Correlation of Plasma Fibroblast Growth Factor 23 with the Risk of Cardiovascular Disease in a Group of Iraqi Patients with Type 2 Diabetes Mellitus

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ABSTRACT:
Since it is the largest cause of death globally, cardiovascular disease (CVD) poses a serious health issue. Whether or whether they are changeable, several risk factors exist for the onset of CVD. Conventional and most often used approach to estimate cardiovascular risk is Framingham risk score. Still, ongoing research is looking for alternative markers that can better estimate this risk. One of these producers under increasing research attention is fibroblast growth factor 23 (FGF-23). The aim of this work is to investigate in patients with type 2 diabetes mellitus a possible prognostic value of plasma and urine FGF-23 for CVD. Two groups—the patients' group and the control group—will be formed out of the 200 participants split equally. The group of patients will include those with type 2 diabetes mellitus of more than five years. Using the Framingham risk score, all participants will be evaluated for their 10-year CVD risk; the outcomes will be statistically linked to both plasma and urine FGF-23. Our present work revealed a positive association between Framingham risk and cholesterol, TG, LDL, HDL, VLDL, non-VLDL. and also showed favorable link in Atherogentic index and BMI,HDL,LDL,VLDL and non LDL. In Dm.patient group and farmingham risk, the FGF23 in current study show greater signifcant.

1. Introduction

Clearly documented relationships exist between type 2 diabetes and cardiovascular disease. In those with type 2 diabetes, compared to those without type 2 diabetes, the risk of coronary artery disease (CAD), heart failure, and cardiovascular death is substantially elevated. [1, 2]

Lower extremity atherosclerotic disease (LEAD) is mostly presented in peripheral arterial disease (PAD), and it is connected to a higher risk of cardiovascular disease [2, 3] since it reflects systemic atherosclerosis impacting the peripheral vascular [1]. Diabetes is a documented risk factor for LEAD [4] with a more rapid progression, greater spectrum of vascular lesions, and higher sensitivity to stenosis and occlusion than those without diabetes. LEAD often stays clinically undetected in the early stage since neuropathy in diabetes patients is rather common. Usually presented at the terminal stage of LEAD, diabetic patients are often unaware of the early course of LEAD since they lose pain sensation and have lower frequency of intermittent claudication until the symptoms become severe and advance to ulceration or gangrene. This brings about amputation at last. Therefore, early identification and treatment of this disorder in diabetic individuals depend on an indicator of early-stage LEAD, which will help to avoid amputation and improve patients's quality of life.

Mostly expressed in bone by osteocytes and osteoblasts, fibroblast growth factor (FGF) 23 is a protein regulating mineral metabolism (calcium-phosphate balance). Basic research studies have indicated that FGF23 starts and accelerates atherosclerosis via effects on arterial calcification and endothelial dysfunction [7, 8]. Recent studies in clinical settings have confirmed the connection between increased circulating FGF23 and atherosclerotic cardiovascular disease [9, 10]. Our previous studies shown that serum FGF23 levels linked not only with subclinical atherosclerosis but also coronary artery disease [11–13], suggesting the function of FGF23 in the genesis and evolution of atherosclerosis. Moreover, we have found that blood FGF23 levels are rather highly associated with the presence of abdominal obesity [14]. Still, for a Chinese population the association between blood FGF23 levels and LEAD is yet unknown.

Widely used in the clinical setting for noninvasive PAD (especially LEAD) evaluation in diabetic patients, color Doppler ultrasounds show benefits in the identification of intima-media thickness (IMT) and plaque [15]. In Chinese patients with type 2 diabetes mellitus (T2DM), color Doppler ultra-sound imaging was therefore employed to detect abnormalities in the lower extremities arteries in order to investigate the association between blood FGF23 levels and LEAD as well as the related factors.

In this work, we focus on one of the first and most important elements of the processes leading to CAD and atherosclerosis: endothelium dysfunction [18]. Regarding both diseases, these processes offer a framework for more research and implications during the course of the disease development. This brings us to the rest of the work, which consists of oxidative elements and inflammatory processes affecting diseased tissue.

We also consider the genetic basis; dynamically developing research shows entirely new faces of these diseases known to us and makes it possible to reflect on the actual causes of their diversity and changeable forms as well as generate new possibilities for better diagnostics and considering whether the present judgement that the lifestyle and drugs mostly allow controlling the disease-causing process.

They expand our expertise in this field and let us apply fresh ideas.

1.1. Atherosclerosis Endothelial Dysfunction

Arterial vasculature comprises in sites (branch points, bifurcations, and significant curvatures—arterial geometry)—much more likely to have atherosclerotic lesions [19]. Moreover influencing the endothelial cell are mechanical forces related to the geometry and form of vessels, such a turbulent flow. [19]

Variations in flow, evident at sites of low shear stress, turbulence, and oscillating flow, lead to atherosclerosis in these areas. We do not argue that these elements lead to atherosclerosis but rather that they "prime the soil" on which lesions begin to grow [20]. Different degrees and kinds of shear stress expose endothelial cells, which affects their form, intracellular signaling, and gene expression [21]. Nitric oxide (NO) is generated in the normal state—that of the quiescent state of the endothelium—to bind to cysteine groups in NF-κB and the mitochondria, therefore blocking cellular activities. Furthermore covered by the endothelium layer is a glycocalyx, layer of proteoglycans and extracellular matrix components, important in transendothelial transport, e.g., of lipoproteins, which can be lost or diminished in inflammation due to plasminogen activator inhibitor [21]. By secreting NO, prostacyclin, t-PA, and antithrombin III [21], endothelial cells in homeostasis stop platelet activity, blood clotting, and leukocyte adherence. Adhesion molecules (E-selectin, ICAM, and VCAM) which help leukocytes infiltrate the endothelium layer [22] increase in quantity when inflammation develops there. Lipoproteins enter the endothelium with leukocytes, then get caught in the subendothelial area and oxidatively changed.

In the second stage, NOS catalyses the oxidation of Nω-hydroxy-L-arginine to L-citrulline, hence generating NO [38,39]. For homodimerization and activity, nNOS and eNOS are strongly de-pendent on Ca2+-activated CaM; iNOS is slightly dependent on calcium concentration. These subtleties serve important purposes. Another factor under great focus as a fundamental component in the evolution of vascular dysfunction is NADPH oxidase (NOX). Considered as the principal generator of reactive oxygen species (ROS), NOX serves primarily this purpose in endothelial cells. Mediating the endothelium function depends on eNOS producing NO enzymatically, hence oxidative stress can lead to eNOS dysregulation and endothelial dysfunction. [40].

Considering this, the endothelium dysfunction is exactly correlated with a lower NO production and sensitivity of cells. Consequently, we have an efficient disturbance in the functioning of the whole vessel and its homeostasis, which results in an observation of prothrombotic and proinflammatory events together with reduced susceptibility of the blood vessel wall.

Phospholipase A2 and its effect on the endothelium dysfunction also piques more curiosity. Mostly produced by macrophages, lymphocytes, and foam cells in the atherosclerotic plaques, Lp-PLA2 (lipoprotein-bound phospholipase A2), sometimes known as platelet- activated acetylhydrolase, is a vascular-specific inflammatory enzyme. Lp-PLA2's circulation is mostly linked to lipoproteins carrying apolipoprotein B, hence tightly linked to low-density lipoproteins (LDLs). Proinflammatory and proatherogenic effects in the vascular wall can be set off by Lp-PLA2 On LDL particles in the intima of the artery, the enzyme hydroly oxidized phospholipids to generate two very in-flammatory mediators with proinflammatory and atherosclerotic

consequences. In individuals with a stable CAD, elevated levels of Lp-PLA2 associated with arterial stiffness independent of the risk factors and medication (Figure 1)[41].

1.2. Inflammation in CAD

Systemic vasculitis is the name given to a collection of disorders marked by inflam- mation and fibrinoid necrosis of blood vessel walls. The fundamental pathophysiology consists in several processes including ANCA-mediated inflammation, immune complex (IC)-mediated inflammation, and cell-mediated inflammation. For instance, inflammation in GCA is largely a T-cell-driven mechanism whereby dendritic cells present antigens in blood vessel walls. Other inflammatory cells include monocytes and macrophages, which these T-cells activate, release pro inflammatory cytokines like interleukin-1, interleukin-6, and interferon-γ. IC deposition (antibody-mediated IC development, microaneurysms) drives inflammation in disorders including polyarteritis nodosa and cryoglobuline-mia [42],

Whereas Wegener's granulomatosis, Churg–Strauss syndrome, microscopic polyangiitis, and necrotizing glomerulonephritis originate from interactions between antibodies and enzymes inside inflammatory cells, which is common for ANCA-related vasculitis [43], this is not the case for other diseases. These mechanisms cause produced antibodies and immune complexes to stick to the inner layer of blood vessels. This is a source of increased ET-1 release, which in a positive feedback loop attracts additional monocytes and macrophages. Although vasculitis is a quite varied collection of disorders with multiple cellular mechanisms as discussed above, in terms of size and distribution it affects distinct arteries and veins [44]. Furthermore important in terms of elements maintaining inflammation is artery size. Small vein vasculitis is linked to endothelial involvement, necrose (related to ANCA), destruction of the artery walls, an aneurysm development, and bleeding. It is also marked by leukocytoclasia, the too high neutrophil buildup. Furthermore in vasculitis of big systemic arteries, the response to the inflammation causes restenosis, thickening of the intima, and general remodeling. These changes show up as blood vessels' dysfunction and later events including hemorrhage and infarction [44].

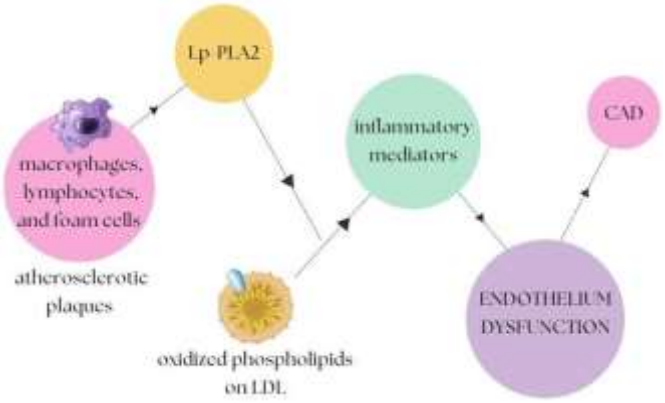

Figure 1. Lp-PLA2-dependent activation cycle [40].

2. Material And Method

Chemicals

1. HRP conjugation.
2. Solution A's chromogeny.
3. Third: Chromogen solution B.
4. 4. Stop the fix.
5. 5. Diluent sample.
6. 6. Wash solution.

Blood sample preparation:

After coagulation, the blood was separated by centrifugation at 2000xg for 10 min. Five CCS were derived from blood samples from diabetic and non-diabetic patients as well as healthy people with diabetic nephropathy. The blood was left for twenty minutes at room temperature.

Experimental Techniques

After incubation and washing to remove the uncombined enzyme add chromogen solution A and B, the microtiter plate included in the kit has pre-coated with antibody add standard samples and HRP conjugated antibody to wells. Under the action of acid, the color of the liquid will become blue; at last, the color turns yellow; spectrophotometric analysis of the color change at 450 nm wavelength By means of comparison between the O.D. of the samples and the standard curve, one can determine the concentration pf FGF23 in the sample.

Table 3. 2 Materials supplied in human FGF23 Elisa kit

FGF23 assay	The Amount of Pıpette
Sample	10 ML
Diluent	40 ML
Hrp conjugate	100 ML
Wash solution	400 ML
Chromogen A-B	50 ML
Stop solution	50 ML

Assay procedure

1- Before beginning the test process, ready all the reagents. All standards and samples should be added on the micro ELISA strip plate in twin copy.

2- Add a conventional set of wells sampling wells for tests Add 50mm to the standards wells.

3- Sample add testing sample 10 ml then add sample diluent 40ml to the testing sample well blank does not contribute anything.

1- To each well cover with an adhesive strip, add 100ml pf HRP conjugate reagent and incubate for 60 minutes at 37c.

2- Using a squirt bottle manifold dispenser or auto washer, aspirate each well and wash four times total, filling each well with wash solution (400 ml). Good performance after the last wash depends on complete removal of the liquid at every stage; remove any residual wash solution by aspirating or decanting invert the plate and blot it against fresh paper towels.

3- To each well gently mix and incubate chromogen solution A 50ml and chromogen B 50ml for 15 minutes at 37c protected from light.

4- 4- Fill every well with a 50ml stop solution. If the color in the wells is agreed upon or if the color shift does not seem consistent, lightly tap the plate to guarantee complete mixing. The color should form blue to yellow.

5- Using a microtiter plate reader, read the optical density (O.D) at 450 nm in 15 minutes.

Theoretical Foundatıons

With ongoing inflation of this health issue, cardiovascular disease is clearly the main cause of death worldwide (1). American Society for Preventive Cardiology (ASPC) has revised the risk factors linked to CVS development; these factors include:

inadequate diet

physical inactivity

dyslipidemia

hypoglycemia

significant blood pressure

obesity factors related to particular populations

disparities in sex

ethnicity/race

smoking-related thrombosis

renal failure

genetics/familial hypercholesterolemia.

Since prediction of CVD seems to be a useful approach to control this group of diseases, various attempts have been made to identify a dependable predictive system to be employed for lessening the high incidence of morbidity and death related to CVD(3). Although some research have indicated that Framingham risk score can overstate CVD risk, it is the most often used technique to quantify this risk (4). Reliable as predictors of some forms of CVD, including high-sensitivity C-reactive protein, fibrinogen, Pregnancy-associated plasma protein A, myeloperoxidase, lipoprotein-associated phospholipase A2 and secretory phospholipase A2(5), other biomarkers have been shown Major control of vitamin D phosphate metabolism is provided by fibroblast growth factor 23 (FGF-23). Osteoblasts and osteoclasts secrete it. Many investigations have revealed a strong relationship between circulatory FGF-23 and several forms of CVD including atherosclerosis, left ventricular hypertrophy, and hypertension(6).

Objectives

The aim of this work is to search for a possible predictive value of urine FGF-23 and plasma for CVD in type 2 diabetic individuals.

Study design

Two groups—the patients' group and the control group—will be formed out of the 200 volunteers split equally each. Patients with type 2 diabetes mellitus of more than five years will be included under the patients' group. Patients visiting several private clinical labs for routine check-up will be chosen at random. Apart from a full blood count, these individuals will be examined for fasting blood glucose, HbA1c, lipid profile, liver and renal function test. Furthermore questioned or measured differently will include age, weight, height, body mass index, sex, smoking, blood pressure, compliance with treatment, type of drugs, past medical and surgical history. Those meeting the inclusion criteria will be examined for urinary FGF-23 as well as plasma. The same factors will be measured or asked for the control group aiming to match age, sex, and body mass index as practically practicable.

Exclusion criteria

1- Patients with recent diabetes mellitus or within the last 5 years.

2- Patients with type 1 diabetes mellitus

3- Patients poorly comply with treatment

4- Patients with established cardiovascular disease

5- Patients with any chronic illness apart from diabetes mellitus

6- Patients with acute or recent illness

 Data analysis

Using the Framingham risk score, all participants will be evaluated for their 10-year CVD risk; the outcomes will be statistically linked to both plasma and urine FGF-23.

Statistical Analysis

2019's SPSS The effect of difference groups—patients and control—in research parameters was found using statistical packages of social sciences-SPSS program. Means were significantly compared using T-tests.

Significant comparison between percentage (0.05 and 0.01 likelihood) using chi-square test Projected correlation coefficient between variables. Calculate the patients' and control groups' respective sensitivity and specificities of parameters in this work.

$$\chi 2 = \Sigma \frac{(O - E)2}{E}$$

$\chi 2$: Chi-square , Σ: Summation , O: Observed No. , E: Expected No.

3. Results:

1. Age distribution of studied groups:

Comparatively to their control counterpart, the tissue samples linked to individuals with diabetes mellitus whose ages ranged from 25 to 78 years with a mean age of 54.62± 12.6 years. Still, between these age groups, no notable differences were found. (> p 0.05) (Table 1).

Table 1: The age distribution of the researched groups

Studied Group	No.	Mean Age (years)	S.D	S.E	Minimum	Maximum
D.M Patients	160	54.62	12.6	1.15	25	78
Apparently Healthy Control (AHC)	40	53.37	13.7	2.01	23	67
Statistical Analysis		Non-significant (P > 0.05) = 0.06				

2. Sex distribution of studied groups:

Of DM cases, men accounted for 88 (55%) and women for 72 (45%). Men to women was 1.2:1; the control group's sex distribution for men was 28 (70%) and for women was 12 (30%). In statistical analysis, the DM patients' group differed significantly from the control group (P 0.05). (Table 2).

Table 2: Distribution of study groups according to their sex

Sex	DM		Control		P-value
	No.	%	No.	%	
Male	88	55	28	70	0.04*
Female	72	45	12	30	
Total	160	100	40	100	

3. Distribution of patients with DM group according to their age stratum:

Ten percent of cases are between the age of ⩽30 years, six.8% between the age of 31 and forty years, eleven.3% between the age of 41 and 50 years, 36.3% between the age of 51 and 60 years, and 35.6% between the age of >60 years. The 51 to 60 year old group had the most frequency. Comparatively between patient age groups and AHC groups, significant difference (P 0.05) in statistical analysis was identified. (Table 3).

Table 3: Patients with DM according to their age

Age	Patients		AHC		P. value
	No.	%	No.	%	
≤30 yr.	16	10	2	5	0.01
31-40 yr.	11	6.8	6	15	
41-50 yr.	18	11.3	6	15	
51-60 yr.	58	36.3	16	40	
>60 yr.	57	35.6	10	25	
Total	160	100	40	100	

4. Distribution of sample study according to smoking and hypertension among groups

The present study comprised 160 patients identified as diabetic; of these, ninety-nine (61.8%) were smokers and sixty-one (38.13%) did not smoke. Thirty seemingly healthy-looking individuals deemed as control group were also included; twenty-seven 27 out of 40 (67.50%) were smokers, and 13 (32.5%) did not smoke.

Moreover, in patients and AHC groups, one hundred thirty three out of 160 patients (81.25%) and 75% (30 out of 40) had hypertension. The groups of smokers and hypertension differed significantly from one another with regard to control group (p value 0.01). (Table 4).

Table 4: Distribution of sample study according to smoking and hypertension among groups

Facto	rs	Patients No (%)	Control No (%)	P-value
Smoking	Yes	99 (61.88%)	27 (67.50%)	0.001 *
	No	61 (38.13%)	13 (32.50%)	
Hypertension	Yes	130(81.25%)	30 (75.00%)	0.001 **
	No	30 (18.75%)	10 (25.00%)	
** (P≤0.01).				

5. Based on patient age and AHC groupings, the BMI findings reflect

Table (5) lists the The BMI values for the AHC groups and DM patients matched their respective ages: 29.36 ±0.44 and 29.22 ±1.02 respectively. Statistical analysis showed non-significant variations in BMI in respect to age (P<0.05).

Table 5: The BMI results according to the age of the patients and AHC groups

Group	Mean ±SE	
	Age (year)	BMI (kg/m^2)
Control	53.37 ±2.01	29.22 ±1.02
Patients	54.62 ±1.15	29.36 ±0.44
T-test	4.962 NS	2.023 NS
P-value	0.6200	0.889
	NS: Non-Significant.	

6. The patients in the FBS and HbA1c categories correspond with AHC groupings.

Table (6) indicates the FBS values in DM patients and AHC groups were determined respectively to be 98.16 ±14.33 and 239.18 ±7.70.HbA1c produced findings of 9.42 ±0.20 and 3.42 ±0.20 respectively. Significant variations in FBS and HbA1c were found by statistical analysis between investigated groups (P<0.0).

Table 6: FBS and HbA1c results in the patients and AHC groups

Group	Mean ±SE	
	F.B.S. (mg/dl)	HbA1c (%)
Control	98.16 ±14.33	3.42 ±0.20
Patients	239.18 ±7.70	9.30 ±0.11
P-value	0.03S	0.04S
S: Significant.		

7. The Comparison among study groups according to biochemical parameters

Table 7 shows that, except from the serum levels of creatinine between the DM group and the AHC group, where a p-value of 0.04 was recorded, the assessment of biochemical parameters including Urea, creatinine, ALT, AST, and LDH serum levels in patients with DM,, and the AHC groups revealed no statistically significant variations.

Table7: Comparison between DM patients and AHC according to biochemical parameters.

Parameters	AHC	DM Patients	P-VALUE
Urea±SD mg/dl	30.42 ±0.56	30.64 ±0.34	0.763
Creatinine±SD mg/dl	0.692 ±0.02	1.859 ±0.57	0.0411*
ALT ±SD IU/L	31.45 ±1.59	30.26 ±0.93	0. 572
AST ±SD IU/L	33.68 ±1.83	34.87 ±0.94	0. 556

8. The SBP and DBP results in the DM patients and AHC groups

Table (8) shows the the SBP results in DM patients and AHC groups were found 14.08 ±0.09and 14.05 ±0.18,respectively.While , the results of DBP were found 8.73 ±0.05and 8.81 ±0.11, respectively. Statistical analysis revealed non-significant differences in SBP and DBP among studied groups (P<0.05).

Table 8: The SBP and DBP results in the DM patients and AHC groups

Group	Me an ±SE	
	SBP (mm)	DBP (mm)
Control	14.05 ±0.18	8.81 ±0.11
Patients	14.08 ±0.09	8.73 ±0.05
T-test	0.395 NS	0.243 NS
P-value	0.876	0.527
	NS: Non-Significa	nt.

9. Comparison between control and patient groups in Lipid profile

In the current study the 160 cases were DM and 40 as AHC at diagnosis of, cholesterol; Triglyceride; HDL; LDL; VLDL and non-VLDL were found160.13 ±5.76; 135.01 ±6.68; 42.72 ±0.87; 90.41 ±5.26; 27.01 ±1.33 and159.56 ±3.23; 132.84 ±3.48; 41.50 ±0.30; 93.63 ±2.54; 26.57 ±0.69and120.26 ±2.86,respectively . Statistical analysis revealed nonsignificant differences in Triglyceride; HDL; LDL; VLDL and nonVLDL among studied groups table (9).

Table 9: Comparison between cholesterol; Triglyceride; HDL; LDL; VLDL and non-VLDL among studied groups.

Group	Mean ± SE (mg/dL)					
	Cholesterol	Triglyceride	HDL	LDL	VLDL	Non-HDL
Patients	160.13 ±5.76	135.01 ±6.68	42.72±0.87	90.41±5.26	27.01±1.33	117.41 ±5.69
Control	159.56 ±3.23	132.84 ±3.48	41.50±0.30	93.63±2.54	26.57±0.69	120.26 ±2.86
T-test	13.962 NS	15.253 NS	1.462 NS	11.279 NS	3.050 NS	12.604 NS
P-value	0.935	0.779	0.149	0.572	0.779	0.656
NS: Non-Significant.						

10. Results of c Framingham, Atherogenic index and FGF-23 among study groups.

By comparing the observed of investigated of c Framingham, Atherogenic index and FGF-23 in DM patients and AHC were found 8.98 ±0.48; 0.491 ±0.01 ; 510.32 ±31.12and 10.76 ±1.04; 0.487 ±0.02 ; 644.62 ±64.93, respectively as shown in Table (10). It was determined that there are statistically significant differences in c Framingham and FGF-23 except for the serum levels of Atherogenic index in the DM group and AHC groups, where a p-value of 0.861 was observed in Table 10.

Table 10: Comparison between control and patient groups in c Framingham, Atherogenic index and FGF-23

Group	Mean ±SE		
	Framingham	Atherogenic index	FGF-23
Control	10.76 ±1.04	0.487 ±0.02	644.62 ±64.93
Patients	8.98 ±0.48	0.491 ±0.01	510.32 ±31.12
T-test	1.167 *	0.0438 NS	118.42 *
P-value	0.048	0.861	0.043
* (P≤0.05), NS: Non-Significant.			

11. Sensitivity and Specificity of Framingham, Atherogenic index and FGF-23 parameters in patients and control groups

Table (11) shown the Sensitivity of Framingham, Atherogenic index and FGF-23 in DM patients and AHC were found 0.71; 0.39; 0.76and 0.44;

0.55 and0.46 , respectively as shown in Table (11). While ,the results of Specificity of Framingham, Atherogenic index and FGF-23 in DM patients and AHC were found 0.48; 0.72; 0.36 and 0.59; 0.43 and0.57 , respectively as shown in Table (11).

Table 11: Results Sensitivity and Specificity of Framingham, Atherogenic index and FGF-23 parameters in patients and control groups

Parameters	Group	Sensitivity	Specificity
Framingham	Control	0.44	0.59
	Patients	0.71	0.48
Atherogenic index	Control	0.55	0.43
	Patients	0.39	0.72
FGF-23	Control	0.46	0.57
	Patients	0.76	0.36

12. Correlation coefficient between Framingham, Atherogenic index and FGF-23 with others parameter study in patients group

The correlation coefficient among study parameters shows:

A positive correlation were found in Atherogenic index and BMI; AST; cholesterol; Triglyceride; HDL; LDL; VLDL and non-VLDL were found (0.17, 0.18 , 0.52 , 0.94, -0.40, 0.40, 0.93and 0.58) respectively. Also, was found positive correlation between Framingham and cholesterol; Triglyceride; LDL; VLDL and non-VLDL were 0.64, 0.33, 0.69, 0.33 and 0.70 ,respectively.

However , non- correlation between FGF-23 and all studied parameters as shown in table (12).

Table 12: Correlation coefficient between Framingham, Atherogenic index and FGF-23 with others parameter study in patients group

Parameters	Correlation coefficient-r		
	Framingham	Atherogenic index	FGF-23
BMI	0.08 NS	0.17 *	-0.06 NS
F.B.S.	-0.03 NS	-0.02 NS	-0.04 NS
HbA1c	-0.02 NS	-0.06 NS	0.01 NS
ALT	-0.009 NS	0.09 NS	0.06 NS
AST	0.10 NS	0.18 *	0.07 NS
Urea	-0.08 NS	-0.10 NS	0.06 NS
Creatinine	-0.06 NS	0.11 NS	-0.09 NS
SBP	0.08 NS	-0.03 NS	0.08 NS
DBP	-0.01 NS	0.12 NS	0.11 NS
Cholesterol	0.64 **	0.52 **	-0.02
Triglyceride	0.33 **	0.94 **	0.13 NS
HDL	-0.02 NS	-0.40 **	-0.04 NS
LDL	0.69 **	0.40 **	-0.08 NS
VLDL	0.33 **	0.93 **	0.13 NS
Non-HDL	0.70 **	0.58 **	-0.04 NS
* ($P \leq 0.05$), ** ($P \leq 0.01$), NS: Non-Significant.			

4. Discussion

FGF23's and TG&HDL's relationship

One can connect diabetes to several other diseases. Untreated, it could finally cause serious medical issues including heart disease, vascular disease, renal disease, and ultimately blindness ((Singh & Prasad, 2014)). Since type 2 diabetes in humans is expensive, demands a lot of time and money, and compromises a person's quality of life, researchers have focused on its causes and consequences. This study sought to find any possible relationship between urine FGF23 levels and plasma FGF23 levels as well as CVD risk in Iraqi type 2 diabetes mellitus (T2DM) sufferers. Although FGF23 is a hormone recognized to control phosphate homeostasis, new

studies point to a connection between high FGF23 and higher CVD risk.Studies have revealed that patients with T2DM and normal or modestly impaired renal function show higher FGF23 levels and increased risk of significant adverse cardiovascular events [4].Studies indicate a strong linkage between triglycerides (TG) and FGF23; evidence of HDL's association with FGF23 is not clear-cut. Increased FGF23 has also been linked with poor heart function and indicators of diabetic cardiomyopathy.In this present work we discovered a favorable link between Framingham risk and cholesterol, TG, LDL, HDL, VLDL, non-VLDL. also revealed favorable relationships in Atherogenic index and BMI, HDL, LDL, VLDL and non-LDL.

Patients with type 2 diabetes have showed a positive association between TG levels and FGF23 according to several research [1][2][3]. Insulin resistance, a frequent trait of both high TG and raised FGF23 [2], may explain this link.Higher TG could cause adipocytes to release more FGF23 [4].FGF23 may raise hepatic TG storage [5].According to several studies, HDL and FGF23 indicate a negative relationship [4][5].

While others discovered no link [6][7], recent research also revealed negative correlation between FGF-23 and all measures (TG, CHOL, LDL, HDL, BMI).Variations in the research population and FGF23 measuring technique could be the causes of these variances.Particularly in type 2 diabetes sufferers, TG and FGF23 show a notable association.HDL and FGF23 have a non-defining association.More study is required to fully grasp the link between FGF23 and lipids.

FGF23 and Framingham Risk Score: Correlation in Type 2 Diabetes Mellitus

A marker of 10-year cardiovascular disease (CVD), several studies have shown a notable connection between greater FGF23 levels and higher Framingham Risk Score (FRS) in patients with type 2 diabetic mellitus (T2DM).

FGF23-FRS Correlation Evidence for T2DM:

FGF23 levels were independently linked with FRS and predicted long-term unfavorable cardiovascular outcomes [1] according a study including 1,563 T2DM patients with coronary artery disease (CAD). Higher FGF23 levels were linked, according another study in 4,889 T2DM patients, to a higher risk of all-cause and cardiovascular mortality [2].A sign of subclinical atherosclerosis, FGF23 has also been linked to higher carotid intima-media thickness (IMT) in T2DM patients [3].

In the Dm.patient group and farmingham risk, the FGF23 in present study show more signifcant. .

5. Conclusion:

- Particularly among type 2 diabetes sufferers, there is evidence of a strong link between TG and FGF23.
- There is not definitive link between HDL and FGF23.
- Significant in patient and healthy groups is smoking and hypertion.
- Neither the DM patient group nor the control group have any notable anticipated serum creatinine.
- More study is required to better grasp how FGF23 and lipids interact.
- FGF23 could be involved in inflammation in obesity and insulin resistance, therefore raising the risk of both chronic kidney disease and cardiovascular disease.
- More study is required to better grasp FGF23's contribution to obesity and create fresh remedies.
- Other variables including age, sex, and ethnicity could potentially influence the FGF23 to BMI association.

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