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A Study on the Effect of Type 2 Diabetes Mellitus on Serum Vitamin A Level in Patients from Rawalpindi and Azad Jammu and Kashmir

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ABSTRACT

Diabetes Mellitus is a chronic metabolic condition resulting from abnormalities in insulin signaling, secretion, or both, leading to symptoms such as high blood sugar and disruptions in fat, protein and carbohydrate metabolism. Vitamin A could potentially influence the secretion of insulin. Insufficient levels of vitamin A over an extended period may result in decreased hormone levels in the pancreas. The presence of vitamin A affects cell development, including pancreatic cells, which is advantageous for insulin synthesis. Research on animals has shown that the deficiency of vitamin A may lead to a reduction in pancreatic β-cell mass and decreased insulin secretion, ultimately causing hyperglycemia as a result of triggered β-cell apoptosis. The current study was carried out to estimate the vitamin A level in diabetic patients from Rawalpindi and Azad Jammu and Kashmir (Rawalakot). One hundred (N=100) diabetic patients and 100 age-matched healthy subjects were selected. Inclusion criteria for the patients were: consent to participate in the study, no physiological abnormality, and, for female patients, not currently pregnant or lactating. Serum samples were collected from the blood of all the selected subjects. Blood glucose level and HbA1c were collected from patients' reports. Vitamin A level was estimated through the ELISA technique. Statistical analysis was done by SPSS software using independent sample t-test, ANOVA, and chi-square tests. The mean value of vitamin level in diabetic patients was (263.07 ± 19.67), and in control subjects it was (342.05 ± 38.75). Results showed significantly reduced vitamin A levels in the diabetic patients compared to the control group ($p < 0.036$). There was a significant difference in the vitamin A levels of diabetic patients based on location ($p < 0.01$), age ($p < 0.0001$), diabetes duration ($p < 0.0001$), HbA1c ($p < 0.0001$), and vegetarian food consumption ($p < 0.0001$). Vitamin A levels were positively correlated with location, occupation, sunlight exposure, symptoms of diabetes, vitamin A deficiency signs, taking any medication for diabetes, taking any vitamins, exercise, vegetable consumption, and dairy consumption. Vitamin A was lower in the residents of Rawalpindi (251.65 ± 38.64) than in Azad Jammu and Kashmir (272.21 ± 21.23). The study concluded that vitamin A levels are significantly reduced in patients with diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) is one of the earliest diagnosed diseases known to man. About 300 years ago, it was first mentioned in an Egyptian manuscript. A metabolic disorder known as diabetes mellitus is characterized by consistently elevated blood sugar levels and varying levels of protein impairment and carbohydrate metabolism (Baynes, 2015; Chaudhary and Tyagi, 2018). Higher glycated hemoglobin in the blood or higher glucose concentrations in venous plasma are indicators of diabetes. Diabetes is commonly classified into different categories, such as type 1 or type 2 diabetes mellitus, gestational diabetes, and other distinct forms that result from additional factors such as genetics, exocrine pancreatic problems, and drug interactions (American Diabetes Association 2014; American Diabetes Association Professional Practice Committee 2024).

T2DM is one of the most prevalent diseases in the world today, and its incidence is rising significantly. An approximate number of 366 million people worldwide, or 8.3% of people between the ages of 20 and 79, were estimated to have T2DM in 2011. This number is expected to increase to 552 million (9.9%) by 2030 (Wild et al., 2004; Sami et al., 2017). Diabetes mellitus was more common in the districts of Muzaffarabad (1.05%), Poonch (0.98%), and Bagh (0.84%). The average disease prevalence in the selected areas of Azad Jammu and Kashmir did not differ significantly. The minor variation

may be created by the district's urbanization. In Azad Jammu and Kashmir, the overall prevalence of diabetes mellitus was 0.95 percent (Danish et al., 2002).

Genetics and lifestyle changes are the primary risk factors for diabetes, especially in adults. These include eating more processed meals that are higher in sugar, being obese, and leading a sedentary lifestyle. 73.1% of people were assessed to have central obesity (62.7% of women and 37.3% of men) (Basit et al., 2021; Azeem et al., 2022). Vitamin A influences cell formation in pancreatic cells, which is beneficial for the synthesis of insulin. Research on animals suggests that a deficiency of vitamin A may lead to a reduction in insulin release and a loss of mass in the pancreatic β-cells, which would cause β-cell death and result in hyperglycemia (Zhou et al., 2020; Liu et al., 2023). Conversely, it has been demonstrated that the risk of T2D is positively correlated with retinol-binding protein 4 (RBP4), the primary circulating retinol transporter that moves retinol from the liver to peripheral target organs (Fan et al., 2019; Liu et al., 2023).

It has been demonstrated that consuming vitamin A daily increases pancreatic β-cell function and can either stop or slow the development of T2D from pre-diabetes (Amisten et al., 2019; Said et al., 2021). Studies on mice have demonstrated that vitamin A has both antihyperglycemic and antioxidant characteristics, making it a viable dietary intervention for individuals with T2D (Meerza et al., 2016; Said et al., 2021).

MATERIALS AND METHODS

The cross-sectional study was carried out at Rawalpindi Women's University from July 2024 to December 2024. Patients were selected from multiple hospitals in Rawalpindi and Azad Kashmir, including Chaudhary Muhammad Hussain Natt Trust Eye Hospital, Khanna Pul, Rawalpindi, and Ali Imran Hospital, Poonch, Rawalakot. A total of 100 patients with T2DM and 100 non-diabetic individuals, including both males and females, between the ages of 22 and 65 years, were selected. Random blood sugar, HbA1c, two-hour postprandial, and fasting glucose level was used to diagnose diabetes mellitus. Blood samples were taken from the cubital vein of all patients using a sterile needle and syringe of 5 cc. The data were collected about location, medical history, type of medication, intake of dietary supplements, duration of diabetes diagnosis, light exposure, routine of exercise, HbA1c, signs and symptoms of vitamin A deficiency, smoking habits, and vegetable and dairy consumption through in-person interviews using a standardized questionnaire. The serum vitamin A will be estimated using ELISA through a commercially available ELISA kit. The data analysis was conducted using SPSS (Statistical Package for the Social Sciences) version 21.0. Independent sample T-test, frequency, Chi-square ANOVA, and correlation were applied to compare the serum vitamin A levels of control and patients.

RESULTS

The mean of vitamin A in the control group was (342.05 ± 38.75), and the diabetic group was (263.07 ± 19.67). The vitamin A levels were significantly higher in the control group compared to the diabetic patient group ($p < 0.036$) (Figure 1).

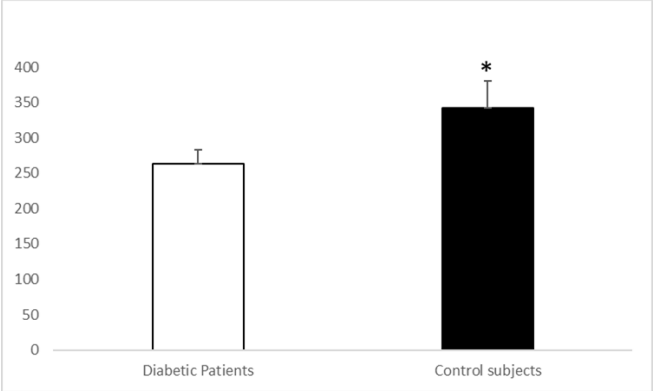

Figure 1: Mean and Standard Error of Mean of vitamin A of the Control and Diabetic groups *p < 0.03

The mean value of diabetic patients from Rawalpindi was (211.59 ± 13.01), while the control group showed a mean of (249.08 ± 28.96). There was no statistically significant difference present between them ($p < 0.86$) (Figure 2). Diabetic patients from Azad Jammu and Kashmir had a mean of (226.64 ± 29.41), and the control group showed (276.26 ± 28.6). Statistically significant difference between them ($p < 0.04$) (Figure 2).

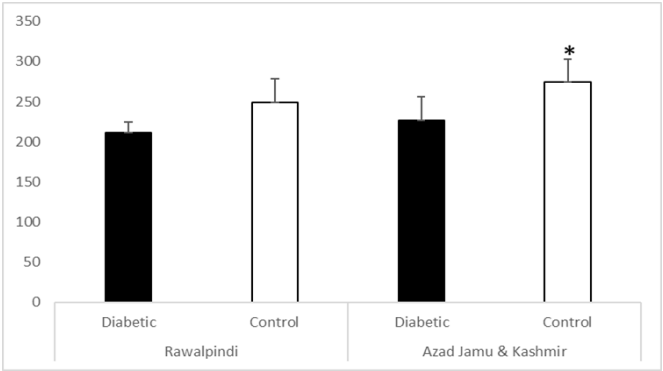

Figure 2: Comparison of Vitamin A Levels between Diabetic and Control Subjects from Rawalpindi and Azad Jammu & Kashmir

Mean of vitamin A in subjects from Rawalpindi was (213.99 ± 12.06) and in subjects from Azad Jammu & Kashmir was (302.43 ± 20.95). Significantly higher vitamin A levels were observed in subjects in Azad Jammu & Kashmir compared to subjects in Rawalpindi ($p < 0.02$) (Figure 3).

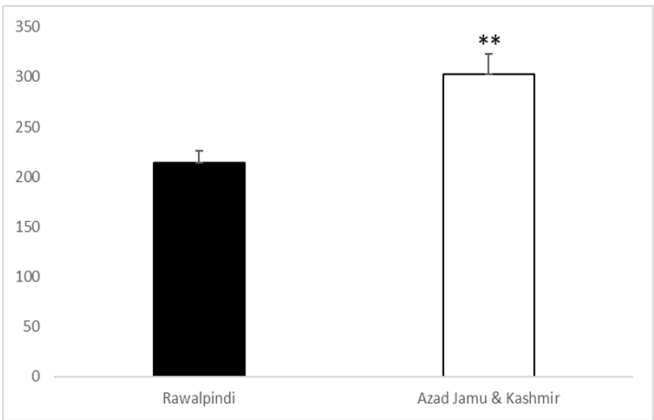

Figure 3: Comparison of Vitamin A Based on Location p < 0.02**

Correlation of Vitamin A with Other Variables of the Diabetic Group

The correlation coefficient of location was 0.78 and ($p < 0.01$), which means there was a significant difference between vitamin A and location. The correlation coefficient of age was -0.82, which showed a negative correlation ($p < 0.006$), which means there was a significant difference between vitamin A and age. The correlation coefficient of diabetes duration was -0.94, a negative correlation ($p < 0.0001$), which showed that as the duration of diabetes increased, the vitamin A level tended to decrease. The correlation coefficient of HbA1c was -0.97, showing a negative correlation ($p < 0.0001$), which means a significant correlation was present between vitamin A and diabetes. The correlation coefficient of vegetable consumption was 0.95, which indicated a negative correlation ($p < 0.001$), showing a significant correlation between vitamin A and vegetable consumption (Table 1)

Table 1: Correlation of Vitamin A with Other Variables of the Diabetic Group

Variable	Correlated to	Pearson Correlation	Sig. (2-tailed)
Vitamin A	Location	0.78	0.01**
Vitamin A	Age	-0.82	0.0001***
Vitamin A	Diabetes duration	-0.94	0.0001***
Vitamin A	HbA1c	-0.97	0.0001***
Vitamin A	Vegetable consumption	0.95	0.0001***

DISCUSSION

The current study aimed to find the effect of T2DM on serum vitamin A (VA) levels in Rawalpindi, Azad Jammu, & Kashmir patients. The results showed reduced VA in the diabetic patients. Similarly, VA levels were lower in Emirati people with T2D in a study done by Taneera et al. (2021). T2DM can be prevented in populations with inadequate vitamin A status by taking vitamin A supplements. According to studies conducted in France and Japan, T2DM patients had noticeably greater levels of circulating retinol than the control group Li et al., 2024. However, in another study by Thakur et al. (2022), the vitamin A levels of diabetics and the control group were not significantly different.

Currently, vitamin A levels were somewhat higher in participants from Azad Jammu & Kashmir than in Rawalpindi, indicating geographical variation. In this study, vitamin A levels varied according to the geographical variation. According to studies on the elderly, vitamin A deficiency was less common in rural areas than in urban areas. In China, studies on the elderly population showed that vitamin A insufficiency was less common in rural areas than in urban areas. The study found that while the deficiency rate was greater in urban regions, it was 0.99% in rural areas (Wang et al., 2021). Regional differences were significant for the majority of dietary micronutrients, food types, and eating behaviors, but not for blood vitamin B6 or any other nutritional biomarker (Kant and Graubard, 2018).

The current study showed lowered vitamin A levels in older subjects. Chronic metabolic abnormalities, which are more common in people with diabetes, such as elevated oxidative stress and age-related alterations in nutritional absorption, could all be the reasons behind. Patients with T2D who are very old have reduced levels of vitamin A and carotenoids in their plasma (Valdes-Ramos et al., 2015). Zhang et al. (2021) have studied reduced serum levels of vitamin A resulting from changes in vitamin A metabolism, which can lead to metabolic dysfunction linked to type 2 diabetes.

In the current study, diabetes duration and vitamin A deficiency were correlated, suggesting that a longer duration of the disease could result in a worse micronutrient status. ROS are produced as a result of chronic hyperglycemia, and these may deplete antioxidant stores such as vitamin A. Lower vitamin A levels may be the consequence of accumulated oxidative stress as diabetes becomes chronic. Chronic diabetes can damage the liver, which can impact the metabolism of vitamin A. As time passes, this impairment may result in lower serum retinol levels. Serum retinol binding protein 4 (RBP4) and transthyretin (TTR) levels declined as type 2 diabetes progressed. This disparity might result from decreased hepatic TTR expression caused by liver damage, since TTR is produced in the liver and binds to RBP4 in the endoplasmic reticulum of hepatocytes. Vitamin A availability to peripheral tissues, including retina, may be restricted as a result of this decrease in hepatic TTR, which also affects retinol binding protein 4 stability and transport (Chang et al., 2025).

HbA1c was correlated with vitamin A levels, supporting the idea that inadequate glycemic management hurts vitamin status. Higher vitamin A levels were linked to lower fasting blood glucose, HbA1c, waist circumference, triglycerides, and BMI. This is similar to previous research suggesting that VAD results in hyperglycemia and the pancreatic β cells, while vitamin A therapy improves insulin resistance, inhibits lipid biosynthesis, and lowers body weight (Taneera et al., 2021).

Currently, high vegetable consumption is correlated with increased vitamin A levels. A lower risk of diabetes is linked to a larger dietary consumption of vitamin A, especially from plant sources high in β-carotene (Su et al., 2022). The human body cannot produce vitamin A, a vital fat-soluble micronutrient that must be obtained from the diet. It is present in dairy products, fish oil, liver, eggs, yellow and orange fruits, and dark green leafy vegetables. Moderate cooking of vegetables increases the release of carotenoids, which helps in absorption. Zinc deficiencies, alcohol use, mineral oil, neomycin, and cholestyramine can all impair the body's ability to absorb vitamin A (Zinder et al., 2019).

CONCLUSION AND RECOMMENDATION

The study concluded that vitamin A (VA) levels were reduced in diabetic patients as compared to the normal subjects. VA was positively correlated with the location, age, diabetes duration, HbA1c, and vegetable consumption. VA was lower in subjects from Rawalpindi in comparison to Azad Jammu and Kashmir. This study found that VA deficiency was prevalent in diabetic patients with

an advanced age of 51-60 years, longer diabetes duration of 1-5 years, and with HbA1c in the range of 9.0-9.9. People who used to consume vegetables daily had significantly higher VA levels.

This study increases understanding of the connection between VA levels and T2DM and emphasizes the need for more research at the molecular level to investigate underlying cellular mechanisms. Additionally, the need of the day is to discover how VA supplementation affects diabetes outcomes and the mechanisms underlying VA insufficiency in diabetic patients.

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