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ORIGINAL RESEARCH PERIOPERATIVE MEDICINE

Evaluation of serum level of furin enzyme activity, fatty acid binding protein-4 (FABP-4) and insulin resistance in patients with pre-diabetes and newly diagnosed type 2 diabetes mellitus

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ABSTRACT

Objectives: To study the levels of furin enzyme activity (FEA) and fatty acid binding protein-4 (FABP-4) in the serum as vital indicators in pre-diabetes patients, newly diagnosed type 2 diabetes mellitus (ND-T2DM) patients, and insulin resistance, and compare with that of healthy control group, as a predictor of risk factors.

Methodology: The current study included 180 adult participants; 50 newly diagnosed with T2DM (28 men and 22 women), 50 with pre-diabetes (27 men and 23 women), compared with 80 healthy volunteers as a control group (44 men and 36 women). We examined serum levels of FEA, FABP-4 levels and insulin hormone.

Results: The results in the current study showed that the average effectiveness of furin enzyme in newly diagnosed T2DM patients was very much lower than it was in the control group(0.53 ± 0.06 pg/mL) and in the pre-diabetes group it was significantly less than the control group (0.85 ± 0.26 pg/mL). The levels of effectiveness of furin enzyme were significantly high in the control group (1.70 ± 0.66) ($P < 0.0001$).

Conclusions: The effectiveness of the furin enzyme in newly diagnosed type 2 diabetes mellitus patients and pre-diabetes has not been previously studied. We conclude that measurements of the furin enzyme activity and fatty acid binding protein-4 in serum, are indicators of risk factors for type 2 diabetes mellitus patients.

Abbreviations: ADA - American Diabetes Association; CAD - coronary artery disease; DM - diabetes mellitus; FEA - furin enzyme activity; FABP-4 - fatty acid binding protein-4; FBG - Fasting blood glucose; T2DM - type 2 diabetes mellitus; ND-T2DM - Newly diagnosed T2DM; IGT - impaired glucose tolerance;

Keywords: Diabetes mellitus; Furin enzyme activity, FABP-4, Insulin resistance, Prediabetics

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1. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is the most prevalent type of diabetes. Nearly 90 to 95% of the diabetics have T2DM. DM of this type was earlier labeled as adult onset, maturity onset or non-insulin dependent diabetes. It is a term applied tp persons with relative (rather than absolute) insulin deficiency.[1] Deficient beta cell activity and insulin-resistance (IR) are the hallmarks of T2DM. With type-2 diabetes, the beta cells, either do not sense

blood glucose levels accurately or produce too little insulin to counteract the IR. Unlike, type 1 diabetes, T2DM is not a result of autoimmune destruction of beta cells, and affected individuals usually have a relative insulin deficiency and not a complete lack of insulin.[2] The premature mortality rate due to diabetes decreased from 2000 to 2010 in high income countries but then increased from 2010-2016 in lower middle income countries.[3] Many genes have been implicated in T2DM. Environmental factors are shown to be risk factors as well, including age, obesity, and lack of physical activity.[2] Several researchers suggest that the ecological pollutants have contributed in the development and evolution of T2DM.[4] The major risk factors are the following: history of prior impaired glucose tolerance (IGT) or impaired fasting glucose (IFG), age above 45 y (although, the recurrence of T2DM happening was increased in young persons as mentioned above), hypertension (BP >140/90 mmHg) or dyslipidemia (HDL < 40 mg/dl or TG level above 150 mg/dl). Individuals diagnosed with T2DM have an increased risk of dyslipidemia; the primary causes of death and disability in this population are macrovascular complications and coronary artery disease (CAD).[5]

According to the American Diabetes Association (ADA), pre-diabetes is defined by glycemic levels that are increased in comparison to the normal but lower than the diagnostic criterion for diabetes.[6] It is a condition with a high risk of developing diabetes, with an estimated annual conversion rate of 5-10%; a comparable percentage is returning to normo-glycemia.[7] Prior to the onset of DM, there is a condition known as prediabetes. These patients have impaired glucose tolerance and impaired fasting glucose levels.[8] Pre-diabetes is linked to a high risk of heart disease, stroke, CAD, and all-cause mortality.[9] 15% to 30% of those with prediabetes who are not treated eventually acquire T2DM in five years.

Furin is considered as a proprotein convertases (PC) model in regulating growth factors and is involved in regulating many pro-proteins. The mammalian target of the rapamycin (mTOR) signaling pathway is another key player in regulating cellular processes and its dysregulation is linked to several diseases including type 2 diabetes (T2D).[10] Fatty acid-binding proteins (FABPs), a family of lipid chaperones, contribute to systemic metabolic regulation via several lipid signaling pathways. Fatty acid-binding protein 4 (FABP4), known as adipocyte FABP (A-FABP) or aP2, is mainly expressed in adipocytes and macrophages and plays important roles in the development of insulin resistance and atherosclerosis.[11,12]

We studied the levels of furin enzyme activity and fatty acid binding protein-4 (FABP-4) in the serum as vital indicators in pre-diabetes patients, newly diagnosed T2DM, and insulin resistance, and compared with that of healthy control group, as predictors of risk of developing DM.

2. METHODOLOGY

The current study included 180 participants; 30-60 y old; 50 of them newly diagnosed with T2DM (ND-T2DM) (28 men and 22 women), 50 with prediabetes (27 men and 23 women), compared with 80 healthy controls (44 men and 36 women) from February 2023 to September 2023, at Diabetes and Endocrinology Specialist Center, AL-Sadder Medical City in Al-Najaf Province. Iraq. Participants underwent a physician consultant's examination as well as a well-structured interview. The following clinical biochemical indicators were studied: furin enzyme activity (FEA) by fluorescence method, FABP-4 and insulin hormone by ELISA method, fasting blood glucose (FBG) and hemoglobin bound to sugar (HbA1c) by using the colorimetric method (Cobas c 501). Body mass index, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), and Quantitative Insulin Sensitivity Check Index (QUICKI) were also measured.

Samples were collected from patients and healthy control group by taking 7 ml of venous blood into an empty tube. The blood was centrifuged, the serum was transferred to a new tube and stored at a temperature of −80 °C to measure the effectiveness of the furin enzyme and −20 °C to measure other clinical biochemical indicators.

The kits were provided from ANASPEC (USA) and Cloud-Clone Corp (USA).

Statistical Analysis

Analysis of data was performed by using SPSS version 23. The results were expressed as (mean ± standard deviation) and percentages. Analysis of variance (ANOVA) was used to compare the results among the three studied groups. $P < 0.05$ was used as a level of statistically significant.

3. RESULTS

3.1. BMI

The mean BMI of the control subjects was 28.32 kg/m^2, of the prediabetic subjects was 28.51 kg/m^2, and in the newly diagnosed T2DM subjects was 30.43 kg/m^2. The differences were statistically not significant ($P = 0.06$) (Table 1).

Table 1 Descriptive statistics and comparisons of clinical BMI between the studied groups

	Subjects	n	Group	1st Q	Median	3rd Q	Mean ± SD	p-value
BMI (kg/m²)	T2DM	50	A	27.08	30.05	34.65	30.43 ± 5.58	0.06
	Prediabetic	50	A	24.19	27.02	33.96	28.51 ± 5.46	
	Control	80	A	24.81	26.14	31.45	28.32 ± 4.52	

**Groups sharing the same letters are not statistically different from each other based on post hoc testing*

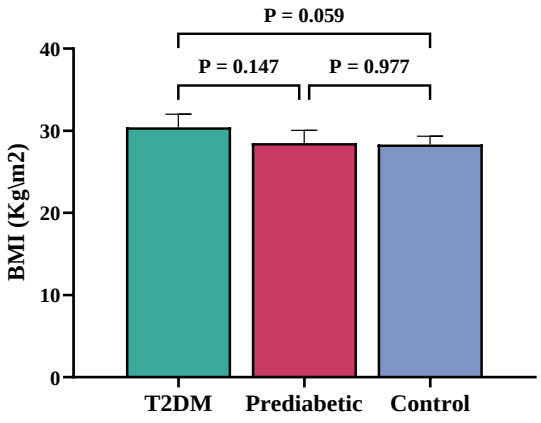

Figure 1: Means of BMI by groups with 95% CI error bars

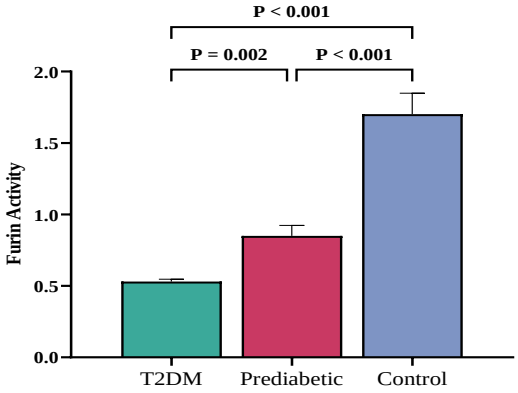

Figure 2: Means of furin activity (IU) by groups with 95% CI error bars

3.2. Furin Enzyme Activity

The analysis of furin activity levels indicated significant differences among the groups. The ANOVA results were highly significant, with an F-statistic of F(2, 177) = 113.69 and a P < 0.001. This suggests substantial variations in furin activity levels among the different groups, as presented in Table 2. The effect size, represented by eta squared (η^2), was notable at 0.56, indicating that approximately 56% of the variance in furin activity can be attributed to the variations among the groups.

To further investigate these differences, t-tests were conducted between each pair of groups. the mean furin activity level for the newly diagnosed T2DM group (0.53 ± 0.06) was significantly lower than that of the prediabetic group (0.85 ± 0.26), with a P of 0.002. Similarly, for the main effect of groups, the mean furin activity level for the T2DM group was significantly less than that of the healthy control group (1.70 ± 0.66), with a P < 0.001. Additionally, for the main effect of groups, the mean furin activity level for the prediabetic group (0.85 ± 0.26) was considerably less than that of the healthy control group, with a P < 0.001.

3.3. FABP-4

The ANOVA results demonstrated statistical significance, with an F-statistic of F(2, 177) = 54.53 and a P < 0.001. This indicates that there were noteworthy differences in FABP4 levels among the groups, as outlined in Table 2. The effect size, as indicated by eta squared (η^2), was 0.38, suggesting that approximately 38% of the variance in FABP4 can be attributed to the variations among the groups.

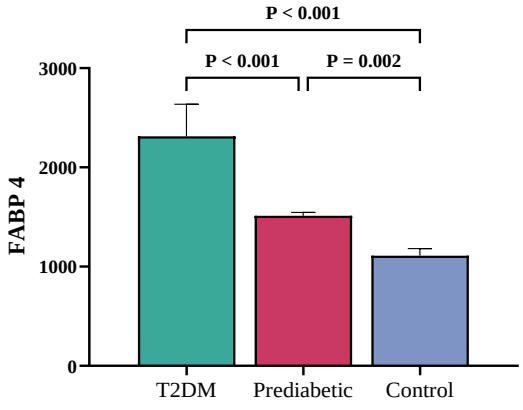

Figure 3: Means of FABP-4 (pg/mL) by groups with 95% CI error bars

Table 2: Descriptive statistics and comparisons of the main markers between the studied groups

Parameter	Subjects	Group	n	1st Q	Median	3rd Q	Mean ± SD	p-value
Furin activity (IU)	Control	A	80	1.06	1.84	2.22	1.70 ± 0.66	< 0.0001
	Prediabetic	A	50	0.70	0.74	0.87	0.85 ± 0.26	
	T2DM	A	50	0.51	0.53	0.57	0.53 ± 0.06	
FABP4 (pg/mL)	Control	C	80	924.55	1144.09	1326.96	1110.34 ± 321.23	< 0.001
	Prediabetic	B	50	1415.79	1492.37	1552.23	1511.87 ± 120.18	
	T2DM	A	50	1893.37	1963.21	2225.76	2312.78 ± 112.49	

**Groups sharing the same letters are not statistically different from each other based on post hoc testing*

For a more detailed analysis of the variations among the groups, t-tests were conducted between each pair of groups. The mean FABP4 level for the T2DM group was significantly more than that of the prediabetic group (P < 0.001). Similarly, the mean FABP4 level for the type 2 diabetes group was also significantly more than that of the healthy control group (P < 0.001). Furthermore, the mean FABP4 level for the prediabetic group was significantly greater than that of the healthy Control group (P = 0.002).

3.4. Correlation between FEA and FABP4

3.4.1. ND-T2DM group

In this section, we explore the correlations between FEA, FABP4, and several other variables in the studied group. The Pearson correlation coefficient is used to quantify these relationships, and the significance levels (p-values) help determine the statistical significance of these correlations. Here are the correlations for the ND-T2DM group:

There was a moderate negative correlation (-0.507) between FEA and FABP4 in the T2DM group, and this correlation was statistically significant (P = 0.0002). indicating that FEA has a significant negative correlation with FABP4, suggesting a potential relationship between these two factors in the disease. The correlation matrix is presented in the table 3 below.

Table 3: Pearson Correlation Matrix Among FEA, FABP4, FBG, HbA1c, Insulin, HOMA-IR, and QUICKI in ND-T2DM

Parameter		Furin activity	FABP- 4
Furin activity (IU)	Correlation coefficient		-0.507
	Significance Level P		0.0002
FABP- 4 (pg/mL)	Correlation coefficient	-0.507	
	Significance Level P	0.0002	
FBG (mmol/L)	Correlation coefficient	0.176	-0.064
	Significance Level P	0.2214	0.6582
HbA1c (%)	Correlation coefficient	0.056	-0.211
	Significance Level P	0.6973	0.1414
Insulin (µU/mL)	Correlation coefficient	-0.465	0.568
	Significance Level P	0.0007	<0.0001
HOMA-IR	Correlation coefficient	-0.317	0.458
	Significance Level P	0.0248	0.0008
QUICKI	Correlation coefficient	0.129	-0.217
	Significance Level P	0.3723	0.1299

3.4.2. Pre-diabetes group

Table 4 presents a Pearson Correlation Matrix among various biomarkers in prediabetic individuals. The correlation coefficients and their significance levels (P-values) are provided to assess the relationships between these biomarkers. There was a weak negative correlation

(-0.199) between FEA and FABP-4, but it is not statistically significant (P = 0.1664).

A positive association was observed (0.204) between FBG and HbA1c levels in prediabetic individuals, but it is not statistically significant (P = 0.1559). There was a moderate negative correlation (−0.353) between Insulin levels and HOMA-IR (a measure of insulin resistance) in prediabetic individuals, and this correlation was statistically significant (P = 0.0119).

Table 5: Descriptive statistics and comparisons of metabolic and Insulin resistance markers between the studied groups

Parameters	Subjects	*Groups	n	1st Q	Median	3rd Q	Mean ± SD	p-value
FBG (mmol/L)	Control	C	80	4.44	4.61	4.94	4.77 ± 0.49	< 0.001
	Prediabetic	B	50	6.11	6.38	6.73	6.21 ± 0.66	
	T2DM	A	50	10.38	11.74	13.89	11.86 ± 2.53	
HbA1c (%)	Control	C	80	4.90	5.10	5.30	5.11 ± 0.31	< 0.001
	Prediabetic	B	50	6.00	6.20	6.30	6.14 ± 0.23	
	T2DM	A	50	7.50	8.62	11.00	9.30 ± 2.02	
Insulin (µU/mL)	Control	B	80	0.61	0.70	0.78	0.73 ± 0.23	< 0.001
	Prediabetic	A	50	1.65	1.98	2.98	3.39 ± 3.87	
	T2DM	A	50	2.20	2.87	3.57	2.94 ± 1.37	
HOMA-IR	Control	C	80	0.12	0.15	0.18	0.15 ± 0.05	< 0.001
	Prediabetic	B	50	0.36	0.55	0.81	0.98 ± 1.15	
	T2DM	A	50	1.04	1.50	1.85	1.53 ± 0.73	
QUICKI	Control	A	80	0.54	0.56	0.59	0.57 ± 0.09	< 0.001
	Prediabetic	B	50	0.40	0.43	0.46	0.42 ± 0.05	
	T2DM	C	50	0.35	0.36	0.38	0.37 ± 0.05	

** Groups that share the same small letters (c, b, a) are not statistically different from each other based on post hoc testing.*

3.5. Insulin Hormone, HOMA-IR, QUICKI, HbA1c, and FBG

In Table 5, the analysis of various metabolic parameters, including Fasting Blood Glucose (FBG) in mmol, HbA1c, insulin levels in µU/mL, HOMA-IR, and QUICKI, was conducted among different groups. the results of this analysis showed significant differences in metabolic parameters (FBG, HbA1c, Insulin, HOMA-IR, and QUICKI) among the control, prediabetic, and T2DM groups the details are presented in each section below.

Table 6: ROC analysis criteria of the main study biomarkers in the context of classifying Type 2 Diabetes, Pre-diabetes, and Control groups.

	Variable	AUC	SE	95% CI	Cutoffs	Sensitivity	Specificity
T2DM vs Control group	Furin activity	1.000	0.000	0.972 to 1.000	≤0.618	100.00	100.00
	FABP-4	0.975	0.0134	0.931 to 0.994	>1640.642	90.00	100.00
	HOMA-IR	0.984	0.0155	0.945 to 0.998	>0.28	98.00	98.75
Pre-diabetes vs Control group	Furin activity	0.865	0.0313	0.793 to 0.918	≤1.039	90.00	75.00
	FABP-4	0.876	0.0324	0.807 to 0.927	>1365.392	100.00	82.50
	HOMA-IR	0.991	0.00490	0.956 to 1.000	>0.22	100.00	91.25
T2DM vs Pre-diabetes	Furin activity	0.986	0.00824	0.938 to 0.999	≤0.618	100.00	92.00
	FABP_4	0.926	0.0316	0.856 to 0.969	>1809.796	82.00	100.00
	HOMA_IR	0.774	0.0540	0.680 to 0.852	>0.81	86.00	82.00

AUC: (Area Under the Curve), SE: (Standard Error), 95% CI: (95% Confidence Interval)

3.6. ROC Analysis

Table 6 provides an overview of the diagnostic and predictive performance of the main study biomarkers in the context of classifying newly diagnosed T2DM, prediabetics, and control groups.

3.6.1. For the ND-T2DM vs. Control comparison:

Furin enzyme activity (FEA) demonstrates perfect discriminatory ability with an AUC of 1.000, using a cut-off value of ≤ 0.618. It achieves both 100% sensitivity and 100% specificity. It achieves a high sensitivity of 98% and perfect specificity of 100%. FABP-4 has a good AUC of 0.975, using a cut-off value of >1640.642. It maintains a sensitivity of 90% and perfect specificity of 100%. HOMA-IR performs well with an AUC of 0.984 and a cut-off value of > 0.28. It has a sensitivity of 98% and a specificity of 98.75%.

3.6.2. Control comparison:

FEA has an AUC of 0.865, with a cut-off value of ≤ 1.039. It achieves a sensitivity of 90% and a specificity of 75%. FABP4 has an AUC of 0.876, using a cut-off value of > 1365.392. It achieves a perfect sensitivity of 100% and a specificity of 82.50%. HOMA_IR demonstrates excellent performance with an AUC of 0.991 and a cut-off value of > 0.22. It maintains both a sensitivity of 100% and a specificity of 91.25%.

3.6.3. For the ND-T2DM vs. Pre-diabetes comparison:

FEA performs well with an AUC of 0.986, using a cut-off value of ≤ 0.618. It achieves a sensitivity of 100% and a specificity of 92%. FABP-4 exhibits good discrimination with an AUC of 0.926 and a cut-off value of > 1809.796. It has a sensitivity of 82% and perfect specificity of 100%. HOMA-IR has an AUC of 0.774, using a cut-off value of > 0.81. It maintains a sensitivity of 86% and a specificity of 82%.

4. DISCUSSION

4.1. Body mass index (BMI)

In the present study there was no significantly difference of (BMI) (P = 0.06), the BMI for three groups control group (28.32 ± 4.52), prediabetics group (28.51 ± 5.46) and ND-T2DM group (30.43 ± 5.58). The result in Table 1 and Figure 1 show there is no significant difference in mean of (BMI) with three groups and this study agreement with study.[12] ND-T2DM and prediabetics had higher weight than normal control group. Also agreement was present no significant difference between (BMI) in the three groups.[13] There were no significant difference between the study groups and control group with respect to BMI this finding also found by Estabraq A. Al-Wasiti et al., 2014.[14]

4.2. General Serum Biochemical Tests:

4.2.1. FBG

A high significant difference existed between the control group and the pre-diabetic group, a highly significant difference existed between the control group and ND-T2DM group, and a high significant difference existed between the pre-diabetic and ND-T2DM group according to the results of the current study (P < 0.001) this result in Table 5. In addition, this study supports previous findings showed that diabetic groups had higher glucose levels than healthy groups, as well as findings showed that prediabetic groups had higher levels of glucose than control groups. Additionally, this study supports research done by,[13] diabetes group and pre-diabetes have high glucose level than healthy control group, also agreement with diabetes group have high level of glucose than pre-diabetes and control group, and the pre- diabetes have higher glucose level than healthy control group.[14,15]

4.2.2. HbA1c

There was a highly significant difference between the three groups (P < 0.001), as well as a significant difference between the control group and the pre-diabetic group and a highly significant difference between the control group and ND-T2DM group. The present study also found a high significant differences between the pre-diabetic and ND-T2DM group this result in Table 5, which is consistent with studies by[14] also agreement with[16]. The current research discovered that a significant positive correlation between fasting blood glucose (FBG) and glyclated hemoglobin (HbA1c) between three groups and this results agreement with previous study.[17] there was found positive correlation between (HbA1c and FBG) in patients with type 2 Diabetes. Also agreement with study[18] there was found a significant positive correlation between FBS and HbA1c of three groups ,control group, prediabetes group and type 2 diabetes group.

4.2.3. Serum Furin Enzyme Activity

Activity of the furin enzyme is illustrated in Table 2 and Figure 2, and showed great lower activity of the furin enzyme with ND-T2DM (0.53 ± 0.06) and lower activity with pre-diabetes (0.85 ± 0.26) when compared with the healthy control group (1.70 ± 0.66). There was a highly significant difference between the three groups (P < 0.0001). In Table 3 and Figure 2 and Figure 3 show that significant difference between FEA and FABP4 (P = 0.0002) with moderate negative correlation (r = -0.507) in ND-T2DM group. Indicating that FEA has a

significant negative correlation with FABP4, suggesting a potential relationship between these two factors in the disease. In Table 4 and Figure 2 and Figure 3 show that no significant difference between FEA and FABP4 (P = 0.1664) with weak negative correlation (r = -0.199) in pre-diabetics group. The diagnostic precision was examined using ROC analyses, it was found that FEA demonstrates perfect discriminatory ability with an AUC of 1.000, using a cut-off value of ≤0.618. It achieves both 100% sensitivity and 100% specificity with ND-T2DM from a healthy control. FEA has an AUC of 0.865, with a cut-off value of ≤1.039. It achieves a sensitivity of 90% and a specificity of 75% with pre-diabetes from a healthy control. FEA performs well with an AUC of 0.986, using a cut-off value of ≤0.618. It achieves a sensitivity of 100% and a specificity of 92% with ND-T2DM from pre-diabetes this results in Table 6. This study and the results regarding the role of FEA were conducted for the first time in Iraq and the world as a whole with newly diagnosed type 2 diabetes patients and pre-diabetes patients, and no previous studies had been conducted on the role of FEA with newly diagnosed type 2 diabetes patients and pre-diabetes patients compared with healthy control group.

4.2.4. Serum level fatty acid binding Protein-4 (FABP-4)

The current investigation's findings showed that Serum (FABP-4) levels were high in patients with ND-T2DM (2312.78 ± 112.49), pre-diabetes (1511.87 ± 120.18) when compared with the healthy control group (1110.34 ± 321.23). There was a highly significant difference between the three groups (P < 0.001) in Table 2 and Figure 3. The diagnostic precision was examined using ROC analyses, it was found that FABP-4 has a good AUC of 0.975, using a cut-off value of >1640.642. It maintains a sensitivity of 90% and perfect specificity of 100% with ND-T2DM from a healthy control. FABP-4 has an AUC of 0.876, using a cut-off value of >1365.392. It achieves a perfect sensitivity of 100% and a specificity of 82.50% with pre-diabetes from a healthy control. FABP-4 exhibits good discrimination with an AUC of 0.926 and a cut-off value of >1809.796. It has a sensitivity of 82% and perfect specificity of 100% with ND-T2DM from pre-diabetes this results in Table 6. In addition to FABP-4 involvement in cellular lipid transport and fatty acid metabolism.[19]. FABP-4 has also been shown to participate in atherosclerosis. The pathogenic role of FABP-4 in atherosclerosis was confirmed by a report of [20] that serum levels of FABP-4 are associated with Atherosclerosis is a complex and multifactorial disease, with age, diabetes, dyslipidemia, insulin resistance, and inflammation as is known contributing factors. In Table 3 serum FABP-4 concentrations positive correlated with HOMA-IR (r = 0.458) in newly diagnosed T2DM. In Table 4 serum FABP-4 concentrations positive correlated with HOMA-IR (r = 0.13) in prediabetics. These findings agreement.[21]. They observed independent positive correlation of serum FABP-4 with BMI. Nevertheless, our data are in line with increasing evidence suggesting a prognosis value of FABP4 in a wide range of pathologies. The current study's findings showed that T2DM patients had greater FABP-4 levels than the control group did. The FABP-4 level independent predictor of T2DM, but not age, weight, or sex, is an according to a logistic regression analysis. Comparing patients with T2DM to the control group, there is a greater chance of glucose metabolism abnormalities .[22].

4.2.5. Insulin Resistance (IR)

Numerous techniques can be used to evaluate insulin resistance, an axial disease of the metabolic syndrome and a significant risk factor for type 2 diabetes.[23] Based on anthropometric and biochemical data, a number of indirect markers of insulin resistance have been proposed.[23] The results of the present study demonstrated that Homeostatic HOMA-IR levels were high in patients with ND-T2DM (1.53 ± 0.73) , pre-diabetes (0.98 ± 1.15) when compared with the healthy control groups (0.15 ± 0.05). There was a highly significant difference between the three groups (P < 0.001) in Table 5. The diagnostic precision was examined using ROC analyses, it was found that HOMA-IR performs well with an AUC of 0.984 and a cut-off value of > 0.28. It has a sensitivity of 98% and a specificity of 98.75% with ND-T2DM from a healthy control. HOMA-IR demonstrates excellent performance with an AUC of 0.991 and a cut-off value of > 0.22. It maintains both a sensitivity of 100% and a specificity of 91.25% with pre-diabetes from a healthy control. HOMA-IR has an AUC of 0.774, using a cut-off value of > 0.81. It maintains a sensitivity of 86% and a specificity of 82% with ND-T2DM from pre-diabetes this results in Table 6. The serum insulin concentration showed significant (P < 0.001) higher levels in the group of T2DM compared to the group of healthy controls group, HOMA-IR was significantly (P < 0.001) increased in the T2DM patients compared to its value in the healthy controls this finding also found by Estabraq A. Al-Wasiti et al., (2014).[12] While the results of the present study demonstrated that QUICKI levels were lower in the patients with ND-T2DM (0.37 ± 0.05), pre-diabetes (0.42 ± 0.05) when compared with the healthy control group (0.57 ± 0.09). There was a highly significant difference between the three groups (P < 0.001) in Table 5. The QUICKI was shown to have the advantages of being more reproducible and applicable to a larger range of insulin sensitivity when compared to other traditional insulin resistance indices. Research has demonstrated that QUICKI is one of the most reliable

and practical surrogate indices for assessing human insulin sensitivity. QUICKI and insulin action, however, do not significantly correlate, especially in older patients with poorly managed T2DM or those with moderate insulin resistance or reduced glucose tolerance.[24]

4.3. Study of Correlation

4.3.1. Correlation between FEA and FABP-4

Table 3 and Figure 2 and 3 show that significant difference between FEA and FABP-4 (P = 0.0002) with moderate negative correlation (r = -0.507) in ND-T2DM group. Indicating that FEA has a significant negative correlation with FABP-4, suggesting a potential relationship between these two factors in the disease. In Table 4 and Figure 2 and Figure 3 show that no significant difference between FEA and FABP4 (P = 0.1664) with weak negative correlation (r = -0.199) in prediabetics group.

4.3.2. Correlation between FEA, FABP4 and HOMA-IR

Table 3 shows that significant difference between FEA and HOMA-IR (P = 0.0248) with negative correlation (r = -0.317) in ND-T2DM group. Highly significant difference between FABP-4 and HOMA-IR (P = 0.0008) with positive correlation (r = 0.458) in ND-T2DM group.[25] In Table 4 show that no significant difference between FEA and HOMA-IR (P = 0.1738) with negative correlation (r = -0.195) in prediabetes group. While no significant difference between FABP-4 and HOMA-IR (P = 0.3671) with positive correlation (r = 0.13) in pre-diabetes group.

5. CONCLUSION

The effectiveness of the furin enzyme in newly diagnosed type.2 diabetes mellitus patients and pre-diabetes has not been previously studied in Iraq and even in the rest of the world. We conclude that measurements of the furin enzyme activity and fatty acid binding protein-4 (FABP-4) in serum, are indicators of risk factors for type.2 diabetes mellitus patients.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Acknowledgement

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9. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors' contribution

All authors took part in the conduct of the study, literatures search, data analysis and manuscript preparation. All authors approve the final draft of the manuscript.

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