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Interaction Between Vitamin B12 Status and Lipid Profile Among Children and Adolescents with Type I Diabetes

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ABSTRACT

Background: Vitamin B12(VIT B12), also known as Cobalamin, is a water-soluble vitamin that acts as a coenzyme. It plays pivotal role in keeping healthy neurons and the synthesis of RBCs, making it crucial during early growth stages. Humans fulfill their nutritional needs for vitamin B12 through combined gut microbial biosynthesis and food consumption.

Aim and objectives: To evaluate the serum level of vitamin B12 in children and adolescents with type 1 diabetes.

Methods: This cross-sectional study was conducted on 61 children and adolescents with type 1 diabetes patients were recruited from the endocrine clinic, Military hospitals, Cairo, Egypt and 21 healthy matched control group. Serum vitamin B12 and lipid profile were measured.

Results: There were statistically significant higher levels in cases than control regarding total cholesterol, HDL and LDL, while there was statistically significant decrease regarding triglycerides. Vitamin B12 was statistically lower in patients group than control group. There was no statistically significant relation between VIT B12 and BMI. While, there was significant negative correlation between VIT B12, triglyceride and LDL at p=0.021 and 0.043 respectively.

Conclusions: Our study underscores the necessity of comprehensive clinical and monitoring in type 1 diabetic patients. The correlation of vitamin B12 with lipid biomarkers is particularly relevant for managing cardiovascular risk in this population.

Keywords: *Vitamin B12 , Children, Adolescents, Type I Diabetes*

1. INTRODUCTION

Vitamin B12(VIT B12), also known as Cobalamin, is a water-soluble vitamin that is important for neurological health, healthy hemopoiesis, and DNA synthesis. Therefore, hematological and neurocognitive impairment are mostly seen in vitamin B12 insufficiency (Obeid et al., 2019). However diagnosis of vitamin B12 deficiency may not affect blood picture, especially in mild deficiency (Rasmussen et al.,2001).

Type 1 diabetes mellitus (T1DM) is an auto immune disease caused by the death of the pancreatic beta cells that secrete insulin by the immune system. (Brouwers et al., 2019). The prevalence of biochemical and clinical vitamin B12 deficiency in adults with T1DM has been demonstrated. It displays a wide range of clinical signs, such as, delirium, dementia, peripheral neuropathy, and sub-acute combined degeneration of the spinal cord (Ralapanawa et al., 2015). Hematological abnormalities such as pancytopenia, ovalocytes, hyper segmented (i.e., >5% of neutrophils with 5 lobes), and macrocytosis (mean cell volume [MCV]> 100 FL).
Malabsorption owing to villous atrophy, and mucositis are additional frequent outcomes of inadequate cell repair mechanisms (Sama et al., 2017).
Patients with T1DM frequently get pernicious anemia brought on by long-term autoimmune gastritis. About 1% of the general population, are affected with pernicious anemia. The prevalence is 3 to 5 times higher in persons with T1DM (Jia et al., 2019).

T1DM patients, particularly those with antibodies against glutamate decarboxylase-65 (GAD-65) and the HLA-DQA1*0501-B1*0301 haplotype, actively display autoantibodies intrinsic factor (IF) types 1 and 2 and parietal cell antibodies (PCA). Pernicious anemia, which is 10 times more common in type 1 diabetes patients than non-diabetic people, results from the PCA's inhibition of intrinsic factor release. By preventing vitamin B12 from attaching to IF, type 1 autoimmune IF causes a vitamin B12 deficit. This stops it from being transported to the terminal ileum, where it would be absorbed (Joffe et al., 2010). Therefore, it's crucial to understand potential pathophysiological causes of vitamin B12 insufficiency, screening for vitamin B12 deficiency, and vitamin B12 supplementation among children with diabetes mellitus. Therefore, this study aimed to assess the prevalence of vitamin B12 deficiency and possible interaction with metabolic parameters in infant and adolescents with type 1 diabetes.

2. PATIENTS AND METHODS

A prospective cross sectional study was conducted on 82 children and adolescents aged between 6 up to 16 years. sixty one diagnosed with T1DM and 21 heathy age and sex matched control group.

Criteria for the diagnosis of diabetes: HbA1C ≥ 6.5%. OR Fasting blood glucose ≥ 126 mg/dl (7.0 mmol/l). Fasting means no caloric intake for at least 8h. OR Postprandial blood glucose ≥ 200mg/dl (11.1mmol/l). OR associated with classic symptoms of hyperglycemia, a random blood glucose ≥ 200 mg/dl (11.1 mmol/l) according to American Diabetes Association, 2017 (Payal et al,2017).

They were recruited from the endocrinology outpatient clinic of military hospitals and NRC, Cairo, Egypt. during a period of 10 months (between November 2023 and August, 2024). Children and adolescents were diagnosed with T1DM for at least 2 years duration. Patients with acute diabetic complications, for example, diabetic ketoacidosis or hypoglycemia have been excluded. In addition, patients suffering from congenital, rheumatic heart and left ventricular dysfunction, or patients with any other acute or chronic inflammatory diseases or infectious diseases or immunodeficiency at study entry or patients receiving medications for cardiac disease or on multivitamins or metformin were excluded.

All patients were subjected to full history taking (e.g., age, sex, anthropometric measures, order of birth, consanguinity, allergy, hospital admission, family history, duration of disease and drug history), Full clinical examination including anthropometry and blood pressure measurements to exclude any possible comorbidities. Fasting venous blood samples (5 milliliters) have been obtained from each participant in the investigation & separated into two parts: the first part has been placed in a tube containing EDTA for the analysis of glycosylated hemoglobin, while the second aliquot has been transferred to a serum separator tube. The serum has been divided into aliquots & promptly frozen at minus eighty degree Celsius. All participants, including cases & controls, had the subsequent assessments of lipid profile including: Total Cholesterol, Triglycerides, HDL & LDL, Glycosylated hemoglobin (HbA1c). Fresh morning urine samples for micro albuminuria. Vitamin B12(Cyanocobalmin) has been calculated by Enzyme Linked Immune Sorbent Assay (ELISA) method.

Informed written consent has been obtained from all cases prior to enrolment. Study details, the nature of the investigations was explained to all patients. Approval of the Research Ethics Committee of AFCM, Egypt, has been obtained & the research has been performed in line with the Declaration of Helsinki (2013).

3. STATISTICAL ANALYSIS:

All data have been gathered, organized, & statistically analyzed utilizing the SPSS version 22 statistical software package (SPSS Inc., Chicago, IL, the United States of America). Data presented as mean & standard deviation for normally distributed quantitative variables. Numerical values and percentages are utilized in the characterization of qualitative characteristics. The Chi-square test (χ^2) is utilized for comparing qualitative variables, whilst the independent T-test is utilized for comparing normally distributed quantitative data among groups. All statistical comparisons were two-tailed, with a significance threshold of pvalue £0.05 indicating significance.

4. RESULTS

The mean weight of the studied patients was 46.5±18.08 kg, mean of height was 147.19±16.3 cm, mean of BMI was 20.6±4.8 kilogram per square meter, mean of waist circumference was 70.3±12.3, mean of hip circumference was 84.4±13.9, mean of waist/hip ratio was 0.81±0.09 while mean of waist/height ratio was 0.47±0.06.

The mean onset of DM in the studied cases was 7.06±3.8 years, mean duration of DM was 5.96±3.7 years and mean dose of insulin was 1.07±0.3 units per kilogram.
21.3% of the studied cases had family history of DM. 4 cases (6.5%) of the studied cases took captopril and 2 (3.3%) took atorvastatin drug.
29.5% of the studied cases had palpitation, 26.2% had dyspnea, 8.2% had orthopnea, 1.6% had chest pain, while 3.3% of them sweeting at rest.

As regard renal symptoms, 9.8% had dysuria, 1.6% had vaginal discharge, 1.6% had nocturnal enuresis, 1.6% had blood in urine, 1.6% had Pus cell and 1.6% of them had incontinence.

As regard neurological symptoms, 24.5% had Parathesia and 34.4% had numbness (table 1). Associated autoimmune dysfunction: 1.6% had blurring of vision, 1.6% had familial mediterranean fever and 1.6% had psoriasis.

The mean of Hb A1c was 9.3±2.2, mean of total cholesterol was 164.13±39.5 mg/dl, mean of TGA was 84.4±40.9 mg/dl, mean of HDL was 64.6±24.9 milligram per deciliters, mean of lowdensity lipoprotein was 86.7±30.3 milligram per deciliters, mean of microalbuminuria was 29.8±39 mg/24h and mean of vitamin B12 was 1.07±0.5 ng/ml±0.5 ng/ml.

A statistically significant rise has been detected in case group than control group regarding total cholesterol, HDL & LDL, while a statistically significant decrease has been detected in case group compared to control group regarding Triglycerides.

A significant negative correlation has been detected between vitamin B12, triglycerides & LDL, while there was insignificant correlation between vitamin B12 & other parameters.

Table 1 Demographic and clinical characteristics of diabetic group

Characteristics	**T1DM group(n=61)**
Age (years)Mean ±**SD**	12.74±3.4
Male N(%)	25(41)
Female N(%)	36(59)
Weight (Kg) Mean ±**SD**	46.5±18.08
Height (cm) Mean ±**SD**	147.19±16.3
BMI (kg/m²) Mean ±**SD**	20.6±4.8
Waist circumference(cm) Mean ±**SD**	70.3±12.3
Hip circumference(cm) Mean ±**SD**	84.4±13.9
Waist/Hip ratio	0.81±0.09
Waist/Height ratio	0.47±0.06
systolic blood pressure(mmHg)	106.19±15.7
diastolic blood pressure(mmHg)	73.92±11.7
Onset of diabetes mellitus (years) Mean ±**SD**	7.06±3.8
Duration of DM (years) Mean ±**SD**	5.96±3.7
Dose of Insulin (units/ kg) Mean ±**SD**	1.07±0.3
Family history of diabetes Negative N(%)	48(78.7)
Positive N(%)	13(21.3)
Captopril N(%)	4(6.5)
Atorvastatin N(%)	2(3.3)
Palpitation N(%)	18(29.5)
Dyspnea N(%)	16(26.2)
Orthopnea N(%)	5(8.2%)
Chest pain N(%)	1(1.6)
Sweeting at rest N(%)	2(3.3)
Dysuria N(%)	6(9.8)

Vaginal Discharge N(%)	1(1.6)
Nocturnal enuresis N(%)	1(1.6)
Parathesia N(%)	15(24.5)
Numbness N(%)	21(34.4)
Hb A1c (%)Mean ±**SD**	9.3±2.2
Microalbuminuria (mg/24h) Mean ±**SD**	29.8±39

Table2: Vitamin B12 & Lipid profile in studied groups

Vatriables	**Diabetic group (N=61)** Mean ±**SD**	**Control Group (N=21)** Mean ±**SD**	**P value**
Total cholesterol (mg/dl)	164.13±39.5	131±38.6	**0.012**
Triglycerides(mg/dl)	84.4±40.9	113±46.2	**0.03**
HDL (mg/dl)	64.6±24.9	39±20.2	**0.002**
LDL (mg/dl)	86.7±30.3	69±25.6	**0.04**
Vitamin B12 (ng/ml)	1.07±**0.5**	1.5±0.84	0.02

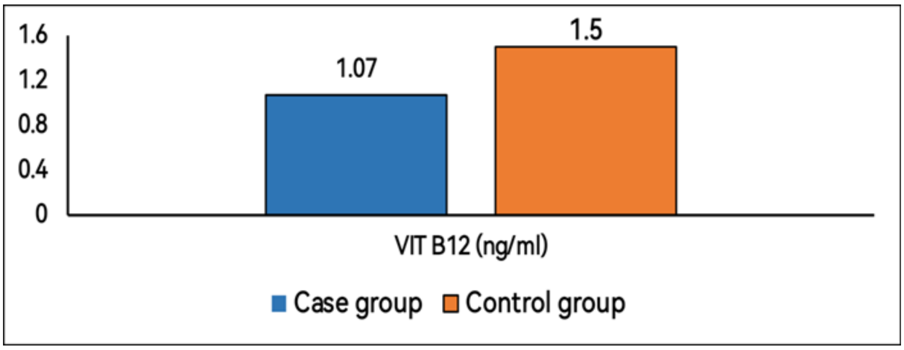

Figure 1: Distribution of Vitamin B12 among studied groups.

Table 3: Correlation between Vitamin B12 and studied parameters

Variables	Vitamin B12	
	r	**p**
Age (years)	0.114	0.379
Height (cm)	0.194	0.131
Weight (kg)	0.130	0.314
Body mass index kilogram per square meter	0.010	0.940
HbA1c	-.045	0.728
Total cholesterol (mg/dl)	-.179	0.163
Triglyceride (mg/dl)	-.293	**0.021**

HDL (mg/dl)	-.050	0.700
LDL (mg/dl)	-.257	**0.043**
Microalbuminuria (mg/24h)	-.061	0.636

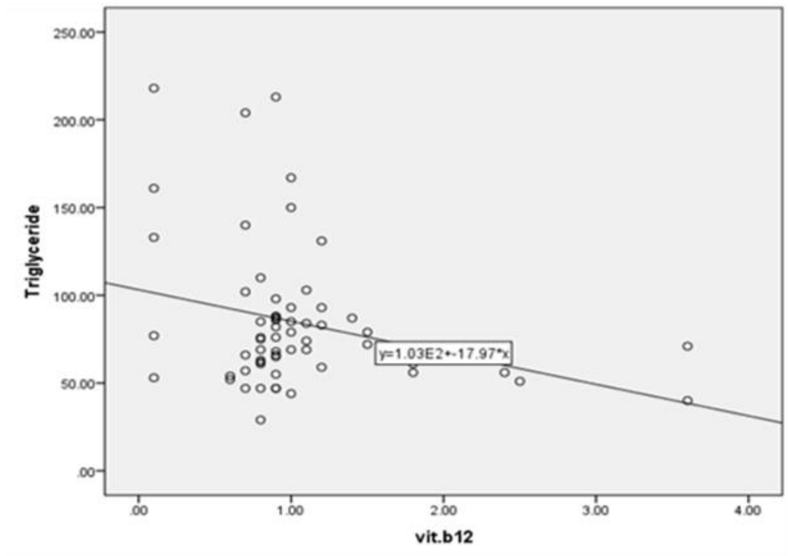

Figure 2: Correlation between Vitamin B12 &LDL

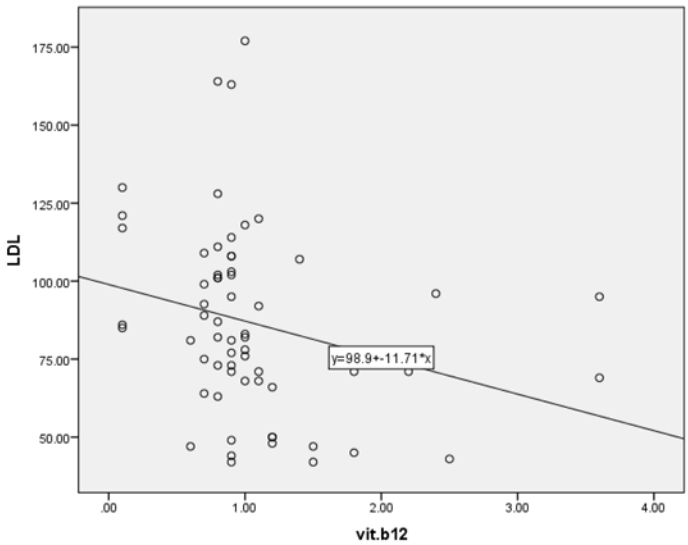

Figure 3: correlation between Vitamin B12 & triglyceride

5. DISCUSSION

Patients with type 1 diabetes are at elevated possibilities for deficiency of vitamin B12 due to autoimmune-related conditions such as pernicious anemia. The occurrence of deficiency of vitamin B12 in this population is a growing concern, as it may exacerbate the complications associated with diabetes, such as neuropathy & poor glycemic control (Infante et al., 2021).

We aimed to evaluate the level of vitamin B12 in children and adolescents with T1DM and explore its association with demographic, anthropometric, and metabolic parameters. The findings revealed significant reduced serum vitamin B12 levels in cases compared to control group, consistent with previous studies reporting a high incidence of vitamin B12 deficiency in T1DM populations (Koshy et al., 2012; Elsayed et al., 2022). Notably, no significant associations were found between vitamin B12 levels and age, gender, diabetes duration, or glycemic control (HbA1c), suggesting that vitamin B12 deficiency in T1DM may arise independently of these factors.

The high prevalence of vitamin B12 deficiency in this population is concerning, given its potential to exacerbate diabetic complications such as neuropathy, anemia, and cognitive impairment (Kibirige et al., 2013; Kim et al., 2019).

In the present study parathesia and numbness were found in 24.5% and 34.4% respectively. Vitamin B12 (Cobalamin) is essential for synthesis of myelin, hence facilitating maintenance & repair of nerve fibres. Vitamin B12 is crucial for energy generation in mitochondria as well as erythropoiesis in bone marrow (Lyon et al., 2020). The manifestations of vitamin B12 insufficiency indicate its impact on the gastrointestinal, hematological, & neurological systems. (Davila and Velez-Yanguas, 2020). Neurological alterations may manifest in the absence of hematological anomalies (Serin and Arslan, 2019).

The lack of a significant association between vitamin B12 levels and glycemic control (HbA1c) contrasts with some hypotheses that poor glycemic management might contribute to micronutrient deficiencies. This finding aligns with prior studies (De Block et al., 2008; Kibirige et al., 2013), which also reported no correlation between vitamin B12 status and diabetes duration or control. Cases with type I diabetes exhibit an almost three fold elevated risk of acquiring vitamin B12 insufficiency relative to general population (Rustgi et al., 2021).

The negative correlations observed between vitamin B12 levels and triglycerides (TGA) and LDL cholesterol are intriguing and warrant further investigation. These findings suggest a potential interplay between vitamin B12 metabolism and lipid profiles, which could have implications for cardiovascular risk in T1DM patients. However, the lack of association with other metabolic parameters, such as total cholesterol, HDL, and microalbuminuria, indicates that vitamin B12 deficiency may not uniformly influence all aspects of metabolic health in this population.

The study also highlights the importance of considering autoimmune comorbidities in T1DM patients, such as pernicious anemia and autoimmune gastritis, which are known to contribute to vitamin B12 deficiency (De Block et al., 2008; Kryssia et al., 2018).

The findings of this study are consistent with global research indicating that reduced level of vitamin B12 is a common but often overlooked comorbidity in T1DM (Wotherspoon et al., 2003). The variability in vitamin B12 status observed in this study, with some participants having normal levels while others were deficient or indeterminate, underscores the need for individualized screening and management strategies.

Our investigation showed that the mean onset of T1DM in the studied cases was 7.06±3.8 years, mean period of T1DM was 5.96±3.7 years & mean dose of insulin was 1.07±0.3 units/ kg. 21% of the studied cases had family history of T1DM. Our research was supplemented by Elsayed et al. 2022, who sought to ascertain the occurrence of a deficiency of vitamin B12 in cases with diabetes mellitus in Egypt & to assess the associated factors of deficiency of vitamin B12 in these cases. They demonstrated longer duration with mean ± SD period of type 1 diabetes mellitus of 9.60±1.133 years (Elsayed et al. 2022).

Moreover, our research was in accordance with an earlier investigation that has been carried out to determine vitamin B12 concentrations in T1DM and to assess the impact of age, diabetic control, and the duration of diabetes on vitamin B12 concentration. Koshy et al. 2012 found that 45.5 percent of the diabetics had reduced vitamin B12 concentration utilizing the manufacturer's cut-off of 180 picograms per milliliter, and fifty-four percent had low B12 levels when utilizing the published cut-off of 148 picomole per litter. Consequently, the occurrence of insufficient serum vitamin B12 concentrations in type 1 diabetics. The investigation didn't show a significant association between the concentration of vitamin B12 & age, tenure of diabetes, or diabetes control (r values of – 0.18, - 0.11, & - 0.08, respectively, at P-value greater than 0.05 (Koshy et al. 2012).

T1DM is often managed by 1ry care physicians who have to be capable to treat both multiple co- morbidities of disease & the disease. Despite the fact that numerous diabetic cases are susceptible to this particular disorder, deficiency of vitamin B12 is frequently disregarded as a possible co-morbidity. The possibility of deficiency of vitamin B12 for diabetic cases is still relevant, despite the absence of metformin in our research. Metformin, a drug that is commonly prescribed to diabetic cases, is known to reduce serum concentrations of vitamin B12 & is related to deficiency of vitamin B12(Pongchaidecha et al., 2004). Our results were consistent with those of Kibirige et al. (2013), who discovered that deficiency of vitamin B12 owing to pernicious anemia was sometimes found among cases with Type 1 diabetes mellitus (Kibirige et al. 2013).

Furthermore, symptoms of deficiency of B12 manifest at a later stage. Nerve damage caused by deficiencies in B12 might be confounded with or contribute to diabetic peripheral neuropathy. It is essential to determine the accurate etiology of neuropathy, as the neurologic symptoms that are misattributed to hyperglycemia may be reversed by the simple replacement of vitamin B12 (Bell et al., 1995).

For cases with Type 1 diabetes mellitus, 1ry autoimmune hypothyroidism & celiac illness are common co-morbidities. (Rewers et al., 2004; Barker et al., 2006). In a cross-sectional investigation conducted in South Africa, the occurrence of associated auto immune hypothyroidism was twenty percent, with a higher incidence among women cases (30.9 percent vs 10.1%-men, p-value less than 0.0002). The investigation included 504 T1DM cases (Joffe et al., 2010). Three cases in this investigation cohort were diagnosed with celiac disease. A correlation has been identified among type 1 diabetes & celiac disease. Both illnesses possess a genetic foundation involving non-HLA & human leukocyte antigen genes. cases who are HLA-DQ2/8 positive have a higher possibility of developing celiac disease (Sharma et al., 2020).

Celiac disease impacts one to ten percent of kids and teens with diabetes. The primary cause of both Celiac disease & diabetes type 1 is wheat gluten, a prevalent environmental component. Gluten elicits an immune response that leads to the generation of anti endomysial (EmA), antireticulin , antigliadin, & anti-tissue transglutaminase autoantibodies. Atrophy of intestinal villi may also occur due to celiac disease.

This results in a significant risk for reduced absorption of vitamin D, folic acid, vitamin B12, fat-soluble vitamins, & calcium. The primary clinical manifestations include of bone demineralization, growth retardation, weight loss, pernicious anemia, & rickets (Arora et al., 2023).

In our results, the mean values of Hb A1c was 9.3±2.2, total cholesterol was 164.13±39.5 mg/dl, triglycerides were 84.4±40.9 mg/dl, HDL was 64.6±24.9 mg/dl, LDL was 86.7±30.3 mg/dl, microalbuminuria was 29.8±39 mg/24h and vitamin B12 was 1.07±0.5 ng/ml. Also, our findings demonstrated that a statistically significant elevation has been detected in case group compared to control group regarding total cholesterol, HDL and LDL, while a significant decrease has been detected in case group compared to control group regarding triglycerides. Low triglycerides in with T1DM could be related to the younger ages of the adolescents in this group (Hickman et al.,1998). These outcomes were in accordance with the outcomes of Elsayed et al. (2022), who discovered that the control group exhibited statistically higher levels of high density lipoprotein cholesterol (Elsayed et al. 2022).

Additionally, our research was corroborated by Koshy et al. (2012), who stated high mean glycated hemoglobin (HbA1c) was 10.13 percent. Our study found that a statistically significant variance has been detected among cases and control under investigation in terms of vitamin B12.In the same line. Koshy et al. (2012) corroborated our findings, determining that the incidence of low serum vitamin B12 was 45.50 percent, with a ninety-five percent confidence interval (CI) of 17.07 to 58.04 percent at p (0.05. twenty -eight percent had deficient level, while seventeen percent were in indeterminate level. The values of the remaining 55 percent were within normal level (Koshy et al. 2012).

Furthermore, our research was corroborated by (De Block et al., 2008; Kibirige et al., 2013), who stated that there was no positive association between low vitamin B12 concentration &level of glycemic control, age, duration of diabetes mellitus & gender. In addition, there was no association among vitamin B12 concentration & duration of diabetes (r = - 0.11), diabetic control (r values for HbA1c , mean fasting blood sugar, & post-prandial blood sugar were 0.02, - 0.08, & - 0.21, respectively), or age (r = - 0.18).

Furthermore, our results were in agreement with those of Elsayed et al. (2022), who stated that the serum B12 concentration was statistically reduced in when compared to the control group. Nevertheless, the concentration of vitamin B12 wasn’t significantly different among type 2 & type 1 diabetic cases (P-value equal 0.774) (Elsayed et al. 2022).

In the current investigation, we demonstrated that a significant negative association has been observed between vitamin B12, triglyceride & LDL, while there was insignificant association between vitamin B12 & other parameters including (height, weight, Microalbuminuria, HbA1c, Age, total cholesterol, high density lipoprotein, or BMI. Thus, vitamin B12 could exerts a role against a spectrum of health conditions, including neurological disorders, diabetes, and dyslipidemia (Harikrishnan et al,2025).

6. CONCLUSIONS

In conclusion, this study highlights the low level of vitamin B12 in children and adolescents with T1DM, emphasizing the need for routine screening and targeted supplementation. The findings contribute to growing evidence underscoring the value of micronutrient management in diabetes care, particularly in populations at risk for autoimmune and metabolic complications. Additionally, a significant negative association has been detected between vitamin B12 & both triglycerides & LDL, suggesting a potential link among vitamin B12 status and lipid profile. The correlation of vitamin B12 with lipid markers is particularly relevant for managing cardiovascular risk in this population. These findings merits the need of more research on a larger population to investigate the benefit of B12 supplementation in type 1 diabetic patients.

Competing interests

The authors declare no competing interests.

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