

Original Research Article

CORRELATION OF SERUM THIAMINE WITH PHYSICAL AND BIOCHEMICAL PARAMETERS AMONG TYPE 1 AND TYPE 2 DIABETES

ABSTRACT

Objective: Thiamine or vitamin B1 is a fundamental vitamins and minerals and enzyme cofactor that are 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 assess various biochemical and anthropometric parameters with serum thiamine levels in patients with type I and type II diabetes.

Methodology: This was a case-control study carried out in outpatient department (OPD) of Diabetes Department of Jinnah post graduate medical institute, Karachi by using non-probability convenient sampling technique. This study comprised of 6 months duration 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 interpret correlation between thiamine levels and height, weight, heart rate, temperature, Total cholesterol, Triglycerides, creatinine, urea in type I and II diabetic patients.

Results: The 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, among type II diabetics, significantly negative correlation was observed between height and 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.

Conclusion: This study concluded that all anthropometric and biochemical parameters were insignificantly correlated with thiamine levels in type I and II diabetes 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: Creatinine, Thiamine levels, total cholesterol, type I diabetes, type II diabetes, Urea,

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 pH and temperature, diuretic intake, high-calorie diet comprising carbohydrates, prolonged use of alcohol, pyrexia, too much exercise, lactation and pregnancy, tension and trauma. [2,3] Furthermore, thiamine has a half-life of about 1–12 hours with limited body stores .[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 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, angina diabetes, myocardial infarction (MI), dyslipidemia, obesity and psychological disorders.[7]

Diabetes mellitus (DM) is the most serious health concerns; 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 cause to develop DM are inappropriate absorption of nutrients, being overweight, laziness, and hormonal discrepancy [8,9]. Generally, DM is classified 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 causing an incapable to make insulin by pancreatic beta cells, whereas type II DM is frequently prevailing disease particularly in Pakistan that is caused by the 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 development of disproportion between free radical creation and their regulation by natural antioxidants trigger consequences and complications of diabetes [10].

Prolonged use of diuretics leads to Thiamine deficiency, causing an abrupt reduction in excretory thiamine that may lead to renal impairment [11]. Most severe complication of diabetes is Diabetic nephropathy, 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 diabetes along with cardiovascular disorders [13,14]. Development of diabetic nephropathy in type I DM can be controlled 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 raised renal clearance of thiamine leads to reduced 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 75% in type II diabetes and 76% in type I and that was related to higher renal clearance and partial elimination of thiamine from the body [22].

Nonetheless, there is ambiguity regarding association between thiamine ingestion and diabetes, CVDs, lipid parameters and renal clearance. Therefore, this 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 cross sectional study carried out in outpatient department (OPD) of Diabetes Department of Jinnah post graduate medical institute, Karachi by using non-probability convenient sampling technique. This study comprised of 6 months duration after approval of synopsis. The ethical approval was approved by the Ethical Review Board of concerned Department. A total of 60 participants were chosen; 30 participants with type I diabetes whereas 30 participants had type II diabetes of both genders with age < 25 to > 46 years were included in the study whereas those patients who were taking diuretics, had co-morbidities like chronic Liver diseases, Ischemic heart diseases, patients who undergone major transplant surgery, end phase renal disease and gastro intestinal disease were excluded from the study.

After getting 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. The collected blood samples were centrifuged instantly at 2000 rounds per minute (rpm) for duration of 20 minutes in non-heparinized tube. The clear supernatant serum was evaluated to assess biochemical parameters comprising of random blood sugar (RBS) levels, fasting blood sugar (FBS) levels, creatinine, urea, hemoglobin A1c (HbA1c), blood and urinary thiamine levels. The height and weight was measured, and blood pressure was estimated by Sphygmomanometer.

The data was analyzed by using SPSS Statistics version 20. The Pearson's correlation test evaluated the correlation between thiamine level and height, weight, heart rate, temperature, dyslipidemia, creatinine, urea in patients of type I and II diabetes. P value of less than 0.05 was considered as statistically significant.

RESULTS

A total of 60 patients were enrolled 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	
	ρ	p
Height	-0.036	0.850
Weight (kg)	-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	
	ρ	p
Height	-0.369	0.045
Weight	-0.054	0.776
Heart Rate	-0.342	0.065
Temperature	0.133	0.484
Triglycerides	0.010	0.956
Total Cholesterol	0.337	0.069
Urea	0.094	0.622

Creatinine	0.120	0.529
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DISCUSSION

Diabetes Mellitus has been observed to be linked with low level of thiamine deposits, as thiamine concentration in the human body directly influences on carbohydrate formation, breakdown, and inter-conversion. This study demonstrated the influence of thiamine level on anthropometric and biochemical parameters in patient with type I and II diabetes.

Thiamine has significant role in inhibition of atherosclerotic plaque as it has a protective influence on proliferation mediated by insulin and glucose on smooth muscle cells of arteries.[23] Another research agreed with this statement that consistent thiamine management augments endothelial activities 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 as compared to in controls (p=0.008) [26]. Likewise, another analysis revealed that triglycerides levels were significantly greater in type II Diabetes 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 that there was no considerable 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 considerably 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 included 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 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 types of 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 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 no correlation observed between thiamine levels and Triglycerides and total cholesterol in both types of diabetes. Nonetheless, this study can have selection and observer bias owing to a non-probability sampling technique. Therefore, it is recommended that prospective researches with a probability sampling technique are used to detailed this association in bigger samples to acquire further accurate results.

CONCLUSION

This study concluded that all anthropometric and biochemical parameters were insignificantly correlated with Thiamine levels in type I and II diabetes 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. Diet, Nutrition, and the Prevention of Chronic Diseases: Report of a Joint WHO/FAO Expert Consultation, vol. 916. Geneva, Switzerland: World Health Organization. 2003.
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. Afkhami-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.

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