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Impact of smoking and environmental toxins on diabetic retinopathy: role of trace elements, lipid profiles, and vitamin A

Nagham Hadi Alrikabi[1,2,3,5*], Hajer Chemingui[1], Soheir N. Abd El-Rahman[4], Madiha Kamoun[1]

[1] *Laboratory of Water, Membranes and Environmental Biotechnology, Water Researches and Technologies Center, BP 273, Soliman 8020, Tunisia*
[2] *Department of Chemistry, Faculty of Science, Al-Manar University, Tunisia*
[3] *Department of Pharmacy, Mazaya University College, Thi Qar, Iraq*
[4] *Crops Technology Research Department, Food Technology Research Institute, Agricultural Research Center, Giza 12619, Egypt*
[5] *Thi Qar Health Directorate, Center for Hereditary Blood Diseases, Thi Qar, Iraq*

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Abstract

Diabetic retinopathy (DR), a leading cause of adult blindness, is influenced by physiological factors such as lipid profiles, vitamin A, and trace elements, as well as environmental factors like smoking. This study investigated the relationship between HbA1C, glucose levels, trace elements (lead, zinc, selenium, magnesium), vitamin A, and lipid profiles (TC, TG, HDL, LDL, VLDL) in type 2 diabetes (T2D) and DR patients, considering the impact of smoking. The study, conducted at Nasiriya General Hospital and the Center for Endocrinology and Diabetes (May 2023–March 2024), included three age groups (15–35, 35–55, and 55–75 years) divided into smokers and non-smokers. Results showed significantly higher glucose, HbA1C, lipid and selenium levels in T2D and DR patients compared to controls ($p \leq 0.05$), with smokers exhibiting greater lead levels. Zinc and vitamin A were significantly lower in DR patients, particularly among smokers. The findings highlight smoking as a source of lead and other toxins that exacerbate DR and diabetes-related complications, emphasizing the critical link between environmental health and chronic disease management.

Keywords: Diabetic retinopathy, Smoking, environmental toxins, Trace elements, Lipid profile, Vitamin A.

1. Introduction

Type 2 diabetes mellitus (T2D) is a chronic metabolic disorder characterized by persistent hyperglycemia and either partial or complete insulin deficiency, leading to vascular injury, dyslipidemia, and damage to multiple organ systems. It represents a significant global health challenge, affecting not only individual patients but also placing a considerable burden on society and healthcare systems. The structural and functional alterations caused by T2D are irreversible and result in complications that impact vital organs such as the nervous system, kidneys, cardiovascular system, and eyes. One of the most common and debilitating complications of T2D is diabetic retinopathy (DR), which is a leading cause of blindness in working-age individuals. Studies show that individuals with diabetes have a 25-fold increased risk of vision loss compared to the general population [1,2]. The retina, a highly vascularized tissue in the eye, depends on a complex network of neurons and blood vessels to maintain essential processes like phototransduction and neurotransmission. Endothelial cells in the choroid and retinal vessels play a crucial role in regulating growth factors and metabolites necessary for proper retinal function [3,4]. The development of DR is multifactorial, with key contributing factors including age, sex, duration of diabetes, HbA1C levels, trace element deficiencies, and lipid imbalances [5]. Trace elements, play a critical role in cellular function and enzyme activation. Their deficiency or imbalance can disrupt metabolic pathways, contributing to the onset and progression of diabetic complications [6,7]. Specific trace elements such as zinc (Zn), selenium (Se), lead (Pb), magnesium (Mg), and others have been implicated in T2D and its complications [8,9]. These elements support insulin receptor activation, act as antioxidants, and improve insulin sensitivity [10,11]. Environmental factors, particularly smoking, further exacerbate the risk of developing DR and other diabetic complications. Smoking is a major source of harmful substances like lead (Pb) and other toxins, which

* Corresponding author.
E-mail address: naghamhadi55@gmail.com (N. H. Alrikabi).
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contribute to oxidative stress and vascular damage, worsening the effects of T2D. Elevated blood lipid profiles and smoking-induced toxins promote endothelial dysfunction, increasing the risk of retinal damage [12]. While some studies have confirmed a link between lipid profiles and DR severity [13,14], other large-scale studies have failed to establish consistent associations [15]. Furthermore, smoking-related toxins, including lead, have been shown to play a significant role in exacerbating retinal damage, particularly in diabetic patients. The primary aim of this study is to investigate the role of key trace elements, specifically zinc (Zn), selenium (Se), lead (Pb), and magnesium (Mg) in the development and progression of diabetic retinopathy (DR) among Type 2 diabetes (T2D) patients, with a particular focus on the environmental health impact of smoking. This research seeks to examine the relationship between smoking-related toxins, such as lead, and DR severity, while also assessing the effect of blood lipid levels on DR progression. By linking the influence of trace elements, smoking, and lipid profiles, this study aims to provide critical insights into how environmental factors and metabolic dysregulation contribute to diabetic complications, with implications for both prevention and management.

2. Material and methods

The current investigation was conducted from May 2023 to March 2024 at the Diabetes Center at Nasiriya General Hospital and the Endocrinology and Diabetes Center. The study included (270) subjects from Iraq, which were divided into ninety subjects as healthy Control group, ninety patients with T2D without complications and ninety Clinically diagnosed cases of T2D with DR. Consent for all sampling was obtained beforehand.

2.1. Blood sugar analysis

Blood sugar and cumulative blood sugar were measured (every week for 30 days) for all control and DM groups with blood sugar kits used by (Roch- Germany, Biolabo – France).

2.2. Determined vitamin A level

Vitamin A was measured by using (kit Aviva Systems Biology, USA) with an (Enzyme-linked immunosorbent assay ELISA device, ELISA reader ELX-800 USA and ELISA washer FLX-50, USA), and (HbA1C analyzer Nycocard TM, Germany).

2.3. Determined the trace element levels

Magnesium and zinc tests were conducted on a (British-made BIOREX monarch/240 device.). Selenium and lead elements were determined by using an atomic absorption device in the Chemistry department, Science College, University of Thi-Qar.

2.4. Calculation of Body Mass Index (BMI)

BMI was calculated as weight divided by height squared (kg/m2). The BMI chart was used to categorize an individual as underweight, normal weight, overweight, or obese, as illustrated in Table 1.

2.5. Collection of blood samples

After 8–12 hours of fasting, five-milliliter venous blood samples were taken from each group. The blood test was divided into two aliquots, 1 and 4 milliliters. In a test tube filled with ethylene diamine tetra acetic acid (EDTA), the main aliquot was transferred. In less than three hours, this blood was built up and utilized to estimate the HbA1c. The second aliquot was transferred to a plain tube without anticoagulant, allowed to clump for thirty minutes, and then the samples were centrifuged for fifteen minutes at 400 rpm. Serum was then separated and quickly stored at -20ºC until it was needed to estimate serum glucose, lipid profile (TC, TG, HDL-C, LDL-C, VLDL-C), Se, Zn, and Pb [16].

An overview of the study structure and the allocation of measured parameters across the different groups is presented in Figure 1

2.6. Lipid profile determination:

Total Cholesterol (TC) and high-density Lipoprotein Cholesterol (HDL-C) were measured according to Allain *et al*. [17] and Lopez-virella *et al.* [18], and the levels of Low-Density Lipoprotein Cholesterol (LDL-C) were calculated by using the formula of Friedewald *et al.* [19], VLDL-C was estimated by: VLDL-C = TG/ 5 (Friedewald's formula). (Triglycerides (TG) with a UV/VIS spectrophotometer, T 60, PG Instruments Ltd, Germany).

2.7. Statistical Analyses

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 22.0 for Windows (SPSS Inc., USA). A p-value of less than 0.05 was considered statistically significant. Descriptive statistics, including mean and standard deviation (SD), were calculated, and group comparisons were conducted using analysis of variance (ANOVA) with LSD post hoc tests.

3. Results

3. 1. Demographic data

The groups were divided according to the three groups distributed (controllers, T2D, and DR patients). The study was done by choosing three variables, including studying the groups according to gender category, where the men category was higher than the women. It was also divided according to age into three age groups starting from the

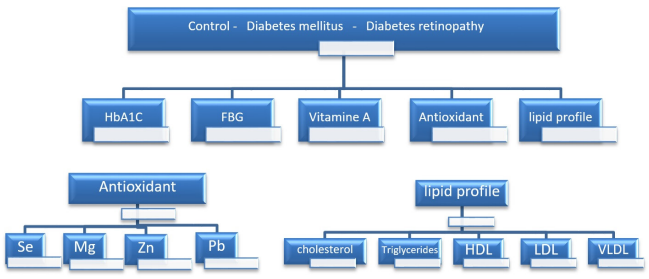

Fig. 1. The general form of the study and distribution of parameters.

Table 1. Categories and cut-off values for Body Mass Index (BMI).

Classification	BMI (Kg/m2)
Underweight	>18.5
Normal weight	18.5-24.9
Overweight	25-29.9
Obese	≥ 30

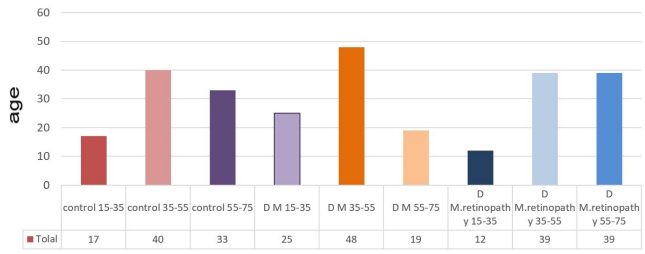

Fig. 2. Characteristic data for studied groups DM and DR and control (age).

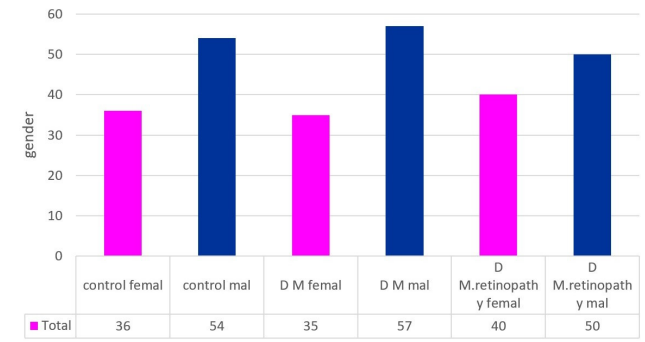

Fig. 3. Characteristic data for studied groups DM and DR and control (gender).

category (15-35), (35-55), (55-75), (Figures 2 and 3). The study population was divided into diabetic smokers (21%) and non-smokers (79%) based on smoking status. The proportion of participants in the 35–55 age group was relatively higher in both the smoker and non-smoker groups, with the non-smoker group having a slightly greater representation (Figure 4).

3.2. Fasting serum glucose levels and HbA1c levels

In this study, the results show that the significant increases in glucose concentration at ($P < 0.05$) in diabetic patients and diabetic with retinopathy patients groups compared with control group are indicated in (Table 2 and Figures 5 and 6). Also, smoking patients are more affected than non-smokers in all age groups. According to reports from the World Health Organization and the American Diabetes Association, the current study on Iraqi patients revealed that subjects with diabetes retinopathy (DR) and those with type 2 diabetes (T2D) had significantly higher HbA1c levels when compared with control subjects. Additionally, DR subjects showed an increased HbA1c level (8.19±0.73, 8.33±0.56), (9.97±0.59,7.33±0.56), (8.46± 0.55, 7.92± 0.94) more than T2DM (8.15±0.59, 8.17±0.77), (8.78±0.77, 7.15±0.73), (7.85± 0.35, 7.26±1.01), at age 15-35, 35-55, 55-75, and smoker and non-smoker groups, respectively as shown in Table 2. Diabetes is characterized by decreased hepatic glucose synthesis, impaired glucose disposal in skeletal muscle, and deficiencies in glucose metabolism in multiple organs. As a result, there is increased insulin-dependent glucose absorption in nerve and lens tissue. These factors together account for the increase in glucose and HbA1c.

3.3. Comparison of some trace element levels

The present study demonstrated a significant decrease in zinc (Zn) levels ($p < 0.05$) and a significant increase in selenium (Se) levels ($p < 0.05$) in both T2D and DR patients compared to controls. Additionally, lead (Pb) levels were significantly higher in diabetic patients, particularly among smokers, as shown in Table 3 and Figure 7. Magnesium (Mg) levels were also significantly elevated in the DR group compared to controls, with a slight increase

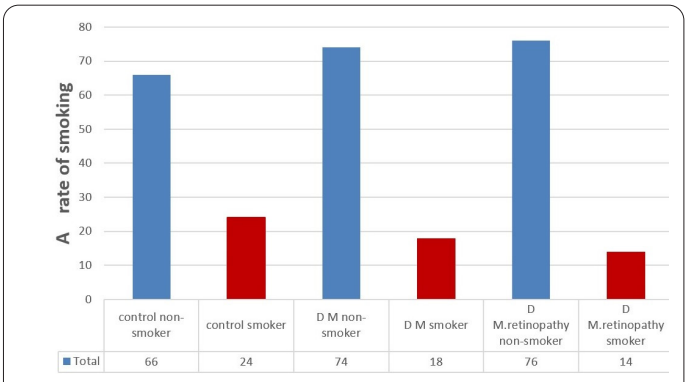

Fig. 4. Distribution according to smoking and non-smoking groups diabetic.

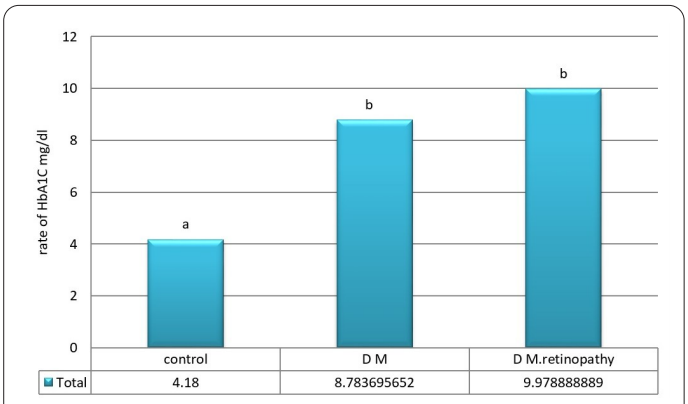

Fig. 5. Explaining Average diabetes according to HbA1C group (35-55) years.

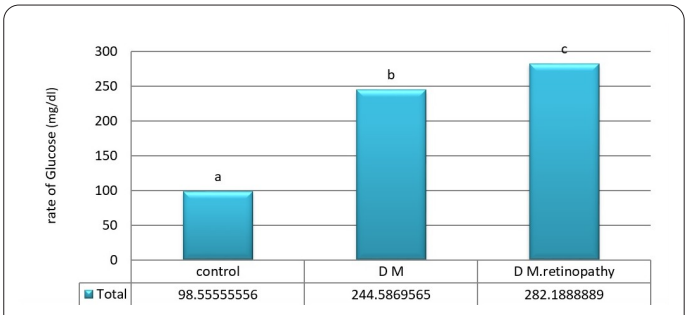

Fig. 6. Explaining Average diabetes according to Glucose group (35-55) years.

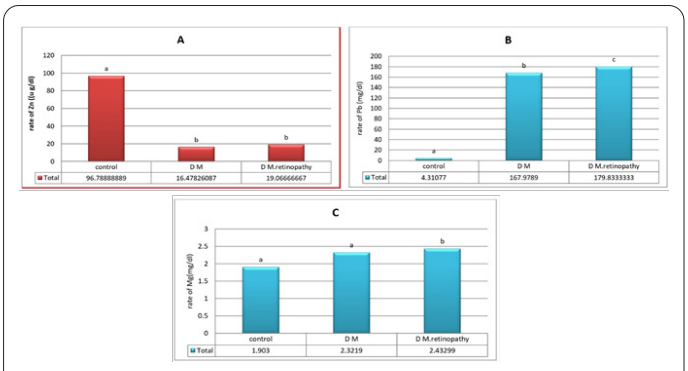

Fig. 7. Average diabetes according to group (35-55) years: A- Zn group. B- Pb group. C- Mg group. D- Se group.

Table 2. Fasting blood glucose and HbA1c levels in control subjects, Type 2 diabetes patients, and diabetic retinopathy patients.

Group	Age Group (years)	Smoking Status	Fasting Glucose (mg/dL)	HbA1c (%)
Control	15–35	Non-Smoker	85.33±8.11	5.12±0.41
Control	15–35	Smoker	87.11±6.92	5.18±0.33
T2D	15–35	Non-Smoker	168.41±12.19*	8.15±0.59*
T2D	15–35	Smoker	175.22±14.21*	8.17±0.77*
DR	15–35	Non-Smoker	187.98±15.22*	8.19±0.73*
DR	15–35	Smoker	193.44±13.99*	8.33±0.56*
Control	35–55	Non-Smoker	88.25±7.41	5.22±0.55
Control	35–55	Smoker	90.14±6.88	5.26±0.39
T2D	35–55	Non-Smoker	171.41±13.22*	8.78±0.77*
T2D	35–55	Smoker	182.15±14.77*	7.15±0.73*
DR	35–55	Non-Smoker	199.22±17.33*	9.97±0.59*
DR	35–55	Smoker	207.41±16.21*	7.33±0.56*
Control	55–75	Non-Smoker	89.11±8.22	5.31±0.49
Control	55–75	Smoker	91.44±7.15	5.34±0.37
T2D	55–75	Non-Smoker	169.22±12.88*	7.85±0.35*
T2D	55–75	Smoker	179.33±15.11*	7.26±1.01*
DR	55–75	Non-Smoker	188.77±16.44*	8.46±0.55*
DR	55–75	Smoker	195.22±15.88*	7.92±0.94*

*Significantly different from control group ($p < 0.05$). Each value is presented as mean±SD for each group. Values significantly different from controls ($p < 0.05$) were identified by ANOVA with multiple range tests.

Table 3. Serum levels of magnesium, lead, selenium, and zinc in control subjects, Type 2 diabetes patients, and diabetic retinopathy patients by age group and smoking status.

Age Group	Case	Mg (mg/dL) Non-Smoker	Mg (mg/dL) Smoker	Pb (µg/dL) Non-Smoker	Pb (µg/dL) Smoker	Se (ng/mL) Non-Smoker	Se (ng/mL) Smoker	Zn (µg/dL) Non-Smoker	Zn (µg/dL) Smoker
15–35	Control	1.91±0.18	2.09±0.24	4.55±2.20	4.69±2.35	108.83±23.77	90.33±16.74	86.33±14.31	95.83±1.58
15–35	T2D	1.88±0.49	1.40±0.47	77.18±21.29	130.66±34.90	110.20±4.67	111.18±3.60	31.00±1.72	33.36±5.85
15–35	DR	2.43±0.48	2.51±0.47	95.25±31.35	150.00±24.43	116.33±5.90	165.00±12.12	23.50±2.61	32.19±4.67
35–55	Control	1.88±0.18	1.90±0.24	4.06±2.20	4.31±2.35	82.47±16.58	91.26±16.74	95.83±14.31	96.78±12.58
35–55	T2D	1.88±0.49	2.92±0.47	80.18±21.00	167.97±34.90	149.67±13.51	154.11±3.60	15.36±1.72	16.47±1.85
35–55	DR	2.13±0.48	2.23±0.47	100.25±31.35	179.83±24.43	159.00±10.87	169.55±12.12	18.67±2.19	19.06±2.19
55–75	Control	1.84±0.17	1.90±0.16	3.92±2.20	5.49±3.03	96.73±4.67	88.75±15.81	93.00±2.37	97.50±1.20
55–75	T2D	1.87±0.10	1.95±0.07	60.00±10.58	132.25±36.05	110.38±7.58	123.75±1.20	33.43±7.67	44.50±3.87
55–75	DR	2.16±0.58	2.30±0.43	71.00±7.98	165.64±4.28	126.38±4.71	133.57±3.47	18.59±3.19	19.00±4.92

Abbreviations: T2D: Type 2 Diabetes; DR: Diabetic Retinopathy. *Significantly different from control group ($p < 0.05$). Each value is presented as mean±SD for each group. *Significantly different from controls ($p < 0.05$) by ANOVA multiple range test.

observed relative to the T2D group (Table 3). The precise roles of trace elements such as lead, zinc, magnesium, and selenium in diabetes remain unclear. This study aimed to determine serum concentrations of these trace elements in both DM and DR patients in comparison to healthy controls.

3.4. Vitamin A levels

The present study has shown a significant decrease in Vitamin A levels at ($p< 0.05$) in T2D and DR groups in all ages in comparison to control group as in (Table 4 and Fig 8). It was also observed that Vitamin A has significantly decreased in DR (7.11±0.69, 12.70±4.09 ng/ml), (16.20±0.69, 16.77±1.09 ng/ml), (20.38± 3.48, 22.35± 1.01ng/ml) compared to DM (19.44±7.72, 21.47±1.85 ng/ml), (31.24±7.72, 31.48±1.85 ng/ml), (25.89±5.27, 27.87± 7.30 ng/ml) and control (46.17± 4.06, 55.32±3.37 ng/ml), (36.17± 2.06, 43.60±13.37 ng/ml), (34.08± 7.40, 55.04±6.49 ng/ml) at age 15-35, 35-55, 55-75, and smoker and non-smoker groups, respectively (Table 4). Moreover, the results in Table 4 indicate that smoking leads to significant decrease in vitamin A in DR, T2D, and control groups. It is believed that vitamin A will play a significant part in the angiogenesis, and fibrosis processes that are the cause and mechanism of DR. Numerous prior studies have demonstrated a connection between vitamin A and DR. Vitamin A works to maintain healthy retinal and corneal layers in the eyes, reducing the risk of certain eye diseases such as keratitis and retinitis. Foam deposits (beot stains) may appear in the whites of the eyes and, the cornea may become dirty and damaged, which may lead to blindness. Vitamin A deficiency is also a common cause of blindness in countries with high rates of food insecurity.

3.5. Comparison of lipid profile levels

The present study showed that all serum lipids and lipoproteins were significantly higher at ($P< 0.05$) in diabetic and diabetic retinopathy groups Compared to control subjects (Table 5 and Fig 9). The average value of Cholesterol (TC), Triglyceride (TG) and Low-density lipoprotein cholesterol (LDL-Cholesterol) levels in diabetics and retinopathy patients increased significantly compared to control. The mean HDL-C value was significantly lower ($P< 0.05$) in both DM and DR compared to control. The mean value of Very Low-density lipoprotein (VLDL-C) in DM and DR was significant ($P< 0.05$), and increased compared to the control as shown in Table 5.

Table 4. Serum vitamin A levels (ng/mL) in control subjects, Type 2 diabetes patients, and dsiabetic retinopathy patients by age group and smoking status.

Age Group	Case	Vitamin A (ng/mL) Non-Smoker	Vitamin A (ng/mL) Smoker
15–35	Control	55.32±3.37	46.17±4.06
15–35	T2D	21.47±1.85	19.44±7.72
15–35	DR	12.70±4.09	7.11±0.69
35–55	Control	43.60±13.37	36.17±2.06
35–55	T2D	31.48±1.85	31.24±7.72
35–55	DR	16.77±1.09	16.20±0.69
55–75	Control	55.04±6.49	34.08±7.40
55–75	T2D	27.87±7.30	25.89±5.27
55–75	DR	22.35±1.01	20.38±3.48

Abbreviations: T2D: Type 2 Diabetes; DR: Diabetic Retinopathy. Each value is presented as mean±SD for each group.

4. Discussion

4.1. Fasting glucose and HbA1c

The present study found significantly elevated fasting glucose and HbA1c levels in both T2D and DR patients compared to controls, with the highest levels observed in DR patients and among smokers. These findings are consistent with global reports from the World Health Organization and the American Diabetes Association, as well as regional studies. HbA1c is a well-established biomarker for glycemic control and diabetic complications. The increased HbA1c levels in DR patients reflect poor long-term glycemic control, a key risk factor for the development and progression of diabetic retinopathy. Similar observations were reported in studies from Africa and Palestine, where diabetic patients with complications had significantly higher fasting blood glucose (FBG) and HbA1c levels compared to healthy controls. These results reinforce the importance of strict glycemic management to reduce the risk of microvascular complications such as DR.

A trait that is objectively tested and assessed as a sign of pathogenic processes, normal biological processes, or pharmacologic reactions to a therapeutic intervention is called a biomarker. In clinical medicine, biomarkers include things like HbA1c values [20].

Patients with diabetes who have high blood glucose levels because of a shortage or resistance. The same out-

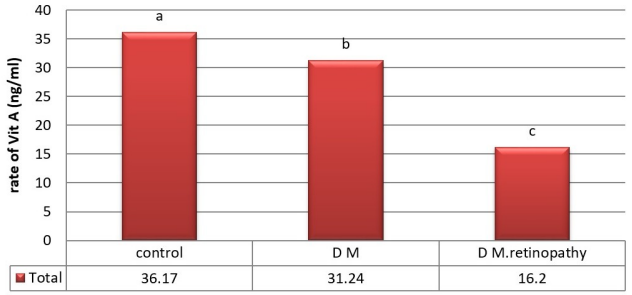

Fig. 8. Explaining Average diabetes according to (Vit A) group (35-55) years. Each value is mean ± SD in each group. Significantly different from controls ($p < 0.05$) by ANOVA multiple rage test.

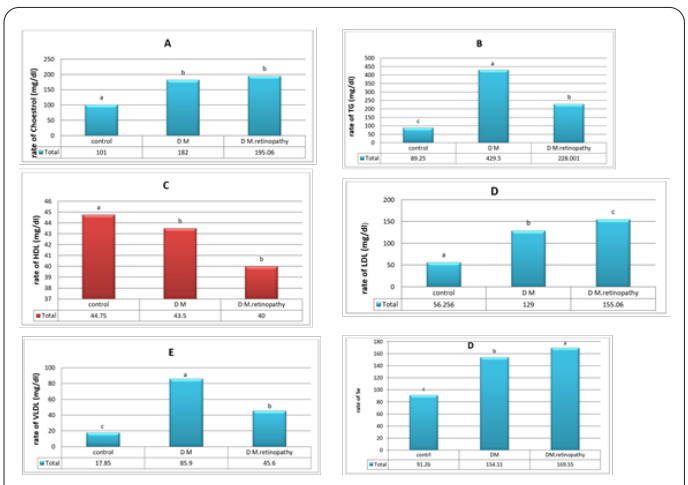

Fig. 9. Average diabetes according to group (35-55) years: A- TC group. B-TG group C-HDL group. D-LDL group. E- VLDL group.

Table 5. Lipid profile parameters (VLDL, LDL, HDL, Triglyceride, Cholesterol) in control subjects, Type 2 diabetes patients, and diabetic retinopathy patients by age group and smoking status.

Age Group	Group	VLDL (mg/dL) Non-Smoker	VLDL (mg/dL) Smoker	LDL (mg/dL) Non-Smoker	LDL (mg/dL) Smoker	HDL (mg/dL) Non-Smoker	HDL (mg/dL) Smoker	Triglyceride (mg/dL) Non-Smoker	Triglyceride (mg/dL) Smoker	Cholesterol (mg/dL) Non-Smoker	Cholesterol (mg/dL) Smoker
15–35	Control	19.68±3.34	21.30±0.57	51.10±15.87	61.83±15.30	56.60±2.96	52.16±4.93	98.40±21.59	106.50±15.82	107.70±16.51	114.00±29.95
15–35	T2D	44.20±21.21	51.56±7.99	150.00±39.90	168.33±35.35	58.00±8.49	41.00±14.14	221.00±18.89	257.81±21.45	208.00±24.04	209.33±23.09
15–35	DR	38.08±12.02	52.51±1.53	161.01±24.03	190.69±42.42	51.38±9.20	38.20±3.53	190.40±22.93	262.56±47.54	212.40±27.98	228.89±47.72
35–55	Control	16.49±3.11	17.85±1.70	53.60±20.98	56.25±27.16	43.00±7.57	44.75±4.03	82.47±16.58	89.25±8.30	96.60±18.21	101.00±33.24
35–55	T2D	64.07±18.05	85.90±7.37	132.37±16.45	129.00±23.33	49.62±9.31	43.50±7.77	320.38±10.87	429.50±57.27	172.50±27.57	182.00±24.20
35–55	DR	43.58±4.22	45.60±4.58	135.91±43.26	155.06±10.26	46.41±8.29	40.00±7.21	217.94±13.51	228.00±6.08	182.33±15.88	195.06±34.06
55–75	Control	16.49±3.11	17.85±1.70	43.60±20.98	56.25±27.16	53.00±7.57	46.00±2.00	82.47±16.58	89.25±8.30	96.60±18.21	101.00±33.24
55–75	T2D	25.60±2.05	43.58±1.37	122.87±36.45	138.50±23.33	49.62±9.31	44.75±4.03	128.00±6.08	217.94±13.51	172.50±27.57	182.00±4.20
55–75	DR	64.07±4.22	85.90±4.58	129.97±13.26	148.50±10.26	51.41±8.29	43.50±7.77	320.38±10.87	429.50±5.27	182.33±5.88	195.06±34.06

Abbreviations: T2D: Type 2 Diabetes; DR: Diabetic Retinopathy. Each value is presented as mean±SD for each group.

comes with insulin were discovered by our last research [16], that During a fast, blood glucose levels increase, which is a sign of inadequate blood sugar regulation then [15,16]. According to an African study, the group of patients with diabetes and comorbidities had FBG and HbA1c levels 2.06 and 2.33 times higher, respectively, than the group of healthy individuals [19], our study's high percentage of HbA1c levels indicates that the type 2 diabetic participants had inadequate glycemic control. The present study's findings are consistent with a study conducted in Palestine titled "Total Antioxidant Status in T2D Patients," which discovered a strong correlation between HbA1c and various groups at ($p = 0.05$). A trait that is reliably measured and assessed as a sign of pathogenic processes, normal biological processes, or pharmacologic reactions to therapeutic intervention is known as a biomarker [21].

4.2. Trace elements

Our study demonstrated a significant decrease in serum zinc (Zn) and an increase in selenium (Se) and lead (Pb) levels in T2D and DR patients compared to controls, with the highest lead concentrations among smokers. Magnesium (Mg) levels were also significantly elevated in the DR group. The role of trace elements in diabetes and its complications is increasingly recognized. Zinc is essential for insulin synthesis, storage, and secretion, and plays a vital role in antioxidant defense. Zinc deficiency in diabetic patients can lead to increased oxidative stress and cellular damage, as supported by previous studies. Zinc also possesses antiviral properties and protects against beta cell death. Our findings are consistent with those of Chausmer et al., Nsonwu et al., and Viktorinovaa et al., who reported decreased zinc and magnesium levels in diabetic populations [37–39]. Selenium, an essential micronutrient with antioxidant properties, was found to be elevated in diabetic groups, possibly as a compensatory response to oxidative stress. Selenium supplementation has been considered for the prevention of metabolic diseases such as diabetes. Lead, a toxic environmental element, was significantly higher in diabetic smokers, highlighting the contribution of smoking to increased lead exposure and vascular damage. Magnesium, which was elevated in DR patients, may reflect altered renal handling or an adaptive response in advanced diabetic complications. These findings underscore the importance of monitoring trace elements in diabetic patients, especially those at risk for retinopathy.

4.3. Vitamin A

Serum vitamin A levels were significantly lower in T2D and DR patients, particularly among smokers. Vitamin A is crucial for retinal health and visual function. Its deficiency has been linked to an increased risk of retinopathy and impaired phototransduction. Measuring serum vitamin A provides a more accurate assessment of its relationship with DR than dietary intake alone. Our results are in agreement with previous studies that reported lower vitamin A levels in diabetic patients, especially those with microvascular complications. The lowest vitamin A levels in DR patients, particularly smokers, may reflect increased oxidative stress and impaired absorption or metabolism associated with diabetes and tobacco exposure.

Dietary vitamin A is absorbed into the blood and acts in different forms when it acts on the retina [31]. Therefore, we think measuring vitamin A levels in the blood type rather than the dietary type is more suitable for evaluating the relationship between diabetic retinopathy and vitamin A. This means that identifying associations through blood sampling is a more accurate and effective way to see and interpret the results. Through this study, we were able to find that high levels of blood vitamin A were associated with a low risk of diabetic retinopathy diabetic patients with diabetic retinopathy need health policies or health education supplements. As diabetic retinopathy worsens quality of life decreases and vision decreases which can lead to dangerous accidents and healthcare expenditure rises [24].

In contrast to other blood vitamin A concentrations, our study indicated that vitamin A was more strongly linked to a lower risk of diabetic retinopathy in males and those under 60. Yu-Jin Choi et al, 2024, 's study found a high level of vitamin A in the blood is associated with a low risk of diabetic retinopathy. In particular, there is a more effective relationship between males and young people under the age of 60. Increasing vitamin A in the blood to reduce the incidence of diabetic retinopathy is thought to help prevent diabetic retinopathy. Therefore, it is necessary to create a good environment for consuming vitamin A to increase vitamin A or synthesize it on its own. Further research on future care, health policies, or health education for patients vulnerable to diabetic retinopathy is thought to be needed in the future [32].

The risk of developing diabetic retinopathy was also found to be lower when blood vitamin A levels were above 0.51 and below 0.64. The mechanism of diabetic retinopathy development and the mechanism of action of vitamin A account for the observed reduction in the risk of diabetic retinopathy. The development of diabetic retinopathy is caused by inflammatory responses, fibrosis, and angiogenesis [33]. Due to this pathophysiology, problems from diabetic retinopathy might arise, including vitreous hemorrhage, traction retinopathy, and non-proliferative diabetic retinopathy [34,35]. Conversely, vitamin A contains anti-inflammatory, anti-fibrotic, and anti-angiogenesis properties that work against the formation of diabetic retinopathy [36,37]. In addition to its immunomodulatory and antiangiogenic properties, vitamin A is a potent regulator of cell differentiation and proliferation [38-40].

One of the most prominent antioxidants, vitamin A works as an anti-inflammatory to shield the body from inflammation by eliminating active oxygen and enhancing immunological function [41]. Studies have been done on the use of vitamin A-binding medications to treat conditions like skin, liver, and pulmonary fibrosis since vitamin A possesses anti-fibrotic properties. Additionally, it is anticipated that vitamin A will have anti-fibrotic properties in our eyes' retinas [42,43]. These explanations help to explain why vitamin A can lower the risk of DR. In this study, vitamin A was found to be associated with a low risk of diabetic retinopathy, especially in men. These results can be explained by biological, social behavior, and cultural differences between men and women. There are several studies on vitamin A and diabetic retinopathy. Ruamviboonsuk et al (2022), reported that serum vitamin A levels were lower in diabetic participants without retinopathy than in the DR group. Patients with DR had significantly lower serum vitamin A levels than control ($P = 0.01$). Higher serum vitamin A levels reduced the risk of DR development by 31.1% ($P = 0.007$) [44]. Rostamkhani

et al (2019) reported that the low concentration of vitamin A in the blood was related to the severity of diabetic retinopathy, followed by the group without diabetic retinopathy, the group with non-proliferative diabetic retinopathy, and the group with proliferative diabetic retinopathy [45]. Zhang C et al (2019). reported that dietary vitamin A intake was lower in the group with diabetic retinopathy than in the group without diabetic retinopathy [46].

4.4. Lipid profile

T2D and DR patients in this study exhibited significant dyslipidemia, with higher levels of total cholesterol, triglycerides, LDL, and VLDL, and lower HDL compared to controls. These abnormalities were more pronounced in smokers. Dyslipidemia is a recognized risk factor for diabetic complications, including retinopathy, as it contributes to endothelial dysfunction and microvascular damage. While some large-scale studies have reported inconsistent associations between lipid levels and DR severity, our findings support the role of lipid abnormalities in the pathogenesis of DR, especially when combined with other risk factors such as smoking and trace element imbalances.

The increase noticed in Table 5 is due to study that lipid profile disorders were higher in DM compared to apparently controls [47,48]. The presence of lipid peroxidation from lipoproteins, in blood vessel wall leads to the internal production of free radicals, including reactive carbonyl compounds. Highly effective against some components of cell membranes, as well as chemical modification of blood vessels [49]. Hence, it has been proposed that hyperlipidemia may result in endothelial dysfunction and blood-retinal barrier collapse, which would then cause serum lipids and lipoproteins to exude [50].Regarding the impact of lipid profiles on retinopathy in people with type 2 diabetes [51]. Established that, in comparison to patients with normal lipid profiles, those with high levels of total and LDL were more likely to have solid retinal secretions. Additionally, individuals with increased levels of TG, LDL, or total serum Nonexistent cholesterol. More research has demonstrated a correlation between retinal secretions and TC, LDL, or both [52,53].

4.5. Integrated perspective

Overall, this study highlights the multifactorial nature of diabetic retinopathy, involving metabolic dysregulation, trace element imbalances, vitamin deficiencies, dyslipidemia, and environmental exposures such as smoking. The findings emphasize the importance of comprehensive risk factor management—including smoking cessation, glycemic control, and monitoring of trace elements and lipid profiles—to prevent or delay the onset and progression of diabetic retinopathy.

Type 2 diabetes (T2D) represents a major public health concern, particularly due to its complications such as diabetic retinopathy (DR), a leading cause of blindness. The present study demonstrates a significant increase ($p \leq 0.05$) in glucose, HbA1c, and lipid concentrations in both T2D and DR groups compared to the control group. Additionally, significant reductions ($p \leq 0.05$) in Vitamin A and zinc levels were found in patients with retinal weakness, compared to both diabetic and control patients. Interestingly, magnesium (Mg) levels showed a significant increase in the DR group compared to controls, with a slight increase compared to T2D patients. Notably, lead and selenium levels were elevated in all T2D and DR groups, particularly in smokers, highlighting the environmental influence of smoking. The findings emphasize the impact of trace elements and Vitamin A on retinal health in diabetic patients, with environmental factors such as smoking exacerbating the condition. This study recommends further research to explore the relationship between these factors and diabetic complications, particularly retinopathy, to inform strategies for prevention and management.

Declarations

Ethics approval and consent to participate

Ethical approval was received from the ethical and research committee of the Thi-Qar Directorate Diabetes and Endocrinology Center. Informed consent was obtained from all caregivers of participants.

Consent for publication

Informed written consent was obtained from all the study participants.

Availability of data and material

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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