

## Original Research Article

### **CORRELATION OF SERUM THIAMINE WITH PHYSICAL AND BIOCHEMICAL PARAMETERS AMONG TYPE 1 AND TYPE 2 DIABETICS: A CROSS-SECTIONAL ANALYSIS**

#### **ABSTRACT**

**Objective:** Thiamine or vitamin B1 is an essential micronutrient and enzyme cofactor that is needed for most of the anabolic and catabolic reaction that occurs in organisms. Deficiency of Thiamine has been associated with numerous complications in diabetes mellitus (DM) patients. Therefore, this study was intended to evaluate various biochemical and anthropometric parameters with serum thiamine levels in type I and type II diabetic patients.

**Methodology:** This was a case-control study carried out in diabetic outpatient department (OPD) of Jinnah post graduate medical institute, Karachi by using non-probability convenient sampling technique. The duration of the study was about six months after approval of synopsis. A total of 60 participants with type I and II diabetes mellitus of both genders with age < 25 to > 46 years were selected; 30 participants with type I diabetes whereas 30 participants had type II diabetes. The Pearson's correlation test was used to evaluate correlation between thiamine levels and height, weight, heart rate, temperature, dyslipidemia, creatinine, urea in type I and II diabetic patients.

**Results:** The study results showed that among type I diabetics, none of the patient characteristics studied were significantly correlated with the thiamine levels of these patients. On the other hand, the study results showed that among type II diabetics, height was significantly negatively correlated with the thiamine level ( $p=0.045$ ) where patients with greater height had lower thiamine level and vice versa. Moreover, both heart rate and total cholesterol were marginally insignificantly correlated with thiamine level ( $p=0.065$  and  $p=0.069$  respectively) where patients with higher heart rate and lower total cholesterol had lower thiamine level and vice versa.

**Conclusion:** This study concluded that all anthropometric and biochemical parameters were insignificantly correlated with thiamine levels in type I and II diabetic patients. However, height had significant negative correlation with the thiamine level among type II diabetics reflecting patients with more height had lower thiamine level.

**Keywords:** Thiamine levels, total cholesterol, type I diabetes, type II diabetes, Urea, Creatinine

## INTRODUCTION

Thiamine is also termed as vitamin B1 which is a water-soluble vitamin and a coenzyme that participated in carbohydrate metabolism and branched-chain amino acids. [1]Thiamine is a essential dietary element that is found in different food sources; however multiple factors are involved in variation of its serum levels for instance elevated temperatures and pH, use of diuretics, high-calorie diet comprising simple carbohydrates, prolonged use of alcohol, pyrexia, too much exercise, lactation and pregnancy, tension and trauma. [2,3] Moreover, thiamine has a short half-life of about 1–12 hours with limited body store .[4] Over the past years, prompt alterations in food regimes and standard of living that have happened owing to industrialization, urbanization, economic progression and globalization that led to modify dietary regimes to high-saturated, high-fat, and low-energy providing diet resulting an insufficient intake of thiamine.[5,6] It is evidently supported that thiamine insufficiency is related to multiple diseases such as CVDs and diabetes, angina, myocardial infarction (MI), dyslipidemia, obesity and psychological disorders.[7]

Diabetes mellitus (DM) is one of the most serious health concerns, and its prevalence is rising promptly in all age groups. Multiple environmental, genetic, host factors are associated with DM. The two basic courses that develop diabetes are autoimmune and metabolic paths. The noticeable possible factors to develop DM are inappropriate absorption of nutrients, being overweight, laziness, and hormonal discrepancy [8,9]. Generally, DM is categorized into two types; type I (insulin-dependent diabetes mellitus) and type II (insulin-independent diabetes mellitus). Type I DM arises because of the autoimmune devastation of pancreatic beta cells causing an incapable to produce insulin by pancreatic beta cells, whereas type II DM is

frequently prevailing disease particularly in Pakistan that is caused by the development of insulin resistance and reduced insulin receptor sensitivity [8,9]. Multiple factors typically associated with fat and carbohydrate metabolism including many micronutrients to some extent causes Type II DM. The consequences and complications of diabetes are triggered by developing imbalance between free radical formation and their control by natural antioxidants [10].

Prolonged use of diuretics leads to Thiamine deficiency, causing an abrupt reduction in excretory thiamine that may lead to renal impairment [11]. One of the most severe complications of diabetes is Diabetic nephropathy that is clinically manifest as the existence of micro-albuminuria that eventually develops macro-albuminuria. Therefore, at this phase, acceptable renal replacement treatment for kidneys is necessary for effective functioning [12]. The prevalence of micro-albuminuria is recognized as indicator of diabetic nephropathy in diabetic patients and also shows cardiovascular disorders [13,14]. The development of diabetic nephropathy in patients with type I DM can be inhibited by regulating glucose level in blood and blood pressure with administration of angiotensinogen-converting enzyme (ACE) inhibitor remedy that decreases the chances of micro-albuminuria [15]. It is proposed that increased renal clearance of thiamine leads to reduction of thiamine level in diabetes [16]. It is recommended that thiamine therapy at higher doses may have a remedial influence on diabetic nephropathy which is effective at an early-stage [17]. Thiamine therapy is also suggested for averting renal impairment and cardiovascular illnesses in type II DM people, in this manner improving the quality of life and decreasing the probability of complications [18].

As far as the association between DM and thiamine is concerned, substantial percentage of healthy individuals (36-47%) presented as deficiency of thiamine in a hyperglycemic episode for instance in a high carbohydrate diet, pregnancy and diabetes [19]. It was reported in one research that low plasma level of thiamine was observed in type I diabetes [20]. It was also revealed in another research that low thiamine level in blood, low functional activity of erythrocyte transketolase (Tk) and high functional activity of erythrocyte thiamine pyrophosphate (TPP) are associated with diabetic patients [21]. Thiamine level was assessed by transketolase activity in mammals. The low level of thiamine in diabetes may be due to the fact that decreased level of apo-enzyme from the disease itself instead of thiamine deficiency [9]. Furthermore, plasma

thiamine level has been revealed to be reduced by 76% in type I and 75% in type II diabetes that was related to higher renal clearance and fractional elimination of thiamine from the body [22].

Nonetheless, there is ambiguity regarding association between thiamine ingestion and diabetes, CVDs, dyslipidemia and renal clearance. Therefore, the present study was intended to explore the correlation of anthropometric and biochemical parameters such as Triglycerides, Total Cholesterol, Urea, and Creatinine with the thiamine level in patients of diabetes type I and II.

## **METHODOLOGY**

This was a case-control study carried out in diabetic outpatient department (OPD) of Jinnah post graduate medical institute, Karachi by using non-probability convenient sampling technique. The duration of the study was about six months after approval of synopsis. A total of 60 participants were selected; 30 participants with type I diabetes whereas 30 participants had type II diabetes. Patients with type I and II diabetes mellitus of both genders with age < 25 to > 46 years were included in the study whereas those patients who were taking diuretics, had significant comorbidities like chronic Liver diseases, Ischemic heart diseases, patients who undergone major transplant surgeries, end phase renal disease and gastro intestinal disease were excluded from the study.

After receiving informed consent from the participants, data was documented from diabetic clinics of medical wards of Jinnah Post graduate Medical Center (JPMC) Karachi. Blood Samples were gathered from the diabetic clinics of Jinnah Post graduate Medical Center (JPMC), Karachi and Dow University Ojha Campus, Karachi. Collected Blood samples in the non-heparinized tube were immediately centrifuged at 2000 rounds per minute (rpm) for 20 minutes duration. The clear supernatant serum was used for the evaluation of many biochemical investigative parameters comprising random blood sugar (RBS) levels, fasting blood sugar (FBS) levels, creatinine, urea, hemoglobin A1c (HbA1c), blood and urinary thiamine levels. The height, weight, and blood pressure were estimated by usual method.

The data was entered and analyzed by SPSS Statistics version 20. The Pearson's correlation test was used to evaluate correlation between thiamine levels and height, weight, heart rate,

temperature, dyslipidemia, creatinine, urea in type I and II diabetes patients. P value < 0.05 was taken as statistically significant.

## RESULTS

Secondary data analysis of total 60 patients was performed for this study, 30 each in type 1 and type 2 diabetes group.

The study results showed that among type 1 diabetics, none of the patient characteristics studied was significantly correlated with the thiamine levels of these patients (table 1).

On the other hand, the study results showed that among type 2 diabetics, height was significantly negatively correlated with the thiamine level ( $p=0.045$ ) where patients with greater height had lower thiamine level and vice versa. Moreover, both heart rate and total cholesterol were marginally insignificantly correlated with thiamine level ( $p=0.065$  and  $p=0.069$  respectively) where patients with higher heart rate and lower total cholesterol had lower thiamine level and vice versa (table 2).

**Table 1: Correlation between serum thiamine and patient characteristics among type 1 diabetics**

Variables (n=30)	Serum Thiamine	
	$\rho$	<b>p</b>
Height	-0.036	0.850
Weight	-0.183	0.333
Heart Rate	0.147	0.438
Temperature	-0.020	0.915
Triglycerides	-0.075	0.994
Total Cholesterol	-0.280	0.134
Urea	0.205	0.276
Creatinine	0.288	0.123

**Table 2: Correlation between serum thiamine and patient characteristics among type 2 diabetics**

Variables (n=30)	Serum Thiamine	
	$\rho$	<b>p</b>
Height	-0.369	0.045

<b>Weight</b>	-0.054	0.776
<b>Heart Rate</b>	-0.342	0.065
<b>Temperature</b>	0.133	0.484
<b>Triglycerides</b>	0.010	0.956
<b>Total Cholesterol</b>	0.337	0.069
<b>Urea</b>	0.094	0.622
<b>Creatinine</b>	0.120	0.529

## DISCUSSION

Diabetes has been observed to be linked with low thiamine level deposits in the body, as thiamine concentration in the body directly affects carbohydrate formation, breakdown, and inter-conversion. The present study demonstrated the influence of thiamine level on anthropometric and biochemical parameters in patients with type I and II diabetes mellitus.

Thiamine has a significant role in inhibition of atherosclerotic plaque as it has a protective influence on proliferation mediated by glucose and insulin on human arterial smooth muscle cells.[23] Another data support this statement that consistent thiamine management augments endothelial functions and impedes atherosclerosis development, [24] One of the researches demonstrated that both types I and II DM patients showed significantly higher level of triglycerides and cholesterol as compared to controls.[25] These findings were similar to another research by Tai VML, who demonstrated type I DM patients had significantly higher triglycerides and cholesterol level than in controls ( $p=0.008$ ) [26]. Similarly, another analysis revealed that triglycerides levels were significantly greater in type II DM patients than in controls ( $p<0.001$ ) [27]. The present study did not endorse the above reported researches and showed that there was no association existed between the thiamine level and triglycerides and total cholesterol in both types of diabetes mellitus ( $p>0.05$ ) indicating there was no significant change seen in thiamine level with reference to types of diabetes.

Importantly, another research observed that most of the biochemical parameters are associated with diabetes type I and revealed that extremely significant differences was observed between adults with and without diabetes type I. In their study, it was observed that total cholesterol, serum glucose and triglycerides levels were significantly higher ( $p<0.001$ , 0.001 and 0.008),

correspondingly in diabetes type I patients as compared to controls. Therefore, it demonstrated a robust relationship between blood thiamine levels with various biochemical indicators including blood glucose, HDL and serum creatinine level ( $p < 0.008$ ,  $0.001$  and  $0.001$ ), correspondingly. It was evidently proved the significant function of thiamine and thiamine phosphate esters in averting the metabolic variations and probably the complications associated with diabetes type I; reflecting these thiamine levels and thiamine phosphate esters were interrelated with diabetes along with associated biomarkers, such as blood glucose, HDL, triglycerides and cholesterol in addition to microalbuminuria and excretory thiamine. [28] The present study was inconsistent with the above findings and showed that there was no association reported between thiamine levels with biochemical parameters ( $p > 0.05$ ) including total cholesterol, triglycerides, urea and creatinine in both diabetes type I and type II.

Similarly, one prospective study assessed the thiamine levels and serum creatinine in diabetes mellitus. It showed a positive and significant association between serum creatinine and urinary thiamine levels in both Type I and type II diabetes ( $p < 0.001$ ). [10] The present study was not supported the above research and revealed that levels of thiamine was insignificantly associated with urea and creatinine levels in both types of diabetes. ( $p > 0.05$ ).

Likewise, in a cross-sectional comparative analysis of healthy controls, micro-albuminuria and macro-albuminuria in diabetic patients, reported that lower thiamine level was found in diabetics, with a gradual reduction in albuminuria, as well as in macro-albuminuria. It was also showed that a negative correlation found between thiamine and lipid parameters in micro-albuminuria. Additionally, Thiamine had greatly significant negative correlation with total cholesterol, triglycerides, and LDL cholesterol, whereas it had an extremely significant positive correlation with HDL cholesterol in all diabetic groups [27]. These findings were not in agreement with our study and revealed that there was no correlation observed between thiamine levels and Triglycerides and total cholesterol in type I and II diabetes. Nonetheless, this study can have selection bias owing to a non-probability sampling technique and observer bias. Therefore, it is recommended that prospective researches with a probability sampling technique are used to elaborate this association in bigger samples to acquire more accurate results.

## CONCLUSION

This study concluded that all anthropometric and biochemical parameters were insignificantly correlated with Thiamine levels in type I and II diabetic patients. However, height had significant negative correlation with the thiamine level among type II diabetics reflecting patients with more height had lower thiamine level.

## REFERENCES

1. Manzetti S, Zhang J, van der Spoel D. Thiamin function, metabolism, uptake, and transport. *Biochemistry*. 2014;53(5):821–835. doi: 10.1021/bi401618y.
2. Goel A, Kattoor AJ, Mehta JL. Thiamin therapy for chronic heart failure: is there any future for this vitamin?, *The American Journal of Clinical Nutrition*. 2019 Dec;110(6):1270–1271, <https://doi.org/10.1093/ajcn/nqz246>.
3. Kiela PR. Unraveling the pathophysiology of alcohol-induced thiamin deficiency. *Am J Physiol Renal Physiol*. 2010 Jul; 299(1): F26–F27. doi: 10.1152/ajprenal.00266.2010.
4. Whitfield KC, Bourassa MW, Adamolekun B, Bergeron G, Bettendorff L, Brown KH, et al. Thiamine deficiency disorders: diagnosis, prevalence, and a roadmap for global control programs. *Ann N Y Acad Sci*. 2018 Oct;1430(1):3-43. doi: 10.1111/nyas.13919. Epub 2018 Aug 27. PMID: 30151974; PMCID: PMC6392124.
5. WHO (2003) *Diet, Nutrition, and the Prevention of Chronic Diseases: Report of a Joint WHO/FAO Expert Consultation*, vol. 916. Geneva, Switzerland: World Health Organization.
6. Song S, Song H. Dietary and lifestyle factors associated with weight status among Korean adolescents from multicultural families: using data from the 2017–2018 Korea Youth Risk Behavior Surveys. *Korean J Community Nutr*. 2019; 24(6):465–475. <https://doi.org/10.5720/kjcn.2019.24.6.465>.
7. Eshak ES, Arafa AE. Thiamine deficiency and cardiovascular disorders. *NutrMetabCardiovasc Dis*. 2018 Oct;28(10):965-972. doi: 10.1016/j.numecd.2018.06.013.
8. American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care*. 2005 Jan;28Suppl 1:S4-S36. Erratum in: *Diabetes Care*. 2005 Apr;28(4):990. PMID: 15618112.

9. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2014 Jan;37Suppl 1:S81-90. doi: 10.2337/dc14-S081.
10. Al-Attas OS, Al-Daghri NM, Alfadda AA, Abd-Alrahman SH, Sabico S: Blood thiamine and derivatives as measured by high-performance liquid chromatography: levels and associations in DM patients with varying degrees of microalbuminuria. *J Endocrinol Invest*. 2012, 35(11):951- 956. 10.3275/8126.
11. Zatalia SR, Sanusi H. The role of antioxidants in the pathophysiology, complications, and management of diabetes mellitus. *Acta Med. Indones*. 2013;45(2):141–147.
12. Alicic RZ, Rooney MT, Tuttle KR. Diabetic Kidney Disease: Challenges, Progress, and Possibilities. *Clin J Am SocNephrol*. 2017 Dec 7;12(12):2032-2045. doi: 10.2215/CJN.11491116.
13. Pasko N, Toti F, Strakosha A, Thengjilli E, Shehu A, Dedej T, et al. Prevalence of microalbuminuria and risk factor analysis in type 2 diabetes patients in Albania: the need for accurate and early diagnosis of diabetic nephropathy. *Hippokratia*. 2013 Oct;17(4):337-41.
14. Afkhani-Ardekani M, Modarresi M, Amirchaghmaghi E. Prevalence of microalbuminuria and its risk factors in type 2 diabetic patients. *Indian J Nephrol*. 2008 Jul;18(3):112-7. doi: 10.4103/0971-4065.43690.
15. Nix WA, Zirwes R, Bangert V, Kaiser RP, Schilling M, Hostalek U, Obeid R. Vitamin B status in patients with type 2 diabetes mellitus with and without incipient nephropathy. *Diabetes Res ClinPract*. 2015 Jan;107(1):157-65. doi: 10.1016/j.diabres.2014.09.058.
16. Bempah OA. Vitamin B blood plasma deficiency model for the study of diabetes complications demonstrates potential for the cure and prevention of complications in type 2 diabetes mellitus patients. *J Diabetes MetabDisord Control*. 2015;2(2):49-52. DOI: 10.15406/jdmdc.2015.02.00033.
17. Lonsdale D. Thiamine and magnesium deficiencies: keys to disease. *Med Hypotheses*. 2015 Feb;84(2):129-34. doi: 10.1016/j.mehy.2014.12.004.
18. Pácal L, Kuricová K, Kaňková K. Evidence for altered thiamine metabolism in diabetes: Is there a potential to oppose gluco- and lipotoxicity by rational supplementation? *World J Diabetes*. 2014 Jun 15;5(3):288-95. doi: 10.4239/wjd.v5.i3.288.

19. Luong KV, Nguyen LT. The impact of thiamine treatment in the diabetes mellitus. *J Clin Med Res.* 2012 Jun;4(3):153-60. doi: 10.4021/jocmr890w.
20. Thornalley PJ, Babaei-Jadidi R, Al Ali H, Rabbani N, Antonysunil A, Larkin J, et al. High prevalence of low plasma thiamine concentration in diabetes linked to a marker of vascular disease. *Diabetologia.* 2007 Oct;50(10):2164-70. doi: 10.1007/s00125-007-0771-4.
21. Michalak S, Michałowska-Wender G, Adamcewicz G, Wender MB. Erythrocyte transketolase activity in patients with diabetic and alcoholic neuropathies. *Folia Neuropathol.* 2013;51(3):222-6. doi: 10.5114/fn.2013.37706.
22. Alam SS, Khan AH, Akhtar MW. Thiamine and the Cellular Energy Cycles: A Novel Perspective on Type 2 Diabetes Treatment. *Proceeding S.Z.P.G.M.I.* 2013; 27(1):27-60.
23. Duc HN, Oh H, Yoon IM, Kim MS. Association between levels of thiamine intake, diabetes, cardiovascular diseases and depression in Korea: a national cross-sectional study. *J Nutr Sci.* 2021 Apr 27;10:e31. doi: 10.1017/jns.2021.23.
24. Arora S, Lidor A, Abularrage CJ, Weiswasser JM, Nylen E, Kellicut D, et al. Thiamine (vitamin B1) improves endothelium-dependent vasodilatation in the presence of hyperglycemia. *Ann Vasc Surg.* 2006 Sep;20(5):653-8. doi: 10.1007/s10016-006-9055-6.
25. Anwar A, Ahmed Azmi M, Siddiqui J, PanhwarG, Shaikh F, Ariff M. Thiamine Level in Type I and Type II Diabetes Mellitus Patients: A Comparative Study Focusing on Hematological and Biochemical Evaluations. *Cureus.* 2020 May 08;12(5): e8027. doi:10.7759/cureus.8027.
26. Tai VML. A case report on the use of oral thiamine in a palliative care patient in the management of peripheral edema in a community setting in New South Wales, Australia. *Int J Case Rep Images* 2016;7(1):15–17. doi:10.5348/ijcri-201603-CR-10590.
27. Waheed P, Naveed AK, Ahmed T. Thiamine deficiency and its correlation with dyslipidaemia in diabetics with microalbuminuria. *J Pak Med Assoc.* 2013, 63(3):340-345.
28. Al-Daghri NM, Alharbi M, Wani K, Abd-Alrahman SH, Sheshah E, Alokail MS. Biochemical changes correlated with blood thiamine and its phosphate esters levels in patients with diabetes type 1 (DMT1). *Int J ClinExpPathol.* 2015 Oct 1;8(10):13483-8.

UNDER PEER REVIEW