

**ASSOCIATION OF AGE, GENDER AND TYPE OF DIABETES WITH
THIAMINE LEVEL: A CROSS-SECTIONAL ANALYSIS**

ABSTARCT

Objective: Diabetes Mellitus has been observed to be related with low thiamine levels in the body, as it affects directly on carbohydrate metabolism. Therefore, this study was intended to assess demographic characteristics and serum thiamine levels in type I and type II diabetic patients and healthy control group.

Methodology: This was a case-control study carried out in diabetic outpatient department (OPD) of Urban Health Center and New Karachi, Hospital . The duration of the study was about six months after approval of synopsis. The study sample included 90 participants and divided into three groups, 30 participants each in the control, type I diabetes and type II diabetes groups. Patients with type I and II diabetes mellitus of both genders with age < 25 to > 46 years were included in the study. One Way ANOVA was applied to find out the significance of differences among the groups.

Results: The study results showed that out of 90 participants, 33(36.7%) were males and 57(63.3%) were females; 1(1.1%) of them had low thiamine level, 17(18.9%) had normal thiamine level whereas 72(80.0%) had high thiamine level. It was observed that significant association found between thiamine levels and age groups ($p < 0.001$). Furthermore, 18(60.0%) had Low/Normal thiamine level and 12(40.0%) had high thiamine level in type I diabetes patients while 30(100%) in control group and Type II Diabetic patients had high thiamine level with significant association between them ($p < 0.001$). On the other hand, an insignificant association was found between gender and low and high thiamine levels ($p = 0.743$).

Conclusion: This study concluded that both the age and group types were significantly associated with thiamine levels of the participants. Furthermore, type I Diabetes patients had

significantly lower thiamine levels as compared to type II Diabetes and controls. On the other hand, there was no significant relationship of gender with thiamine levels.

Keywords:Thiamine level, Type I and II diabetes mellitus, age, gender

INTRODUCTION

Thiamine, also regarded as vitamin B1 characteristically a water-soluble vitamin and act as a coenzyme in carbohydrates metabolism and essential amino acids.[1]Thiamine is a fundamental dietary element that can be gained by a variety of food sources, however many factors can affect its serum level for instance elevated temperatures and pH, use of diuretics, high-calorie diet comprising simple carbohydrates, prolonged drunkenness, pyrexia, undue workout, pregnancy and lactation, tension and trauma[2,3]. Additionally, the thiamine half-life in the body ranges only 1 to 3 weeks.[4] It is evidently reported that thiamine insufficiency is directly or indirectly linked with various diseases such as cardiovascular diseases (CVD) and diabetes, lipid abnormalities, obesity, angina, myocardial infarction (MI) and psychological disorder such as depression. [5] Thiamine is richly existing in many food sources for instance meat, whole grains, mushrooms, beans, and nuts. In high socio-economic status countries, cereals, wheat flour, and infant formulations with thiamine fortification; thiamine-fortified foods give around half of the overall quantity of vitamin consumed in these surroundings.[6]

The Biosynthesis of thiamine is composed of distinct branches for creation of pyrimidine and thiazole ring that are compressed to make thiamin monophosphate (ThMP) and consequently changed into thiamin diphosphate (ThDP) which is an active form.[7]

Thiamine exists in the body by way of free thiamine, in addition to numerous phosphorylated forms: thiamine monophosphate (ThMP), thiamine diphosphate (ThDP), and thiamine triphosphate (ThTP) [7]. ThDP is a vital cofactor in many enzyme complexes contributed in the carbohydrates and amino acids metabolism.[8]

The recommended nutrient intake (RNI) of thiamine is 1.2 mg per day for males and 1.1 mg/day for females, and rises to 1.4 mg/day for expecting women and 1.5 mg/day for breastfeeding women. In period of early childhood, 0.2 mg/day (0–6 months) and 0.3 mg/day (7–12 months) is considered as sufficient ingestion of thiamine. The RNI progressively rises to 0.5 mg/day for ages 1–3 years, 0.6 mg/day for children 4–6 years and 0.9 mg/day by age's 7–9 years. After the age of 10 years, children and adult's thiamine requirement is similar.[9]

Evaluation of Thiamine status can be executed by two means, by measuring the degree of ThDP-capacity of a thiamine-dependent enzyme (erythrocyte transketolase (ETK) assay), and by quantifying thiamine metabolites in nearby tissues. The ETK assay is reflected to be more helpful, as it shows definite vitamin functionality. Both methods indicate deficient thiamine status in areas of the world where beriberi happens than where it does not happen. Though in populations, both non-affected and affected persons with beriberi may have equally lower thiamine levels.[10,11] Thiamine esters and other metabolites are exist in urine and blood. Total blood thiamine level (free thiamine plus its esters) normally ranges from 75-195 nmol/L, that is mostly found in the form of ThDP (70–180 nmol/L).[12] The degree of ThDP reduction in red blood cells is same to that of other organ tissues, and it is well associated with nutritional status.[8]

Type 2 Diabetes Mellitus is a disease that is caused by multiple factors characteristically concomitant to carbohydrate and fat metabolism, though, many essential dietary elements are also involved to some extent either as part of the cause or influence of this chronic pathology. The complications and consequences of diabetes are caused by forming disproportion among free radical creation and their regulation by natural antioxidants [13]. Thiamine works as a coenzyme in the active transference of aldehyde groups and glycation, along with neural transmission and conduction of neural activity, and may have influence on the progression of numerous diabetic complications [14].

Reduced thiamine levels and raised renal clearance have been observed in both Types I and II Diabetes mellitus [15]. It was evidently proved by a cross-sectional comparative study included healthy controls, microalbuminuric and macroalbuminuric DM patients. Low thiamine levels were reported in diabetes, with a progressive reduction of albumin in urine, more so in

macroalbuminuria. Moreover, thiamin level was negatively correlated with lipid profile in microalbuminuria [16].

It is proposed that several thiamine supplementation researches revealed with encouraging outcomes, such as ingestion of thiamine supplementation in one month has been revealed to decline glucose and leptin in diabetic patients than healthy controls [17].

Nonetheless, the association between thiamine ingestion and diabetes, CVDs, lipid abnormalities and psychological fitness are still vague. Thiamine remedy is also recommended to be beneficial in prevention of renal and cardiovascular disorders in patients with type II DM, in this manner improving the quality of life and decreasing complications [18]. This study was aimed to evaluate various demographic factors such as age and gender and variation of serum thiamine levels in type I and type II diabetic patients and associate them with healthy controls.

METHODOLOGY

This was a case-control study carried out in diabetic outpatient department (OPD) of Urban health Center and New Karachi Hospital by using non-probability convenient sampling technique. The duration of the study was about six months after approval of synopsis. A total of 90 participants were selected and divided into three groups, each with 30 participants. Group A was the control group and included healthy non-diabetic participants, while group B included patients with type I DM, and group C included patients with type II DM. 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 therapy, had significant co-morbidities such as chronic Liver diseases, Ischemic heart diseases, patients who have undergone major transplant surgeries, end stage renal disease and gastro intestinal disease were excluded from the study.

After getting informed consent from the participants, data was recorded from diabetic clinics of Karachi. Collected Blood samples in the non-heparinized tube were instantly centrifuged at 2000 rounds per minute (rpm) for duration of 20 minutes. The clear supernatant serum was utilized for the valuation of many biochemical investigative parameters comprising creatinine, urea, random blood sugar (RBS) levels, fasting blood sugar (FBS) levels, hemoglobin A1c (HbA1c), blood and urinary thiamine levels.

The data was entered and analyzed by SPSS Statistics version 20. The data was reported as frequencies and percentages. One Way ANOVA was applied to find out the significance of differences among the groups. P-value < 0.05 was considered as statistically significant.

RESULTS

The study sample comprised of 90 participants and divided into three groups, 30 each in the control, type 1 diabetes and type 2 diabetes groups. Descriptive analysis showed that 23(25.6%) of the participants were aged up to 25 years, 20 (22.2%) were aged from 26 to 35 years, 28 (31.1%) were aged from 36 to 45 years whereas 19 (21.1%) were aged 46 years or above. Moreover, 33(36.7%) were males whereas 57 (63.3%) were females; 1 (1.1%) of them had low thiamine level, 17 (18.9%) had normal thiamine level whereas 72 (80.0%) had high thiamine level, as shown in Table I.

Association of age with thymine level reported that 12(52.2%) participants were up to 25 years of age, 5 (25.0%) participants were 25 to 35 years and 1 (3.6%) participant were 35 to 45 years of age had Low/Normal thiamine level. However, 11 (47.8%) participants were up to 25 years of age, 15 (75.0%) participants were 25 to 35 years, 27 (96.4%) participants were 35 to 45 years and 19 (100.0%) participants were above 46 years of age had high thiamine level indicating significant association between thiamine levels and age ($p < 0.001$). As far as the gender is concerned, 6 (18.2%) males had Low/Normal thiamine level while 27(81.8%) had high thiamine level. Furthermore, 12 (21.1%) females had Low/Normal thiamine level while 45 (78.9%) had high thiamine level with an insignificant association between them ($p = 0.743$). Furthermore, 18 (60.0%) had Low/Normal thiamine level and 12(40.0%) had high thiamine level in type I diabetes patients and 30(100%) in control group, and Type II Diabetic patients had high thiamine level with significant association between them ($p < 0.001$), as shown in Table II.

Table I: Demographic characteristics of Participant Profile (n=90)

Variables(n=90)		n (%)
Age	Up to 25 years	23 (25.6)
	26 to 35 years	20 (22.2)
	36 to 45 years	28 (31.1)
	46 years or above	19 (21.1)
Gender	Male	33 (36.7)
	Female	57 (63.3)
Thiamine Level	Low	1 (1.1)
	Normal	17 (18.9)
	High	72 (80.0)

Table II: Association of age, gender and group type with thiamine levels.

Variables(n=90)		Thiamine Level		P value
		Low/Normal (n=18) Count (%)	High (n=72) Count (%)	
Age	Up to 25 years	12 (52.2)	11 (47.8)	<0.001
	26 to 35 years	5 (25.0)	15 (75.0)	
	36 to 45 years	1 (3.6)	27 (96.4)	
	46 years or above	Nil	19 (100.0)	
Gender	Male	6 (18.2)	27 (81.8)	0.743
	Female	12 (21.1)	45 (78.9)	
Group Type	Control	Nil	30 (100)	<0.001
	Type 1 Diabetes	18 (60.0)	12 (40.0)	
	Type 2 Diabetes	Nil	30 (100)	

DISCUSSION

Diabetic patients are usually associated with mild thiamine insufficiency, as is increased renal thiamine clearance.[19] The present study demonstrated the relationship between age, gender and type of diabetes with variation in thymine levels.

Interestingly, one research reported that type I or II DM patients had significantly decreased serum thiamine levels in comparison with controls.[18] The present study showed consistency to some extent in a manner that type I Diabetes had significantly lower serum thiamine levels as compared to type II DM and controls.

Another former research performed in 2016 also described thiamine levels to be substantially reduced in type I DM patients as compared to controls [20]. The present study endorsed the above cited analysis and observed that serum thiamine level was significantly lower in type I Diabetes as compared to type II DM and controls.

Similarly, one more research done in 2007 also reported that plasma thiamine level to be significantly lower in type I and type II diabetic patients in comparison with normal controls [19]. Likewise, another research performed in 2012 stated blood thiamine level to be significantly lessened in DM type I and II patients as compared to controls [21]. The present study endorsed all above reported researches and revealed that blood thiamine concentration to be significantly lower only in patients with DM type I while thiamine concentration was reported high in Type II Diabetes and controls.

A number of researches have revealed deficiency of thiamine in persons with both type I and type II diabetes. Clinical trials have presented altered erythrocyte transketolase action showing a possibility of thiamine deficiency in both type I and type II diabetes, although the frequency of suspected persons differs from 17% to 79% through the trials [22,23].As far as the present study

is concerned, thiamine deficiency was found in 18(60.0%) patients with Type I Diabetes mellitus as compared to Type II Diabetes and controls.

Likewise, one analysis assessed thiamine status by investigation of erythrocytes, plasma, and urine in type I and type II diabetic patients and relates to signs of vascular disorders. Thronalley and associates recruited 26 Type I Diabetic patients and 48 type II Diabetic patients with and without microalbuminuria and 20 healthy control participants. They indicated that low level of plasma thiamine was reported in 76% of patients with type 1 diabetic patients and in 75% of patients with T2D with a significant difference found between them.[19]The present study was not in agreement with the above mentioned research and observed that serum thiamine concentration was significantly decreased in 18 (60.0%) in patients with type I Diabetes than type II DM and controls. On the other hand, all the type II DM patients and controls had high thiamine levels.

Interestingly, further analysis reported that type I diabetes (T1D) patients had significantly lower blood thiamine levels as compared to healthy controls, and there was an inverse relationship existed between thiamine and glucose levels [12]. The present study was consistent with the above reported research and showed that 18 (60.0%) patients with type I diabetes (T1D) had significantly lower blood thiamine levels than healthy controls.

Therefore, it is stated that thiamine ultimately has a part in the diabetic endothelial vascular dysfunction (micro and macroangiopathy), dyslipidemia, nephropathy, retinopathy, cardiopathy, and neuropathy.

CONCLUSION

This study concluded that both the age and group types were significantly associated with thiamine levels of the participants. Furthermore, type I Diabetes patients had significantly lower thiamine level as compared to type II Diabetes and controls. On the other hand, there was no significant relationship of gender with thiamine levels.

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. Wilson RB. Pathophysiology, prevention, and treatment of beriberi after gastric surgery. *Nutr Rev*. 2020 Dec; 78(12): 1015–1029. doi: 10.1093/nutrit/nuaa004.
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. Pacei F, Tesone A, Laudi N, Laudi E, Cretti A, Pnini S, et al. The Relevance of Thiamine Evaluation in a Practical Setting. *Nutrients*. 2020;12: 1-17. doi:10.3390/nu12092810.
5. Eshak E, Arafa A. Thiamine deficiency and cardiovascular disorders. *NutrMetabolCardiovasc Dis*. 2018;28:965–972. DOI: <https://doi.org/10.1016/j.numecd.2018.06.013>
6. Turck D, Bresson JL, Burlingame B, Dean T, Fairweather-Tait S, Heinonen M, et al. Dietary reference values for thiamin. *EFSA J*. 2016;14(12):e04653. DOI: <https://doi.org/10.2903/j.efsa.2016.4653>.
7. Tylicki A, Łotowski Z, Siemieniuk M, Ratkiewicz A. Thiamine and selected thiamine antivitamin - biological activity and methods of synthesis. *Biosci Rep*. 2018 Jan 10;38(1):BSR20171148. doi: 10.1042/BSR20171148.
8. Fattal-Valevski A. Thiamine (vitamin B1). *J. Evid. Based Complement. Alternat. Med*. 2011;16: 12–20. <https://doi.org/10.1177/1533210110392941>
9. FAO & World Health Organization. 2005. *Vitamin and Mineral Requirements in Human Nutrition*. 2nd ed.: 1–20. Geneva: World Health Organization.
10. Jones KS, Parkington DA, Cox LJ, Koulman A. Erythrocyte transketolase activity coefficient (ETKAC) assay protocol for the assessment of thiamine status. *Ann N Y Acad Sci*. 2021 Aug;1498(1):77-84. doi: 10.1111/nyas.14547.
11. Coats D, Shelton-Dodge K, Ou K, Khun V, Seab S, Sok K, et al. Thiamine deficiency in Cambodian infants with and without beriberi. *J. Pediatr*. 2012 Nov; 161(5): 843–847. doi: 10.1016/j.jpeds.2012.05.006.

12. Marrs C, Lonsdale D. Hiding in Plain Sight: Modern Thiamine Deficiency. *Cells*. 2021 Sep 29;10(10):2595. doi: 10.3390/cells10102595.
13. 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.
14. Polizzi FC, Andican G, Çetin E, Civelek S, Yumuk V, BBurçak G. Increased DNA-glycation in type 2 diabetic patients: the effect of thiamine and pyridoxine therapy. *Exp. Clin. Endocrinol. Diabetes*. 2012;120(6):329–334. doi: 10.1055/s-0031-1298016.
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. 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.
17. Valdés-Ramos R, Guadarrama-López AL, Martínez-Carrillo BE, Benítez-Arciniega AD. Vitamins and type 2 diabetes mellitus. *EndocrMetab Immune Disord Drug Targets*. 2015;15(1):54-63. doi: 10.2174/187153031466614111103217.
18. 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.
19. Thornalley P, Babaei-Jadidi R, Antonysunil A, Ahmed A, Rayman G, Bodmer C. 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.
20. 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.
21. Al-Attas OS, Al-Daghri NM, Alfadda AA, Abd-Alrahman SH, Sabico S. Blood thiamine and its phosphate esters as measured by high-performance liquid chromatography: levels and associations in diabetes mellitus patients with varying degrees of microalbuminuria. *J Endocrinol Invest*. 2012 Dec;35(11):951-6. doi: 10.3275/8126.

22. Jermendy G. Evaluating thiamine deficiency in patients with diabetes. *DiabVasc Dis Res.* 2006 Sep;3(2):120-1. doi: 10.3132/dvdr.2006.014.
23. Saito N, Kimura M, Kuchiba A, Itokawa Y. Blood thiamine levels in outpatients with diabetes mellitus. *J NutrSciVitaminol (Tokyo).* 1987 Dec;33(6):421-30. doi: 10.3177/jnsv.33.421. PMID: 3451944.
24. 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. PMID: 26722561; PMCID: PMC4680506.

UNDER PEER REVIEW