Al-Iraqia Medical College Journal (AIMCJ)
ISSN (Online): 3104-4565
ISSN (Print): 3104-4557

ARTICLE INFO
Received: 17/ 6/ 2025
Revised: 20/ 7 / 2025
Accepted: 21/ 7/ 2025
Publish online: 15 /08 / 2025

*Corresponding Author Noora Wael Rasheed
Email: noora.w.rasheed@aliraqia.edu.iq

CITATION
Rasheed NW, Abbood YH, Abd-Alhussain SQ, Abu-Shana JH. Fibronectin as a nexus of inflammation and dysmetabolism in type 2 diabetes. *AIMCJ*. 2025;2(2):49-59

DOI: https://doi.org/10.58564/AIMCJ2.2.2025.128

Fibronectin as a Nexus of Inflammation and Dysmetabolism in Type 2 Diabetes

Noora Wael Rasheed[1*], Yasameen Hussein Abbood[1], Sabah Qusay Abd-Alhussain[1], Jinan Hameed Abu-shana[1]

[1] Department of Chemistry and Biochemistry, College of Medicine, Al-Iraqia University, Baghdad, Iraq

Abstract

Fibronectin (FN) is a major component of the extracellular matrix and participates in essential biological activities, including wound healing, cell adhesion, and vascular remodeling.

Several studies have suggested that FN might be involved in the metabolic disturbances and vascular complications commonly seen in type 2 diabetes mellitus (T2DM). The purpose of this research was to investigate FN concentrations in Iraqi T2DM patients, examine their links to insulin resistance and oxidative stress, and examine their links to insulin resistance and oxidative stress.

We conducted a study at Baghdad Medical City Hospital between January and June 2025. A total of 150 participants were enrolled and divided equally into three groups: patients with T2DM and complications, patients with T2DM but without complications, and healthy controls. For all participants, plasma FN, HOMA-IR, malondialdehyde (MDA), C-reactive protein (CRP), HbA1c, fasting glucose, and total cholesterol were assessed using validated ELISA kits together with routine biochemical techniques.

Our findings revealed that FN concentrations were substantially higher in patients with T2DM who had complications (662.6 ± 6.1 mg/dL) than in those without complications (533.4 ± 6.2 mg/dL) and in the control group (311.5 ± 6.2 mg/dL) ($p < 0.001$). Moreover, FN showed strong positive correlations with HOMA-IR ($r = 0.84$), CRP ($r = 0.88$), and MDA ($r = 0.85$), all of which were statistically significant ($p < 0.01$).

These observations highlight that FN is closely related to insulin resistance, oxidative stress, and inflammatory status in patients with T2DM. Its strong association with diabetic complications supports its potential value as a complementary biomarker to HbA1c. Our study adds new data from a Middle Eastern population, where few studies have examined FN in diabetes.

Keywords: Fibronectin, Type 2 diabetes mellitus, Insulin resistance, Oxidative stress.

Introduction

Diabetes mellitus is a long-term problem with the pancreas that causes high blood sugar levels because the body doesn't make enough insulin, or it doesn't work properly. Type 2 diabetes results from impaired pancreatic beta-cell function and insulin resistance (1-3). Knowledge of the processes underlying diabetes has evolved over the years. T2D accounts for over 90% of all cases of DM. Since several inflammatory molecules play a major role in the development and progression, it is now more evident that T2D is related to metabolic disorders (4-5).

Fibronectin is a versatile glycoprotein that participates in key biological processes, including tissue repair, cell adhesion, and maintenance of extracellular structure (6). It is found in two main isoforms: plasma FN, produced in the liver, and cellular FN, released by fibroblasts, endothelial cells, and macrophages (7). Glycation alters the appearance and function of FN. It cannot bind to integrins effectively, impairing normal blood vessel function (8). One special form, FN-EDA, can activate TLR4. When this happens, inflammation increases, and insulin resistance can become more severe (9-10). CVD risk increases with rising blood sugar levels, even before reaching diabetic thresholds. Diabetes and hypertension (HT) are two of the most important cardiovascular risk factors (11).

HT and type 2 diabetes are frequently coexisting diseases. Diabetes patients have a higher prevalence of hypertension, whereas hypertensive people are more likely to get diabetes. HT raises the probability of acquiring DM, while DM considerably increases the risk of future HT. Almost one-third of adults have HT. Approximately 75% of individuals with diabetes have hypertension (12).

Numerous epidemiological studies show that smoking cigarettes increases the incidence of type 2 diabetes. Additionally, the length of smoking was positively correlated with the incidence of type 2 diabetes. Chronic heavy smoking increases the risk of hyperglycemia, hyperinsulinemia, and hypertension (13-14).

There is a lack of data on FN in Middle Eastern patients with diabetes. Given that genetic background, lifestyle, and environmental exposures can vary across populations, region-specific studies are important. The purpose of this research was to investigate FN concentrations in Iraqi T2DM patients, examine their links to insulin resistance, oxidative stress, and inflammation, and evaluate the predictive power of FN for diabetic complications.

A key factor in the value of our work is the population we studied. Research on fibronectin in diabetes is still limited in Middle Eastern countries. People from different regions may show differences in biomarker levels because of genetic, environmental, or lifestyle factors.

MATERIALS AND METHODS

Study Design and Participants

Our study was conducted in the Department of Chemistry and Biochemistry at the College of Medicine, Al-Iraqia University, in Baghdad. The work extended over six months, from January to June 2025.

The patients were recruited from the (medical city) hospital in Baghdad. The study enrolled 150 participants and divided them into three groups: patients with type 2 diabetes and complications, patients with type 2 diabetes without

complications, and a control group of apparently healthy individuals.

To be part of the study, participants had to be between 40 and 70 years of age and have a confirmed diagnosis of type 2 diabetes according to the ADA guidelines.

Inclusion and Exclusion Criteria

This study included only patients who had been living with diabetes for at least 5 years. Anyone with type 1 diabetes, chronic liver or kidney disease, thyroid problems, cancer, or any acute infection was excluded. We also did not include individuals receiving long-term corticosteroids or antioxidant supplements, or pregnant or breastfeeding women.

Every participant was informed about the purpose and details of the research, and we obtained written consent before drawing any blood.

Ethical statement

The University of Iraq College of Medicine's Ethics Permission Committee, within the Scientific Affairs Division, granted ethical approval for this study, in addition to the original approvals.

Sample collection

Blood samples were taken in the morning after the participants had fasted overnight for 10–12 hours. Around 5 mL of venous blood was collected under sterile conditions. A part of the sample was placed in EDTA tubes for HbA1c testing, while the rest was placed in plain tubes. After centrifugation at 3000 rpm for 10 minutes, the serum was separated and stored at −20 °C until testing.

Biochemical Measurement

Fibronectin levels were measured with a commercial ELISA kit from MyBioSource (USA). The glucose oxidase analyzed fasting plasma glucose using the peroxidase method, and HbA1c was measured using HPLC on the D-10 system from Bio-Rad. Serum insulin was determined with an ELISA kit from DRG Instruments (Germany), and the HOMA-IR index was calculated in the usual way by multiplying fasting insulin by fasting glucose and dividing by 405. Malondialdehyde (MDA) was estimated using the TBARS method, high-sensitivity CRP was measured with an ELISA kit (Thermo Fisher Scientific, USA), and total cholesterol was determined using a colorimetric enzymatic method (Spinreact, Spain). To ensure accuracy, all tests were done twice, and variability within and between runs was kept below 10%.

Statistical analysis

Programs used: IBM SPSS version 30, Graph Pad Prism version 10.4.1
Statistical tests: mean, standard error of mean, independent t-test, ANOVA table (Duncan test) for categorical parameters.
While frequency and percentage, and Pearson's chi-square test were used to calculate the probability for nominal data such as sex, smoking status, and complications.
Pearson's correlation was used to calculate the correlations among the studied parameters.

Results

Table 1 presents the demographic characteristics of patients with complications, patients without complications, and healthy individuals, respectively.

Each group consists of 50 participants. The average age was similar between the groups with and without complications (58.66 ± 1.46 and 58.50 ± 1.46, respectively), whereas the average age of healthy individuals was lower (55.64 ± 1.34). Thus, we conclude that age has no statistically significant effect on the study. Regarding sex, females showed a slightly significant difference. Significant differences were observed in the diabetic group with complications, with males at 58.0% and females at 42.0%. In contrast, in the diabetic group without complications, males showed a clear increase of 62.0%, and females showed a 38.0% increase. The control group was almost equal between males and females, at 52.0% and 48.0%, respectively. When comparing smokers and non-smokers, the values across the three groups were quite close, ranging from 52–54% and 46–48%, respectively. The study concluded that smoking had no bearing on the study.

The results showed that comorbidities in diabetes with complications were approximately 42.0% CVD and 30.0% Hypertension, and the number of those who did not suffer from comorbidities was about 28.0%. In the group without complications, CVD and Hypertension were equal at 30.0%, and 40.% had no other comorbidities. There were no comorbidities in the healthy group.

Table (2) The three groups showed notable differences in biomarkers (fibronectin, HOMA-IR, MDA, CRP, fasting glucose, HbA1c, and total cholesterol): 662.57 ± 6.07, 6.46 ± 0.08, 6.02 ± 0.08, 15.41 ± 0.27, 273.08 ± 7.05, 10.04 ± 0.13, 268.95 ± 2.33, respectively, with diabetic patients with complications showing significantly higher values than those without complications (533.36 ± 6.20, 6.20,4.51 ± 0.08, 3.96 ± 0.07, 8.72 ± 0.27, 153.19 ± 2.43, 7.46 ± 0.08, 209.53 ± 2.54, respectively).

In general, the results for diabetic patients, compared with healthy controls, were 311.53 ± 6.19, 1.74 ± 0.06, 1.71 ± 0.06, 2.64 ± 0.13, 84.42 ± 1.22, 5.12 ± 0.04, and 162.26 ± 3.49, respectively.

Table 1: Bibliography of the study

Demographical data		**Diabetic with complications**	**Diabetic without complications**	**Healthy control**
Age mean ± SE (Years)		58.66 ± 1.46 [A]	58.50 ± 1.46 [A]	55.64 ± 1.34 [A]
Sex No. (%)	Males	21 (42.0)	31 (62.0)	26 (52.0)
	Females	29 (58.0)	19 (38.0)	24 (48.0)
	Total	50 (100.0)	50 (100.0)	50 (100.0)
Smoking status No. (%)	Smokers	27 (54.0)	26 (52.0)	27 (54.0)
	Non-smokers	23 (46.0)	24 (48.0)	23 (46.0)
Comorbidities No. (%)	CVD	21 (42.0)	15 (30.0)	0 (0.0)
	Hypertension	15 (30.0)	15 (30.0)	0 (0.0)
	None	14 (28.0)	20 (40.0)	50 (100.0)

Table 2: Biomarkers result

Parameters	**Mean ± SE**		
	Diabetic with complications	Diabetic without complications	Healthy control
Fibronectin level (mg/dL)	662.57 ± 6.07^{A}	533.36 ± 6.20^{B}	311.53 ± 6.19^{C}
HOMA-IR	6.46 ± 0.08^{A}	4.51 ± 0.08^{B}	1.74 ± 0.06^{C}
MDA (nmol/L)	6.02 ± 0.08^{A}	3.96 ± 0.07^{B}	1.71 ± 0.06^{C}
CRP (mg/L)	15.41 ± 0.27^{A}	8.72 ± 0.27^{B}	2.64 ± 0.13^{C}
Fasting glucose (mg/dL)	273.08 ± 7.05^{A}	153.19 ± 2.43^{B}	84.42 ± 1.22^{C}
HbA1c (%)	10.04 ± 0.13^{A}	7.46 ± 0.08^{B}	5.12 ± 0.04^{C}
Total cholesterol (mg/dL)	268.95 ± 2.33^{A}	209.53 ± 2.54^{B}	162.26 ± 3.49^{C}
Duncan's test: similar letters indicate no appreciable differences across groups.			

Table 3 demonstrates the effect of smoking on three groups: diabetics with complications, diabetics without complications, and healthy controls, while the probability indicates significance within the same group between smokers and non-smokers. We often see that people with diabetes with complications have higher values than people with diabetes without complications and healthy people.

Smoking and non-smoking were not significant overall, but there were exceptions: HOMA-IR group 2 probability (0.016), while group 1 and group 3 were 0.576 and 0.484, respectively. CRP group 1 shows a slight increase (0.022) from group 2 (0.019) and group 3 (0.710).

In Table 4, the diabetic with complications, diabetic without complications, and healthy control groups were subdivided into three groups: CVD, hypertension, and none. Results show high significance for comorbidities versus no comorbidities (675.56 ± 9.83 mg/dL), followed by hypertension (658.74 ± 10.67 mg/dL) and CVD (655.69 ± 10.36 mg/dL) when compared with group 2, which was diabetic without comorbidities.

Fibronectin levels are significantly higher (551.15 ± 9.55 mg/dL) than in hypertension (521.58 ± 12.32 mg/dL) and CVD (521.42 ± 9.04 mg/dL). HOMA-IR and MDA levels show higher significance in diabetic groups than in healthy controls, with no changes in the subgroups of the initial group. CRP levels were highest in patients without comorbidities (15.93 ± 0.45 mg/L) in group 1.

Fasting glucose and HbA1c levels in patients without comorbidities were higher (291.38 ± 10.35 mg/dL and 10.22 ± 0.24%, respectively), and total cholesterol showed no significant differences among comorbidity subgroups.

Table 3: Effect of smoking on parameters

Parameters		**Mean ± SE**		
		Diabetic with complications	Diabetic without complications	Healthy control
Fibronectin level (mg/dL)	Smokers	664.48 ± 7.45^{A}	531.85 ± 9.42^{B}	311.86 ± 9.37^{C}
	Non-smokers	659.45 ± 10.03^{A}	534.99 ± 8.11^{B}	311.16 ± 7.98^{C}
	Probability	0.687	0.801	0.955
HOMA-IR	Smokers	6.49 ± 0.11^{A}	4.69 ± 0.12^{B}	1.79 ± 0.08^{C}
	Non-smokers	6.41 ± 0.13^{A}	4.32 ± 0.10^{B}	1.68 ± 0.09^{C}
	Probability	0.576	**0.016**	0.484
MDA (nmol/L)	Smokers	5.97 ± 0.11^{A}	3.94 ± 0.09^{B}	1.75 ± 0.08^{C}
	Non-smokers	6.09 ± 0.13^{A}	3.97 ± 0.11^{B}	1.65 ± 0.1^{C}
	Probability	0.415	0.857	0.499
CRP (mg/L)	Smokers	14.93 ± 0.35^{A}	9.23 ± 0.38^{B}	2.56 ± 0.17^{C}
	Non-smokers	15.97 ± 0.38^{A}	8.17 ± 0.35^{B}	2.73 ± 0.19^{C}
	Probability	**0.022**	**0.019**	0.710
Fasting glucose (mg/dL)	Smokers	268.20 ± 9.11^{A}	156.74 ± 3.31^{B}	83.02 ± 1.71^{C}
	Non-smokers	278.80 ± 11.09^{A}	149.34 ± 3.46^{B}	86.07 ± 1.71^{C}
	Probability	0.229	0.339	0.728
HbA1c (%)	Smokers	10.0 ± 0.20^{A}	7.40 ± 0.11^{B}	5.07 ± 0.05^{C}
	Non-smokers	10.09 ± 0.15^{A}	7.52 ± 0.11^{B}	5.18 ± 0.07^{C}
	Probability	0.627	0.527	0.564
Total cholesterol (mg/dL)	Smokers	270.97 ± 3.60^{A}	210.33 ± 3.66^{B}	162.27 ± 4.58^{C}
	Non-smokers	266.59 ± 2.77^{A}	208.67 ± 3.57^{B}	162.26 ± 5.48^{C}
	Probability	0.446	0.773	0.998
Duncan's test: similar letters show that there are no appreciable variations across groups				

Table 5 presents the correlation coefficients among biomarker parameters across patient groups. Fibronectin levels showed high correlations with HOMA_IR, MDA, CRP, fasting glucose, HbA1c, and total cholesterol: 0.844, 0.853, 0.875, 0.851, 0.817, and 0.851, 0.817, 0.851, 0.817, 0.752, respectively. Also, all parameters increased when HOMA_IR was evaluated, with MDA, CRP, fasting glucose, HbA1c, and total cholesterol: 0.879, 0.861, 0.806, 0.878, and 0.808, respectively.

From this table, the variables are significantly related to each other.

Table 4: Effect of biomedical parameters on comorbidities

Parameters		**Mean ± SE**		
		Diabetic with complications	**Diabetic without complications**	**Healthy control**
Fibronectin level (mg/dL)	CVD	$655.69 \pm 10.36^{A}{}_{b}$	$521.42 \pm 9.04^{B}{}_{b}$	-
	Hypertension	$658.74 \pm 10.67^{A}{}_{b}$	$521.58 \pm 12.32^{B}{}_{b}$	-
	None	$675.56 \pm 9.83^{A}{}_{a}$	$551.15 \pm 9.55^{B}{}_{a}$	311.53 ± 6.19^{C}
HOMA-IR	CVD	$6.47 \pm 0.11^{A}{}_{a}$	$4.34 \pm 0.16^{B}{}_{a}$	-
	Hypertension	$6.56 \pm 0.18^{A}{}_{a}$	$4.73 \pm 0.15^{B}{}_{a}$	-
	None	$6.32 \pm 0.16^{A}{}_{a}$	$4.48 \pm 0.56^{B}{}_{a}$	1.74 ± 0.06^{C}
MDA (nmol/L)	CVD	$6.0 \pm 0.15^{A}{}_{a}$	$3.88 \pm 0.13^{A}{}_{a}$	-
	Hypertension	$6.05 \pm 0.14^{A}{}_{a}$	$4.05 \pm 0.14^{A}{}_{a}$	-
	None	$6.03 \pm 0.13^{A}{}_{a}$	$3.94 \pm 0.11^{B}{}_{a}$	1.71 ± 0.06^{C}
CRP (mg/L)	CVD	$14.89 \pm 0.46^{A}{}_{a}$	$8.61 \pm 0.51^{A}{}_{a}$	-
	Hypertension	$15.66 \pm 0.42^{A}{}_{a}$	$9.24 \pm 0.54^{A}{}_{a}$	-
	None	$15.93 \pm 0.45^{A}{}_{a}$	$8.42 \pm 0.39^{B}{}_{a}$	2.63 ± 0.13^{C}
Fasting glucose (mg/dL)	CVD	$259.76 \pm 11.87^{A}{}_{b}$	$150.93 \pm 4.25^{B}{}_{a}$	-
	Hypertension	$274.65 \pm 12.87^{A}{}_{ab}$	$153.30 \pm 4.50^{B}{}_{a}$	-
	None	$291.38 \pm 10.35^{A}{}_{a}$	$154.81 \pm 4.06^{B}{}_{a}$	84.42 ± 1.22^{C}
HbA1c (%)	CVD	$10.14 \pm 0.19^{A}{}_{ab}$	$7.38 \pm 0.16^{B}{}_{a}$	-
	Hypertension	$9.73 \pm 0.23^{A}{}_{b}$	$7.59 \pm 0.14^{B}{}_{a}$	-
	None	$10.22 \pm 0.24^{A}{}_{a}$	$7.42 \pm 0.12^{B}{}_{a}$	5.12 ± 0.04^{C}
Total cholesterol (mg/dL)	CVD	$269.57 \pm 3.13^{A}{}_{a}$	$212.15 \pm 5.20^{A}{}_{a}$	-
	Hypertension	$266.30 \pm 3.91^{A}{}_{a}$	$204.68 \pm 3.89^{A}{}_{a}$	-
	None	$270.87 \pm 5.63^{A}{}_{a}$	$211.21 \pm 4.09^{A}{}_{a}$	162.26 ± 3.49^{A}

Duncan's test: Similar capital letters above the line indicate no significant differences between the groups (horizontal comparison), while small letters below the line indicate no significant differences between the subgroups of the multiples (vertical comparison).

Table 5: Correlations between biomarker parameters

	Fibronectin	HOMA_IR	MDA	CRP	Fasting Glucose	HbA1c	Total Cholesterol
Fibronectin	1	0.844**	0.853**	0.875**	0.851**	0.817**	0.752**
HOMA_IR		1	0.879**	0.861**	0.806**	0.878**	0.808**
MDA			1	0.844**	0.858**	0.864**	0.787**
CRP				1	0.835**	0.824**	0.752**
Fasting Glucose					1	0.817**	0.716**
HbA1c						1	0.793**
Total Cholesterol							1

***. Correlation is significant at the 0.01 level (2-tailed).*

Discussion

Our study shows clear, consistent differences among patient groups: higher fibronectin (FN) levels in patients with type 2 diabetes mellitus (T2DM), especially those with complications, compared with healthy controls. HOMA-IR, MDA, CRP, HbA1c, and total cholesterol also followed the same pattern—worse in complicated cases, moderate in uncomplicated diabetes, and lowest in healthy individuals.

It is well known that chronic high blood sugar drives FN overexpression. In experimental diabetes, FN accumulates in tissues such as the kidney, heart, retina, and colon (15). That tissue buildup reflects structural damage and aligns with our finding that circulating FN is higher in patients with complications. Fibronectin may act not just as a bystander but as a signal of ongoing vascular injury (16).

Moreover, glycation alters FN structure, affecting its binding to integrins such as α5β1 and disrupting signaling pathways, including Ang-1/Tie-2, which are essential for endothelial cell function (17). This mechanistic disruption likely links high FN levels with the impaired vascular integrity seen in diabetic complications.

The findings showed strong positive correlations among FN, HOMA-IR, CRP, and MDA. HOMA-IR reflects insulin resistance. That connection is important because some FN isoforms, especially FN-EDA, can activate Toll-like

receptor 4 (TLR4) and directly promote insulin resistance (18).

CRP serves as a broad indicator of inflammation, generated by the liver when exposed to inflammatory cytokines (19). Numerous T2DM patients with complications exhibited elevated CRP and high FN levels. These two markers seem connected: chronic inflammation is likely to enhance FN expression, and FN might additionally play a role in local inflammatory activities within vascular tissue (20).

Malondialdehyde indicates oxidative stress—the harm induced by reactive oxygen species when antioxidant defenses are inadequate. In T2DM, oxidative pathways are excessively active; they harm proteins, lipids, and DNA while fostering inflammation and vascular damage (21). The correlation between FN and MDA in our data indicates that increased stress is associated with higher FN levels

Furthermore, the current findings revealed that the diabetic patients with complications consistently had higher FN, HOMA-IR, CRP, and MDA than those without complications. This suggests FN may reflect disease severity. In other words, FN may help distinguish stable diabetes from diabetes complicated by vascular issues.

Many patients with acceptable HbA1c still develop nephropathy or retinopathy because glycemic control alone doesn't tell the full story (22). FN, along with markers such as CRP or MDA, may help identify patients at higher risk—those whose disease is progressing quietly despite acceptable glycemic levels (23).

The researcher evaluated a Middle Eastern (Iraqi) group, where information on fibronectin in diabetes is limited. The majority of FN studies originate from Europe or East Asia. However, genetic, lifestyle, dietary, and environmental elements vary by region—and these variations may influence baseline biomarker levels and their clinical significance. Our data addresses a gap: they illustrate FN's behavior in a regional setting and reinforce the notion that FN could serve as an effective marker in varied populations.

While this study cannot determine causality because of its cross-sectional design, the findings indicate that fibronectin might serve as a valuable supplementary marker in conjunction with HbA1c. Incorporating markers of endothelial damage with standard glucose assessments could provide physicians a more effective method to recognize patients at greater risk and address their care sooner.

Additionally, HbA1c is crucial as it indicates long-term glucose management; however, it does not provide insights into oxidative stress or vascular remodeling. Incorporating FN into the evaluation toolkit could provide clinicians with a wider perspective on patient risk:
Patients with high FN—even with moderate HbA1c—may require more frequent monitoring.

Fibronectin may be beneficial for making timely choices regarding the prevention of vascular issues.

Conclusions:

This research indicated that fibronectin concentrations were elevated in individuals with type 2 diabetes, particularly in those with existing complications. Furthermore, the findings discovered that fibronectin was associated with insulin resistance, oxidative stress, and inflammation.

These findings indicate that fibronectin could serve as a valuable marker, alongside HbA1c, for assessing diabetic patients.

Our results are significant due to the scarcity of research on fibronectin in diabetic individuals from the Middle East. Incorporating this information contributes to bridging a knowledge gap in this area.

Although our research cannot demonstrate causation, it reveals distinct correlations. Additional studies that track patients over time are required. Should future research validate these findings, fibronectin may be included in a panel of assessments to enhance the prediction of complications and inform the treatment of individuals with diabetes.

Conflict of Interest: None

Funding: Nil

References:

1. Amirasgari F, Torkfar S, Rezazadeh S, Farzaneh M, Tajik E. Effect of vitamin D on glucose homeostasis, sensitivity, and insulin resistance in type 2 diabetes. *Current Research in Diabetes & Obesity Journal*. 2019;11(2):51-5.
2. Abu-Shana JH, Abdulkareem NG, Jasim AO, Abbood YH. Effect of Diabetes Mellitus Type 2 on the Correlation of Vitamin D with Lipid Profile in Iraqi Patients. *Iraqi Journal of Science.* 2024 Sep 30:4881-9.
3. Mezil SA, Abed BA. Complications of diabetes mellitus. *Annals of the Romanian Society for Cell Biology*. 2021;25(3):1546-56.
4. Sinha SK, Carpio MB, Nicholas SB. Fiery connections: macrophage-mediated inflammation, the journey from obesity to type 2 diabetes mellitus and diabetic kidney disease. *Biomedicines.* 2024, 27;12(10):2209.
5. Kanters SD, Banga JD, Algra A, Frijns RC, Beutler JJ, Fijnheer R. Plasma levels of cellular fibronectin in diabetes. *Diabetes care*. 2001, 1;24(2):323-7.
6. To WS, Midwood KS. Plasma and cellular fibronectin: distinct and independent functions during tissue repair. *Fibrogenesis & tissue repair*. 2011, 16;4(1):21.
7. Kanta J, Zavadakova A, Sticova E, Dubsky M. Fibronectin in hyperglycemia and its potential use in the treatment of diabetic foot ulcers: A review. *International Wound Journal*. 2023;20(5):1750-61.
8. Zheng Z, Ma T, Lian X, et al. Clopidogrel reduces fibronectin accumulation and improves diabetes-induced renal fibrosis. *Int J Biol Sci*. 2019, 15(1):239-252.
9. Fan L, Xiao Q, Zhang L, Wang X, Huang Q, Li S, Zhao X, Li Z. CAPE-pNO2 attenuates diabetic cardiomyopathy through the NOX4/NF-κB pathway in STZ-induced diabetic mice. *Biomedicine & Pharmacotherapy.* 2018,1;108:1640-50.
10. Siam NH, Snigdha NN, Tabasumma N, Parvin I. Diabetes Mellitus and Cardiovascular Disease: exploring epidemiology, pathophysiology, and treatment strategies. *Reviews in Cardiovascular Medicine.* 2024, 11;25(12):436.
11. Gunes Y. A brief approach to hypertension in type 2 diabetes mellitus. *Exploration of Endocrine and Metabolic Diseases.* 2025, 4;2:101422.
12. Jia G, Sowers JR. Hypertension in Diabetes: An Update of Basic Mechanisms and

Clinical Disease. *Hypertension.* 2021 ;78:1197–205.

13. Śliwińska-Mossoń M, Milnerowicz H. The impact of smoking on the development of diabetes and its complications. *Diabetes and Vascular Disease Research*. 2017;14(4):265-76.

14. Chen J, Zhang Y, Li X, et al. Fibronectin accumulation and metabolic memory in diabetic vascular complications. *Mol Med.* 2024;30(1):52.

15. Wang Y, Xu H, Zhao L, et al. Role of ECM remodeling and oxidative stress in fibronectin overexpression in T2DM. *Immun Ageing.* 2025;12:5.

16. Rahman S, Kumar R, Singh P. Glycation-induced alterations in fibronectin structure and integrin binding in diabetes. *Front Biosci* (Landmark Ed). 2024;29(4):567–579.

17. Li M, Fang H, Zhou J, et al. Oxidative stress, TGF-β signaling, and extracellular matrix dysregulation in diabetic complications. *Mol Med.* 2024;30(1):33.

18. Huang L, Zhao J, Liu F. FN-EDA isoform triggers TLR4-mediated inflammation and insulin resistance. *Signal Transduct Target Ther.* 2024;9:242.

19. Sun Q, Zhang H, Yu X. Toll-like receptor 4 activation by fibronectin isoforms in diabetes-induced vascular damage. *Front Biosci* (Landmark Ed). 2024;29(4):421–432.

20. Aravindhan V, Kaur H, Narayanasamy S. CRP, fibronectin, and inflammatory crosstalk in diabetic vasculopathy. *Front Biosci* (Landmark Ed). 2023;28(5):142–153.

21. Zhao X, Chen R, Li S, et al. Multimarker approaches for predicting diabetic complications: emerging evidence. *Endocr Rev*. 2024;45(2):227–245.

22. Almusawi ZM, Haddad NI, Husein EA. Dectin-1 levels in obese and overweight women with polycyctic ovary syndrome (PCOS). *International Journal of Pharmaceutical Research.* 2020;12(2):1095-102.

23. Ali IT, Haddad NI, Hussein EA. Correlation of serum adiponectin and C-reactive protein with other biochemical parameters in Iraqi pregnant women. *Chem Methodol*. 2022;6(21):357–65.