found no statistically significant correlation between thiamine levels and HbA1c. While children with HbA1c > 9% had lower mean thiamine concentrations, the difference did not reach statistical significance. These results are consistent with those of Rosner et al., who observed similar trends in children with DKA, where thiamine deficiency was common but not directly linked to chronic glycemic indices [15].

A significant negative correlation between HbA1c and daily insulin dose was observed, suggesting that poorer glycemic control may be associated with suboptimal insulin usage or adherence. However, thiamine levels did not correlate significantly with insulin dosage, random blood glucose (RBS), or disease duration, indicating that deficiency may be influenced more by acute metabolic changes than long-term disease progression [16].

Thiamine plays an essential role in protecting against diabetes-induced microvascular complications. Its active form, thiamine diphosphate, acts as a coenzyme for transketolase, promoting diversion of harmful glucose metabolites into the non-toxic pentose phosphate pathway. This reduces oxidative stress and the accumulation of advanced glycation end products (AGEs), which are implicated in diabetic nephropathy, neuropathy, and retinopathy [17].

Furthermore, preclinical and clinical studies have demonstrated that thiamine and its synthetic derivative, benfotiamine, can restore endothelial function and mitigate early signs of diabetic organ damage. Thiamine supplementation has been associated with decreased protein kinase C activity, lower polyol pathway flux, and improvement in renal biomarkers such as microalbuminuria [18].

Given the biochemical and clinical importance of thiamine in glucose metabolism and vascular protection, routine screening for deficiency in pediatric diabetes care may be warranted. While our findings did not establish a significant relationship between thiamine and HbA1c, the high prevalence and potential pathophysiologic impact of deficiency support the rationale for considering thiamine status in diabetic children, especially during acute illness.

Limitations

The study's main limitations include its small sample size and cross-sectional design, which limit the generalizability and preclude causal inferences. The absence of a healthy control group and lack of dietary assessment further constrain interpretation. Additionally, thiamine was measured only once,

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JCHR (2025) 15(3), 1155-1160 | ISSN:2251-6727

providing no insight into longitudinal changes or treatment effects.

Conclusion

Thiamine deficiency was highly prevalent among children with Type 1 Diabetes Mellitus, especially those presenting with diabetic ketoacidosis. Although no significant correlation was found between thiamine levels and glycemic control, the clinical relevance of this deficiency remains notable. Routine screening may be warranted, and further studies are needed to explore the role of thiamine supplementation in this population.

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