History of Medicine, 2023, 9(1): 1038–1047
DOI: 10.17720/2409-5834.v9.1.2023.122

Clinical Study of Changes Selenium, Zinc, Lead and Lipid Profile in Serum with Retinopathy Diabetic Patients in thi Qar Governorate

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Received: 20 January 2023 **Accepted:** 15 April 2023

Citation: Alsaadi JHH, Alrikabi NH, younis HM (2023) Clinical Study of Changes Selenium, Zinc, Lead and Lipid Profile in Serum with Retinopathy Diabetic Patients in thi Qar Governorate. History of Medicine 9(1): 1038−1047. https://doi.org/10.17720/2409-5834.v9.1.2023.122

Abstract

Diabetic retinopathy is a common complication of diabetes It causes blindness among adults whose ages range from more than twenty years to about seventy-five years. During the past two decades there is a wide prevalence of diabetic patients with retinopathy. A large proportion of blindness is attributable to diabetic retinopathy. Compared to other eye diseases were common. There are some factors that are associated with high blood sugar levels, including changes in some trace elements and changes in lipid levels in the serum Patients with retinopathy due to diabetes. Aims of study : exploration of the correlation between elevation of glucose and HbA1C levels and levels of trace elements lead , zinc and selenium and lipid profile in serum of diabetic and diabetic with retinopathy groups. Patients and methods : The study extended from March 2021 to end of August 2021. The study included (90) subjects , were divided into thirty subjects as healthy Control group , thirty subjects Diabetes type 2 without complications and Clinically diagnosed cases of Diabetes type2 with retinopathy .The kits were used are available in the commercial markets , and Selenium ,zinc and lead elements was determined by using atomic absorption device. Results: The results of the current study showed a significant increase in blood glucose levels and HbA1C in the groups of diabetic and diabetic with retinopathy patients . The study also showed a significant increase of the lead element with a significant decrease in zinc and selenium in both groups of patients compared with control group, while the results showed the presence of Significant increase in the Biochemical variables of the lipid profile in all groups of patients compared with the control group. Conclusion: Our study showed that diabetic and diabetic with retinopathy are associated with higher lead concentration and lower zinc and selenium . addition increase of lipid profile parameters.

Keywords
diabetic , retinopathy , lipid profile , , lead zinc , selenium

Diabetes mellitus (T2D) a chronic condition characterized by absolute or a relative lack of insulin, as well as hyperglycemia . Dyslipidemia and neurovascular damage. Damage can affect every organ system .In the body of patients, Type 2 diabetes mellitus (T2D) a big health problem of present era and cause a burden at the local and global levels society and economy.T2D lead to unchanged irreversible functional and structural alteration in body which lead towards “diabetic complications”, which affecting, cardiovascular, eye, renal and nervous system. Diabetic retinopathy is a Common complications in type 1 and type 2 diabetes. Diabetes is one of the main causes of retinal damage [1, 2] . The risk of vision loss for diabetic patients 25 times that of people without diabetes [2]. The retina, is a very thin tissue in the eye, the retina has a complex structure of neurons and requires a highly customized rotation.

It is supplied primarily by two blood vessels: the retinal vessels and the choroid vessels, in which they integrate the endothelial cells lining the normal physiological vessels of the retina [3]. to perform metabolic steps and the action of neurotransmitters, image transmission, Interactions of metabolites and growth factors. . Both types of diabetes cause damage to the eye's microvasculature, which may lead to damage to the retina; However, type 1 diabetes has a greater impact on the retina than type 2 diabetes [4].DR in different stages, sex, age , duration of type 1or 2 diabetes and HbA1c levels some trace elements and lipids profile levels in the blood are play a major role in the development of retinal damage in diabetic patients[5].

metals and trace elements are necessary micro-nutrients necessary for the performance of certain physiological functions within the body . They are necessary for many biochemical reactions As cofactors for some enzymes. Regulating critical trace elements. Biological processes by interacting with the membrane receptor site or by changing the 3D shape of the receptor to inhibit the infiltration of specific molecules into the cell [6] Micronutrients have a dual function, they maintain the stability of cellular structures at optimal concentrations, but they maintain their insufficiency. It is transmitted to other pathways, causing diseases [5]. These essential micronutrients have significant physiological effects that show direct links to diabetes [7] . The study of changes in the levels of trace elements and minerals in the body is constantly increasing during the past two decades. between them

Copper (Co), zinc (Zn), magnesium (Mg) selenium (Se) ,lead (Pb) Cobalt (Co), Calcium(Ca) and Iron(Fe), etc. Several studies have shown changes in levels of elements in the blood associated with diabetes from type two [8,9]. In many circumstances, a change in the metabolism of these elements occurs, and one of the proposed mechanisms for the stimulation of the action of insulin by trace elements is the activation of insulin receptor sites [10], They act as cofactors or part of a complete enzyme that is involved in glucose metabolism, which raises insulin sensitivity and acts as an anti-oxidant to prevent tissue oxidation [11].

Previous studies have shown that extensive control of risk factors such as high blood sugar and blood pressure, and control of lipid levels can be beneficial in reducing the beginning and development of (D.R) [12]. High blood lipid profile levels are a risk factor for DR. High lipid levels are known to cause a defect in endothelial function due to decrease NO bioavailability, It has also been suggested that endothelial abnormality function has a role in its formation of retinal secretion in D.R [13]. However, large clinical studies have shown a discrepancy about the association of serum lipids with severity of DR or diabetic macular edema (DME). In a study confirming the association of high levels of total cholesterol and LDL with hard retinal secretions. Some studies have also shown that blood lipids are higher in patients with DR compared to those without DR [14] [15]. On the other hand, these findings have not been confirmed by other large studies such as the Multiethnic Study of a disease of the arteries characterized and the Australian Study of Diabetes, Obesity and Lifestyle[16] . Therefore, the main research objectives are assessment whether serum lipids have an effect on the severity of DR and identify the role of trace elements Se , Zn and Pb in diabetic complications and to find out their relation with diabetes patients .

Material and methods

The present examination was led at the Center of Diabetes at Nasiriya in General Hospital for the period from beginning March 2021 to end of August 2021. The study included dealing with 90 people divided into three groups, the age range within 35 to 65 years

Group 1- healthy without Diabetes type 2 (T2D)

Group 2- Clinically diagnosed cases of Diabetes type 2 without complications

Group 3- Clinically diagnosed cases of Diabetes type2 with retinopathy

blood sample collection

(5) mL of venous blood were drawn from both groups after fasting 8-12 hours, using. The blood test was partitioned into two aliquots; 1 and 4mL. The primary aliquot was moved in

a test tube containing ethylene di amine tetra acetic acid (EDTA). This blood was set up in less than three hours and was used for HbA1c estimation, while the second aliquot were moved into plain tube without anticoagulant, permitted to clump for thirty minutes following which examples were centrifuged for 15 minutes at 4000 xg. At that point, serum was isolated and put away promptly at (-20єC) until used in the estimation of serum glucose level, lipid profile, Se , Zn and Pb .The kits were used are available in the commercial markets and equipped by (Roch-Germany and Biolabo − France), and Selenium ,zinc and lead elements was determined by using atomic absorption device in Chemistry department , Science college, University of Thi Qar .

Statistical Analyses

Statistical analysis of the current study was carried out using the Statistical Package for the Social Sciences (SPSS) version 22.0 for Windows (SPSS inc, USA). p-value less than 0.05 and 0.01 as statistical significance. Descriptive analysis was used to show the mean value; Standard deviation and LSD combinations were performed by ANOVA

Results and Discussion

Demographic Data

Table 1: Characteristic data for studied groups

Diabetic with Retinopathy (n = 30)	Diabetic without complications (n = 30)	healthy without Diabetic (n = 30)	Mean ± SD	Groups Characteristics
59.1± 6.24	57.8± 6.46	49.9± 9.21		Age (years)
11(36.66%) 19(63.33%)	14(46.66%) 16(53.33%)	13(43.33%) 17(56.66%)		Gender Male Female
16.23± 4.30	8.64± 2.61			Diabetes duration (years)

Fasting Serum Glucose Levels

In this study, increases significant glucose conc. at (P< 0.05) in diabetic patients group while high increases significant fasting glucose conc. at (P< 0.01) in diabetic with retinopathy patients group compared with control group are indicated in table (2)and fig. (1).

Table 2: Mean values of fasting glucose in type2 diabetic and type2 diabetic with retinopathy patients and non diabetic subjects.

P-value	FSG (mg/dL) Mean ± SD	Parameter Groups
	91.666 ± 26.87	control
P< 0.05	262.84 * ± 63.50	T2D
P< 0.01	302.16 ** ± 98.00	T2D Retinopathy
SD : Standard deviation.		

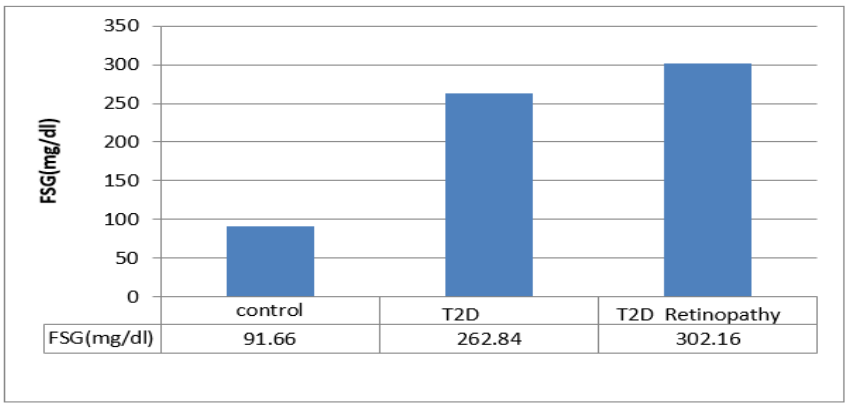


Figure 1: Mean values of fasting glucose in type2 diabetic and type2 diabetic with retinopathy patients and non diabetic subjects.

Diabetics is a defect in glucose metabolism in several Organs, glucose disposal in skeletal

muscle, and hepatic glucose production is reduced Increased insulin-dependent glucose uptake in the lens and nerve tissue Increase [17] [18]. Although the actual mechanisms Insulin resistance in type 2 diabetes is still unknown [19]. Reducing the level of glucose in the blood is one way to monitor diabetes Threads. High blood glucose levels in diabetic patients due to deficiency or resistance To insulin, the same results were found by [20] [21]. In their studies of the population with diabetes, they concluded that .The level of glucose in the blood rises during fasting and this indicates poor blood sugar control . In fact, diabetes mellitus is characterized by high blood sugar combined with biochemistry Changes in glucose [22] .

HbA1c Levels

The results showed in in table (3)and fig. (2). that increases significant in HbA1c at (P< 0.05) in diabetic patients and high increases significant at (P< 0.01) in diabetic with retinopathy patients group compared with control group.

Table 3 : Levels of HbA1c in Diabetic Patients and Control Subjects.

p-value	HbA1c (mg/dL) Mean ± SD	Parameter Groups
	4.35 ± 0.53	control
P< 0.05	7.268 * ± 1.168	T2D
P< 0.01	7.942* *± 1.26	T2D Retinopathy
SD : Standard deviation.		

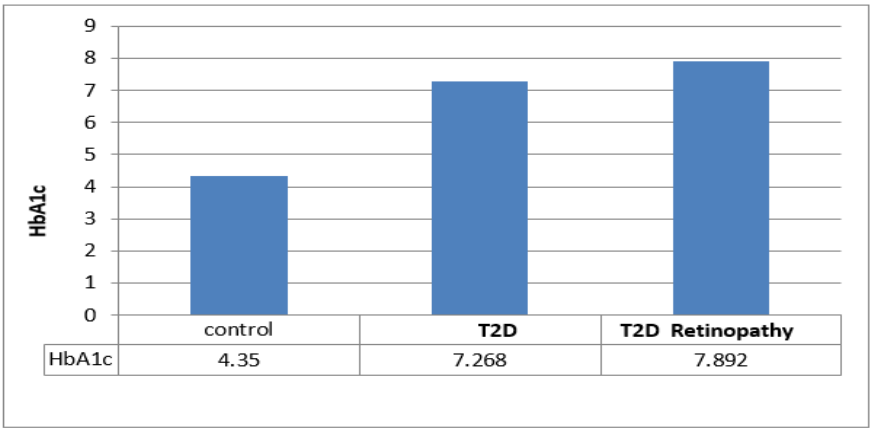


Figure 2: Levels of HbA1c in Diabetic Patients and Control Subjects.

A biomarker can be defined as a characteristic that is impartially measured and assessed as point of reference of normal biological processes, pathogenic processes, or pharmacologic responses to a intervening of healing process [23]. Examples of biomarkers in clinical medicine include HbA1c levels, In the NPDR stage, gender, beginning, , and period of type 1 diabetes and H.b.A1c conc. are It is one of the main indicators involved in the expansion of N.P.D.R [24]

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 non-diabetic subjects except for HLD- which is no significantly compared to non-diabetics . The average value of cholesterol(ch) level in diabetic and diabetic with retinopathy patients The mean value of triglycerides in diabetic patients increased significantly P< 0.05 compared to control group . LDL-cholesterol value in diabetic and diabetic retinopathy groups was statistically significant at P< 0.05 is above the mean value for non-diabetics. The mean serum HDL-Cholesterol value was significantly lower P< 0.05) in both diabetic patients compared to non-diabetic patients . The mean value of VLDL-Cholesterol in diabetic patients was significant (P< 0.05) ,increased compared to the average non-diabetic. As shown in Table (4) and figure (3) .

Table 4: Levels of Serum Lipid Profile in Diabetic Patients and Control Subjects.

ch (mg/dL)	TG (mg/dL)	HDL (mg/dL)	VLDL (mg/dL)	LDL (mg/dL)	Parameters(Mean ± SD) Groups
125.08[a]± 24.78±	88.16 [a]± 14.76	36.33 [a]± 6.394	18.25 [a]± 3.05	77.5a ± 20.30	control
182.30[b]± 44.54	224.73 [b]± 183.76	41.84 [b]± 8.53	44.96 [b]± 36.71	95.69[b] ± 36.50	T2D
190.76[b]± 98.99	243.64 [b]± 176.21	41.44 [b]± 9.09	40.72 [b]± 30.73	80.76 [b]± 32.72	T2D Retinopathy
54.06	80.37	4.65	17.98	16.61	L.S.D

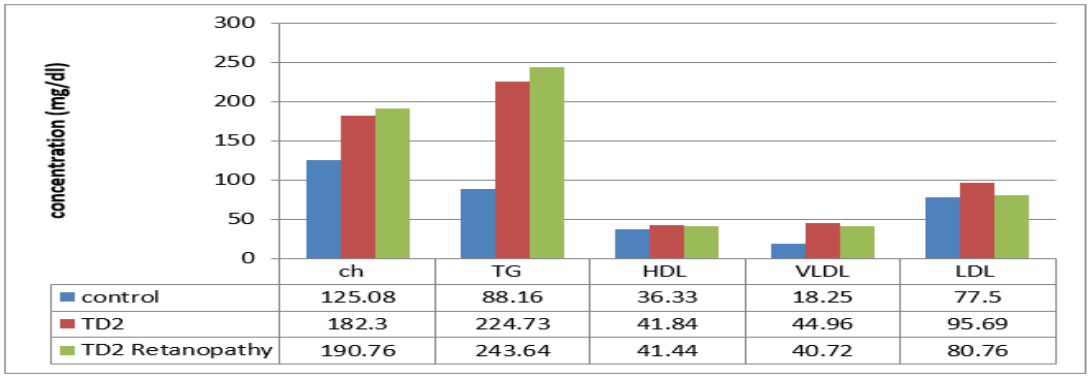


Figure 3: Mean values of lipid profile (TC, TG, LDL, HDL, VLDL mg/dl) of type2 diabetic patients

SD : Standard deviation, LSD: Least Significant Difference
(a, b, c) Means having different letters in the same column differed significantly (P <0.05) .

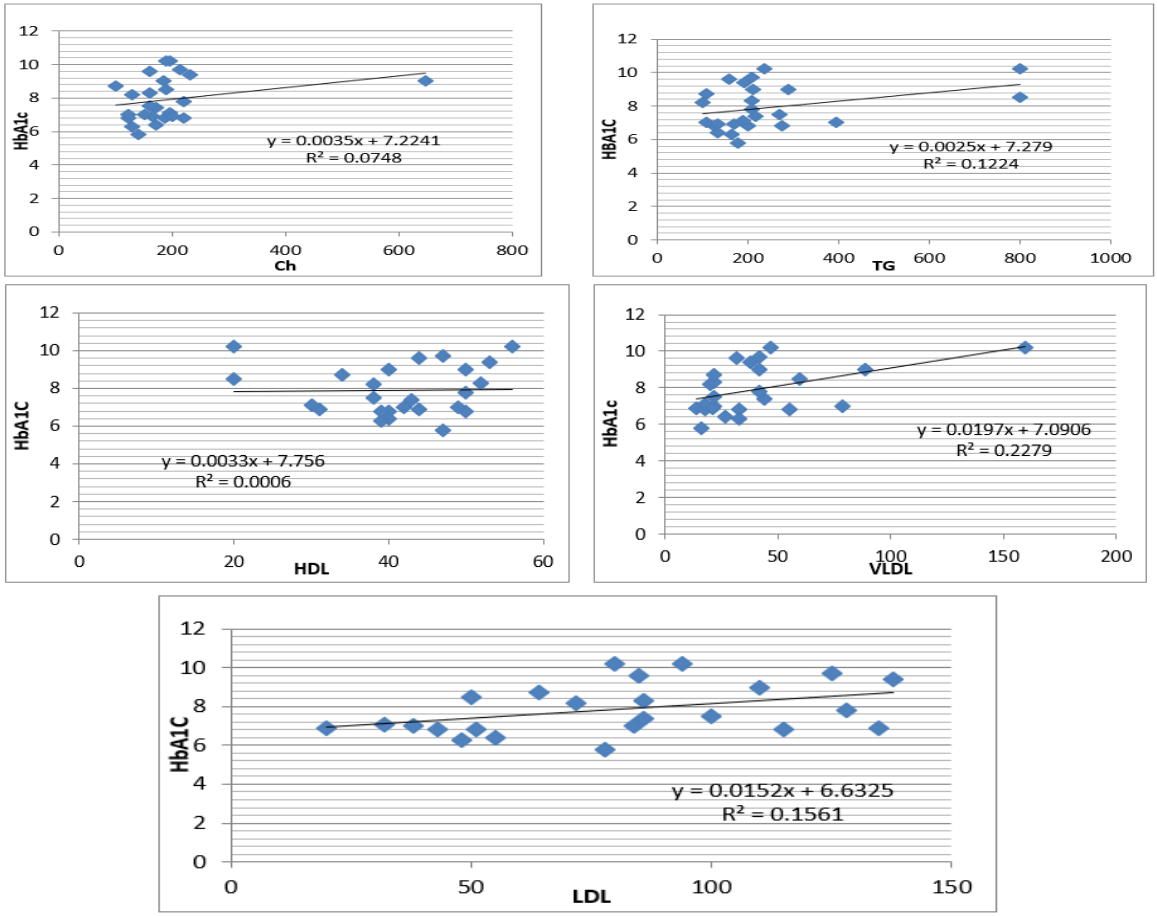


Fig. (4) Correlation coefficient of lipid profile

Lipid peroxidation of lipoproteins in the vascular wall . It leads to the internal production of free radicals, including reactive carbonyls .Highly effective against some components of cell membranes, as well as chemical modification of blood vessels . Proteins through advanced end products of lipid oxidation affecting .Both the structure and function of the vascular wall [25) .Thus, it has been suggested that hyperlipidemia may be Contributes to E via endothelial dysfunction and Breakdown of the retinal blood barrier leading to exudation. Serum lipids and lipoproteins [26]. There are conflicting studies in the literature about Effect of lipid profile on retinal damage in diabetics type -2 .Where The ETDRS report, Chew [27] confirmed that patients with high Total and LDL cholesterol levels were more likely Solid retinal secretions compared to patients with normal fat profile person. Elevated, patients with elevated total serum Non-existent cholesterol, LDLC, or triglyceride levels . Solid retinal exudates were initially at risk Develop a solid retinal exudate during follow-up. Else Studies have also shown that retinal secretions have been associated with Either with LDL or total cholesterol, or both [28] [29][30] .

Comparison of some trace elements levels

Present study has shown a significant increase of lead (pb) levels at P< 0.05 and a significant decreased levels at P< 0.05 of Zinc (Zn) and selenium (Se) in T2D and T2D Retinopathy in comparison to control group ,the table (5) and figure (4) shoe that .

Table 5: Levels of Se , Pb and Zn in Diabetic Patients groups and Control Subjects.

Zn	Pb	Se	Parameters(Mean ± SD) Groups
0.906[a]± 0.38	0.124[a]± 0.05	0.192[a]± 0.10	control
0.348[b]± 0.20	0.146[a]± 0.08	0.071[b]± 0.07	T2D
0.350[b]± 0.13	0.176[b]± 0.09	0.111[c]± 0.08	T2D Retinopathy
0.391	0.042	0.069	L.S.D

SD : Standard deviation.
LSD: Least Significant Difference
(a, b, c) Means having different letters in the same column differed significantly (P <0.05) .

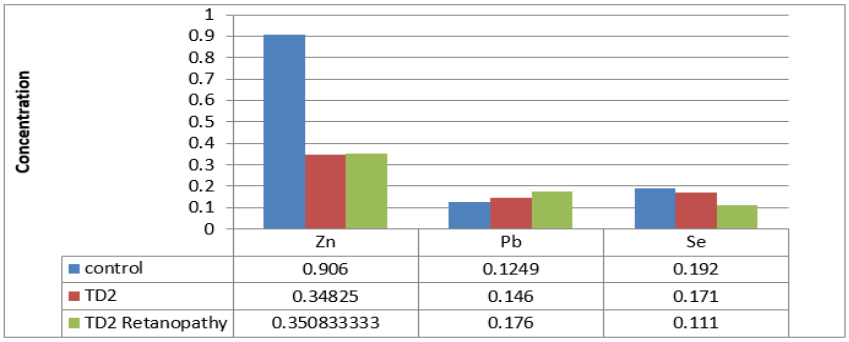
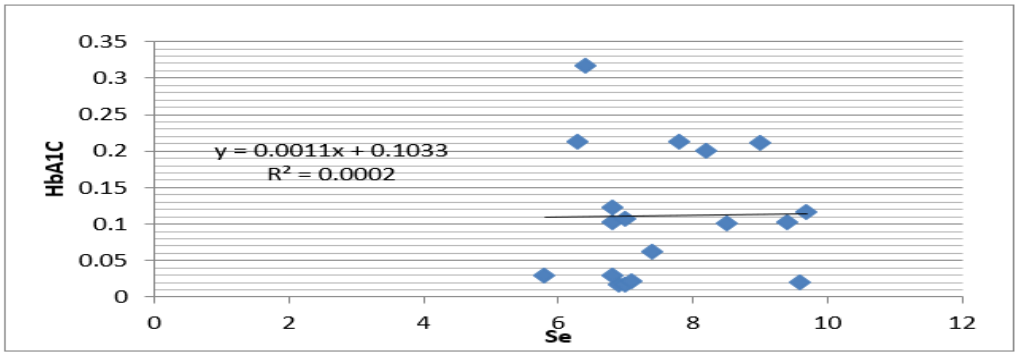


Figure 5: Mean values of Zn ,Pb and Se of type2 diabetic type2 diabetic with retinopathy patients and non-diabetic subjects.



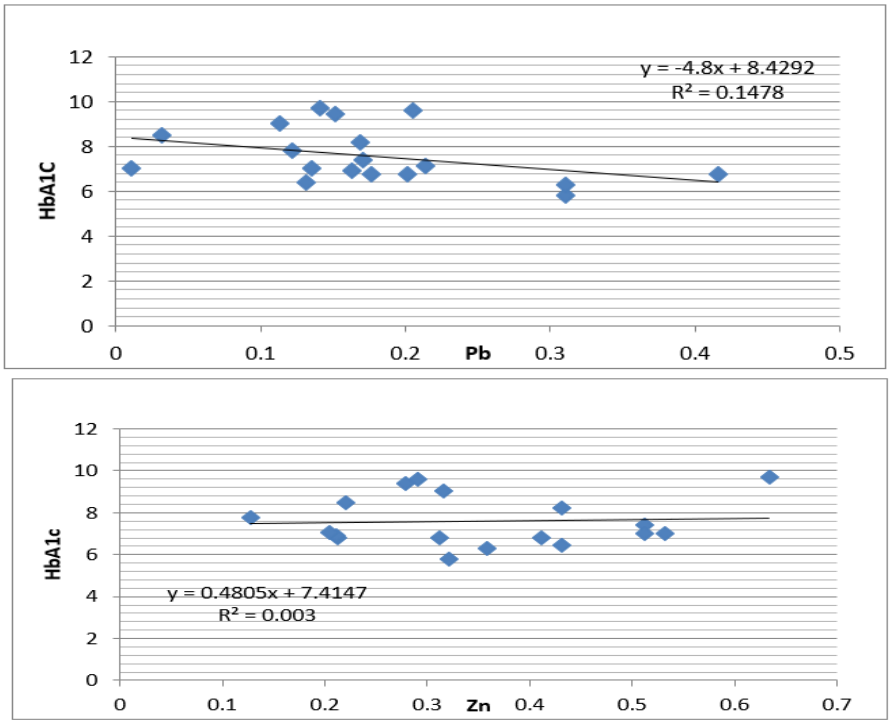


Fig.(6) Correlation coefficient of HbA1C with trace elements

Complications associated with diabetes increased during

In the past two decades, the death rate from this disease has increased Increasing mortality in developing countries and advanced countries about the world .The role of trace elements in diabetes is still unclear Patients, especially lead, zinc and selenium, the study came To determine the levels of lead, zinc and Selenium in the serum of all diabetic and diabetic patients with retinal complications Compared to the controls. The results of the cases were in this study .There was a significant increase at ($P > 0.05$) levels of lead in the two groups of diabetic patients Diabetic patients with retinal complications I found an elevated level of lead in the blood serum Our research is similar to Ghada's study2006) .We found a significantly lower level at ($P > 0.05$) of zinc in patients in comparisons to control. for us The study is similar to that of Mohan Lal, Sudha K et al (KMC, Manipal) significantly reduced In, Zn and Mg. [31] Zinc is a key component of glucose metabolism. It is a cofactor for many enzymes and has important functions in maintaining many tissue properties [32]. The relationship between zinc, the hormone insulin and hyperglycemia is complex, and there is no clear cause-and-effect relationship. Zinc has a major role in the biosynthesis of insulin, as well as a role in the secretion and storage of insulin, as well as the corresponding integration of insulin in the three-dimensional form. Zinc has the ability to regulate some intracellular processes and insulin receptors that determine glucose tolerance and the ability to support a normal pancreatic response to glucose load [33]. It has a protective effect against cell destruction and has strong antiviral effects. The complications of diabetes can be mediated, at least in part, by oxidative stress, and zinc plays a key role in cellular antioxidant defense [34]. Hence, it has been suggested that the abnormal metabolism of zinc may be one of the reasons that lead to diabetes and some of its complications [35]. In this study, serum zinc levels were found to be significantly reduced in the diabetic group ($p < 0.001$), which was related to the findings of Chausmer AB et al. , [36] A C Nsonwu et al., [37] and Alena Viktorinovaa et al., [38]. Dietary selenium (Se) is an essential and important micronutrient that helps in the synthesis of some proteins with biological functions. It has antioxidant and cell-protective properties

Selenium is considered a preventative supplement due to its antioxidant properties for the emergence of metabolic diseases such as

diabetes [39] . The study also confirmed that high serum selenium It has a clear association with the prevalence of diabetes [40][41] . .
.Rats dosed with selenium for three weeks showed reduced blood glucose conc. and amended lipid metabolism [42] . other cross-syllabic study was conducted on 5,423 middle-aged and older Chinese adults To examine the relationship between hyperglycemia and dietary selenium. The spread of diabetes in The study people was 9.7% [39] .
Significant positive linkge between dietary selenium His intake and diabetes were specific by the results of this research, which were in agreement with it epilogue of comparable studies .Selenium is necessary for the effectiveness of the enzyme glutathione peroxidase (GPx.). Where are the causes of diabetes Increased oxidation and produce of reactive oxygen species . GP.x is An internal antioxidant that is important for cellular protectionagainst free radicals [43] . Altering concentrations of trace elements can worsen elevated blood sugar levels and increase complications in diabetic patients, in spite of the fact some micronutrients are recognized to be implicated in The pathogenesis and evolution,of diabetes mellitus, thers may only be the result of depletion or intolerance to carbohydrates and insulin resistance. Often there are studies that have contradictory results. Serum or tissue contents of certain elements, such as zinc, lead, and selenium It may be higher or lower in diabetics than in non-diabetics. The majority of patients with diabetes , Patients without micronutrient deficiencies have been deficient in zinc, chromium and magnesium They were identified in a subset of patients. of patients. More association Research are , needful, to recognize, micronutrients
lackin diabetes mellitus. This survey shows that the shortcomings of tracking items—either Directly or indirectly − linked[44].

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