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Serum and Urinary Fatty Acid-Binding Protein 1 Levels as Markers for Diabetic Nephropathy in Type II Diabetes Mellitus

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Abstract

Background: **Diabetic nephropathy is considered a main microvascular complication of diabetes mellitus (DM) that results in chronic renal failure. Fatty acid-binding protein 1 (FABP1) is expressed in renal proximal tubule cells and released into urine as a result of hypoxia triggered by decreased peritubular capillary blood flow, consequently urinary FABP1 is seen as a hopeful indicator for monitoring tubulointerstitial injury. There is increasing evidence that FABP1 plays a role in the development and progression of chronic kidney disease. This study aimed to assess the correlation of circulating plasma FABP1 level as well as its urinary level to nephropathy in patients with type 2 diabetes mellitus.** ***Methods:*** **Ninety patients were recruited, divided into 3 groups. They were investigated for glycemic and renal biomarkers, then FABP1 concentration was measured in their serum and urine samples. Bioinformatic analysis was done to explore the relation between FABP1 and DN.** ***Results:*** **The presence of DN was associated with increase in both serum and urinary FABP1. A serum FABP1 concentration of >243 ng/L was associated with DN, with a sensitivity of 93% and specificity of 90%, while urinary FABP1 concentration of >155.67 ng/L was associated with DN, with a sensitivity of 90% and specificity of 73%. Bioinformatic analysis revealed interactions between FABP1 and other kidney markers.** ***Conclusion:*** **This study proved that serum and urinary levels of FABP1 were significantly higher in the DN group than the normo-albuminuric groups reflecting the progression of the disease, thus they can be used as diagnostic biomarkers with significant sensitivity and specificity.**

Key words: Diabetic nephropathy, FABP1, bioinformatics

Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia due to either inadequate insulin secretion, defective insulin action or both. Type 2 diabetes mellitus (T2DM) is concerning the public health worldwide as a compelling cause of morbidity and mortality. Diabetic nephropathy (DN), is one of the major microvascular complications of diabetes, it is considered as the most common prominent cause of chronic kidney diseases (CKD) and end-stage renal disease (ESRD) [1, 2].

Diabetic nephropathy is usually diagnosed clinically based on the presence of a

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decreased estimated glomerular filtration rate (eGFR) and persistent albuminuria. However, there have been disputes about the significance of albuminuria (or the urinary albumin-to-creatinine ratio) as a diagnostic or prognostic tool, which has always been considered as the standard marker for early detection of DN. Early recognition of DN can impede the disease progression, here comes the need to find novel biomarkers that can recognize accurately diabetic patients who are more likely to develop DN and predict the disease progression [3-5].

Fatty acid-binding proteins (FABPs) are intracellular, cytoplasmic lipid chaperones that bind reversibly the hydrophobic ligands and transport them throughout cellular compartments. They are widely expressed in body tissues that are involved in fatty acid metabolism and comprise several isoforms [6, 7].

About nine genes coding the FABPs have been found in the human genome. Fatty acid-binding protein 1 (FABP1) (also called L-FABP) is chiefly expressed in renal proximal tubule cells and shed into urine when exposed to hypoxia resulting from the decreased peritubular capillary blood flow [8]. Urinary FABP1 is considered as a promising marker to monitor tubulointerstitial injury owing to its exclusive expression in the renal proximal tubular cells and its increased production in response to hypoxic tubular injury. Using the urinary protein/albumin and FABP1 in combination will help us evaluate glomerular and tubular injury separately in clinical practice [9].

Methods

- **Study population:**

Three groups were involved in this case-control study, each group involved 30 participants. The first group was type II diabetic patients with normo-albuminuria, the second group was type II diabetic patients with diabetic nephropathy either micro- or macroalbuminuria, while the third group was healthy individuals coming for regular check-up as a control group. Diabetic patients were selected according to the American Diabetes Association 2020 diagnostic criteria. Diabetic nephropathy was defined by random spot urinary albumin/creatinine ratio: microalbuminuria: 30 to 300 mg/g and macroalbuminuria: > 300 mg/g. All patients were recruited from SCU hospitals. They were age and sex matched.

Patient history and clinical information were collected by patients' interviewing or by reviewing their medical history. Laboratory work was performed at the Clinical Pathology Department, Suez Canal University Hospitals, Ismailia.

The research protocol was approved by the medical ethics committee of faculty of medicine Suez Canal University. The study aim was explained simply to the patients before they consented to participate.

- **Laboratory investigations:**

The glycemic markers (random blood sugar and glycated hemoglobin) and the kidney function markers (serum creatinine and urinary albumin to creatinine ratio) were investigated for the three groups. They were analyzed using Cobas 6000 automated auto-analyzer using kits supplied by Roche Diagnostics (Mannheim, Germany). Estimated glomerular filtration rate was calculated using the Modified Diet in Renal Disease (MDRD) equation.

- **Determination of serum and urinary levels of FABP1:**

Serum and urinary concentrations of fatty acid-binding protein 1 were measured by sandwich enzyme-linked immunosorbent assay technique using a kit for accurate

quantitative detection of Human FABP1 manufactured by Bioassay Technology Laboratory, Shanghai Korain Biotech Co., Ltd.

- **Bioinformatic analysis:**

KEGG database was used to find the metabolic pathways related to the pathogenesis of DN. Using the STRING database version 12 (https://string-db.org/), protein-protein interactions for FABP1 and other kidney indicators were identified. In order to obtain legend network, protein names were looked for using the "multiple proteins" search option under Homo sapiens.

Statistical Analysis:

All statistical analyses were performed using Statistical Package for Social Science (SPSS) program version 25.0.0.0.

Data normality was analyzed using the Kolmogorov-Smirnov test. Continuous, normally distributed variables were presented as mean ± standard deviation (SD), and non-normally distributed variables as median (interquartile range). Statistical differences in variables were compared by one way analysis of variance (ANOVA) for parametric variables followed by Bonferroni post hoc test and Kruskal-Wallis test was used for non-parametric variables. Categorical variables are presented as frequencies and/or percentages, and inter-group comparisons were analyzed using the chi-square test. Spearman's correlation coefficient analysis was used to examine the correlations and independence among serum and urinary levels of FABP1 and the values of other parameters. The relationship between the presence of DN (dependent variable) and serum FABP1 and urinary FABP1 concentrations (independent variable) was assessed using binary logistic regression analysis to estimate the odd's ratios with 95% confidence intervals. Receiver operating characteristic (ROC) curves were used to compare the diagnostic performance of serum and urinary levels of FABP1. Statistical significance was accepted if $p \leq 0.05$.

Results

1. The bioinformatic study:

KEGG database was used to obtain pathways related to DN pathogenesis. The AGE-RAGE signaling pathway for diabetic complications was the most related pathway (Figure 1). Advanced glycation end products (AGEs) are a complex group of chemicals that result from non-enzymatic glycation and oxidation of proteins, lipids, and nucleic acids. The main causes of this process include ageing and specific medical disorders like hyperglycemia. Among the best chemically described AGEs are N-epsilon-carboxy-methyl-lysine (CML), N-epsilon-carboxy-ethyl-lysine (CEL), and imidazolone. The main receptor for advanced glycation end products (AGEs), also known as the receptor for advanced glycation end products (RAGE or AGER), is a pattern recognition receptor that is a member of the immunoglobulin superfamily. AGE/RAGE signaling initiates many intracellular signal pathways, which subsequently stimulate NF-kappa B activity via the participation of MAPKs, NADPH oxidase, and protein kinase C. The presence of NF-kappa B increases the expression of several genes associated with atherosclerosis, including VCAM-1, tissue factor, VEGF, and RAGE, as well as pro-inflammatory cytokines such as IL-1, IL-6, and TNF-alpha. Additionally, JAK-STAT-mediated and PI3K-Akt-dependent pathways are induced by RAGE and contribute to cell death and proliferation, respectively. The hypoxia-mediated activation of Egr-1 was also shown to need the AGE-RAGE interaction. It has been proposed that the consequences of these signal transductions could be the

mechanism responsible for the onset of diabetes-related problems. To emphasis the significance of FABP1 signaling pathways, we made bioinformatic analysis using the STRING database. Protein-protein interactions found in this database have been determined through experimentation. Proteins are used as nodes in the legend images representing the interactions network, while protein-protein connections are represented by edges connecting nodes. The edges have been color-coded in accordance with Figure 2, where each color denotes evidence that points to a potential functional relationship between proteins. A PPI enrichment p-value of less than 1.0e-16 indicated interactions and biological connections between proteins FABP1, HAVCR1 (KIM-1), LCN2 (NGAL), AGT, B2M, RBP4, PTGDS (Beta-trace protein), CP, TF, TNF, CCL2, VEGFA, and other kidney indicators. The entry's first shell proteins were the twelve proteins. To ensure statistical validity of the enrichment test, "second shell" is set to "none" in the Network Settings box. Gene co-expression of renal markers was produced by the STRING database to emphasis their relationships. The scores produced depend on RNA expression patterns and co-regulation of proteins (Figure 3).

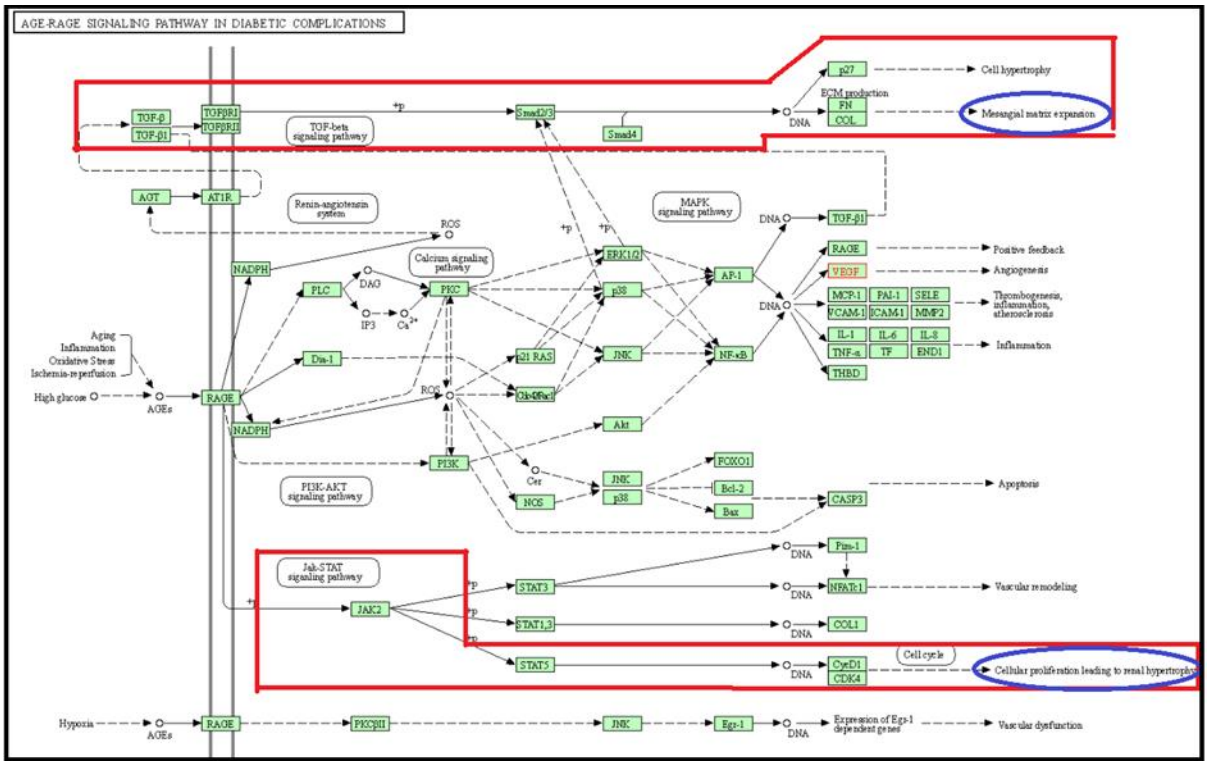

Figure 1: AGE-RAGE signaling pathway in diabetic complications produced by KEGG database.

AGEs; *advanced glycation end products*, RAGE; *receptor for advanced glycation end products.*

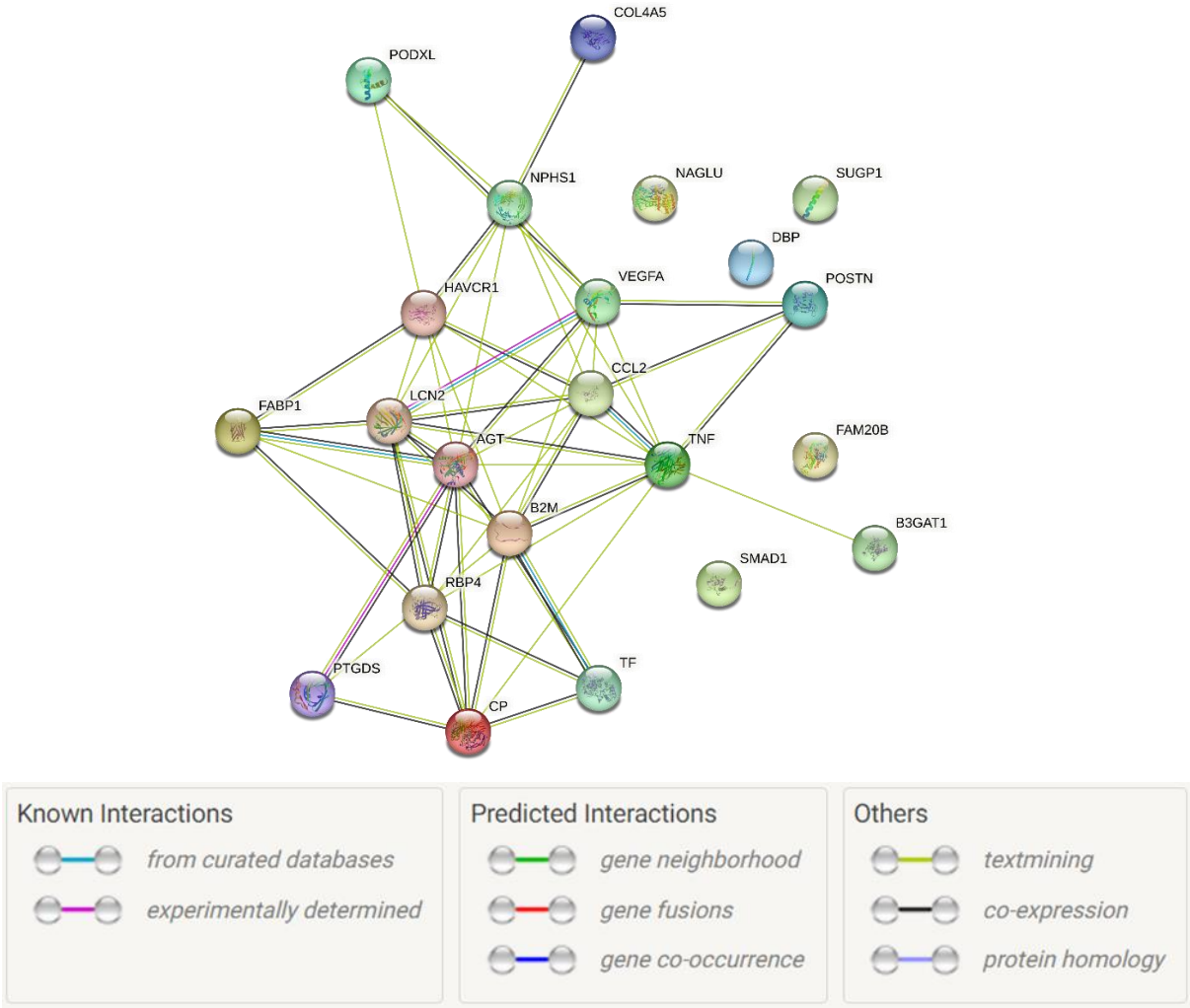

Figure 2: PPI of renal markers. A network diagram produced by STRING database where the nodes represent proteins and the edges show how proteins interact. This network has a disproportionately higher number of interactions than would be predicted from a set of proteins with the same size and degree distribution randomly selected from the genome. Such enrichment demonstrates that the proteins have at least indirect physiological relationships with p-value: < 1.0e-16. FABP1; *fatty acid binding protein 1*, HAVCR1; *Hepatitis A virus cellular receptor 1 (KIM-1)*, LCN2; *Neutrophil gelatinase-associated lipocalin*, AGT; *Angiotensin 1-4*, B2M; *Beta 2 microglobulin*, RBP4; *Retinol binding protein 4*, PTGDS; *Prostaglandin-H2 D-isomerase*, CP; *Ceruloplasmin*, TF; *Serotransferrin*, TNF; *Tumor necrosis factor*, CCL2; *C-C motif chemokine 2*, VEGFA; *Vascular endothelial growth factor A*.

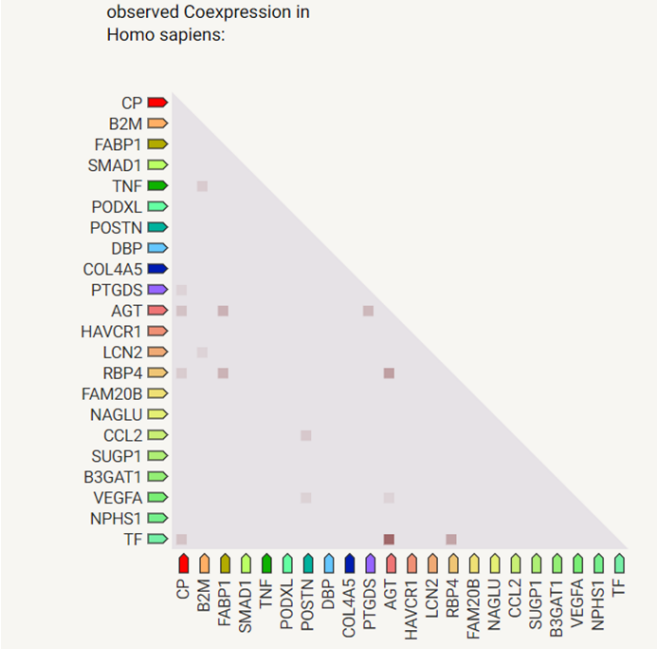

Figure 3: A heatmap produced by STRING database showing gene coexpression of renal markers. Coexpression scores based on RNA expression patterns, and on protein co-regulation provided by ProteomeHD. FABP1 and AGT with score 0.231, FABP1 and RBP4 coexpression with score 0.246

RBP4; *Retinol binding protein 4,* FABP1; *fatty acid binding protein 1,* AGT; *Angiotensin 1-4.*

2. Demographic and clinical characteristics:

Table 1 demonstrates the demographic and characteristics of the study subjects. The three groups under study were all matched in both age and gender. The duration of T2DM showed a statistical significance among the diabetic groups, while the type of treatment did not as shown in table 1.

Table 1: Demographic and clinical characteristics of the study group

		Control group (normo-albuminuric) (n=30)	DM group (normo-albuminuric) (n=30)	DN group (micro- and macro-albuminuric) (n=30)	P value
Mean age + SD (years)		52.63 ± 3.93	54.60 ± 6.055	55 ± 6.046	0.202*
Gender Number (%)	Male	12 (40 %)	13 (43.3 %)	14 (46.7 %)	0.873^
	Female	18 (60 %)	17 (56.7 %)	16 (53.3 %)	
Duration of diabetes (mean ± SD) (years)		-	10.9± 4.2	14.1 ± 2.8	**0.001#**
Type of treatment Number (%)	Oral hypoglycemics	-	16 (53.3%)	10 (33.3%)	0.118^
	Insulin therapy	-	14 (46.7%)	20 (66.7%)	

*****One way ANOVA test.* *^ Chi² test.*

#Student's T test.

SD: standard deviation

Statistical significance was accepted if p ≤0.05.

3. **The biochemical characteristics** of the patients stratified by nephropathy status are given in Table 2. The glycemic markers showed no statistical significance between the diabetic subjects whether with normo-, micro- or macroalbuminuria. The renal biomarkers were higher with a statistical significance in the DN group compared to both the DM group with normo-albuminuria and the control group.

Serum and urinary fatty acid-binding protein 1: There were significant differences in urinary FABP1 levels (p <0.01) across the three study groups, while the main difference in serum FABP1 was detected between overt nephropathic and normoalbuminuric subjects (p <0.01).

Table 2: Biochemical characteristics of study subjects:

	Control group (n=30)	Diabetic group (normo-albuminuric) (n=30)	Diabetic Nephropathy group (micro- and macr albuminuric) (n=30)	*P*-value
RBS (mg/dL) mean ± SD	89.80 ± 12.181	274.47 ± 76.717	237.07 ± 74.351	**< 0.01 *ab**
Glycated hemoglobin (HbA1c) % mean ± SD	4.62 ± 0.4	9.27 ± 2.6	9.09 ± 1.77	**< 0.01*ab**
Serum Creatinine (mg/dl) mean ± SD	0.7 ± 0.15	0.8± 0.18	1.23 ± 0.49	**< 0.01*bc**
UACR (mg/g creatinine) mean ± SD	4.757 ± 2.44	10.43 ± 5.02	180.27 ± 136.6	**< 0.01*bc**
eGFR (mL/min) mean ± SD	105.47 ± 5.374	95.40 ± 16.531	65.70 ± 25.834	**< 0.01*bc**
S. FABP1 (ng/L) Median and IQR	125 (117.2-139.2)	195.5 (170.6-214.3)	405.4 (289.39-538.72)	**< 0.01*bc#**
U. FABP1 (ng/L) Median and IQR	72.8 (70-75.3)	112.5 (92.3-189.3)	243.4 (175-320.7)	**< 0.01*abc#**

RBS: random blood sugar
UACR: urine albumin/creatinine ratio
eGFR: estimated glomerular filtration rate
S. FABP1: serum fatty acid-binding protein 1
U. FABP1: urinary fatty acid-binding protein 1
SD: standard deviation
IQR: inter-quartile range
p- value: probability value
p-values were calculated by one-way ANOVA test followed by the Bonferroni post hoc test.
 # p-values were calculated by Kruskal-Wallis test.
***Statistical significance was accepted if p <0.05.*
a: between control and diabetic groups.
b: between control and diabetic nephropathy groups.
c: between diabetic and diabetic nephropathy groups.

In table 3 Spearman's correlation analysis revealed that serum and urinary FABP1 levels were negatively correlated with eGFR. They showed strong positive significant correlation to the UACR. On the other hand, there was no significant correlation to the glycemic markers.

Binary Logistic regression of serum and urinary FABP1 to predict DN revealed that the presence of DN was associated with increase in both serum and urinary FABP1.

Table 3: Correlation between serum, urinary levels of FABP1, and biochemical parameters among the diabetic groups

	S. FABP1		U. FABP1	
	R	**P – value**	**R**	**P - value**
S. creat (mg/dL)	0.375	**0.003***	0.299	**0.020***
UACR (mg/g)	0.731	**< 0.01***	0.747	**< 0.01***
HbA1c %	-0.063	0.630	-0.141	0.282
RBS (mg/dL)	-0.236	0.069	-0.283	0.029
eGFR (mL/min)	-0.440	**< 0.01***	-0.370	**0.004***

RBS: random blood sugar.
UACR: urine albumin/creatinine ratio.
eGFR: estimated glomerular filtration rate.
S. FABP1: serum fatty acid-binding protein 1.
U. FABP1: urinary fatty acid-binding protein 1.
p- value: probability value.
r: correlation coefficient.
Correlation studies are done by Spearman's correlation analysis. Statistical significance was accepted if p ≤0.05.

4. Receiver Operating Characteristic curve:

The Receiver Operating Characteristic (ROC) curve was used to detect diabetic nephropathy in T2DM patients. It revealed an area under the curve (AUC) of 0.969 for S. FABP1. A serum FABP1 concentration of >243 ng/L was associated with diabetic nephropathy, with a sensitivity of 93% and specificity of 90%, figure 4. While U. FABP1 had an AUC of 0.902. A urinary FABP1 concentration of >155.67 ng/L was associated with diabetic nephropathy, with a sensitivity of 90% and specificity of 73%, figure 5.

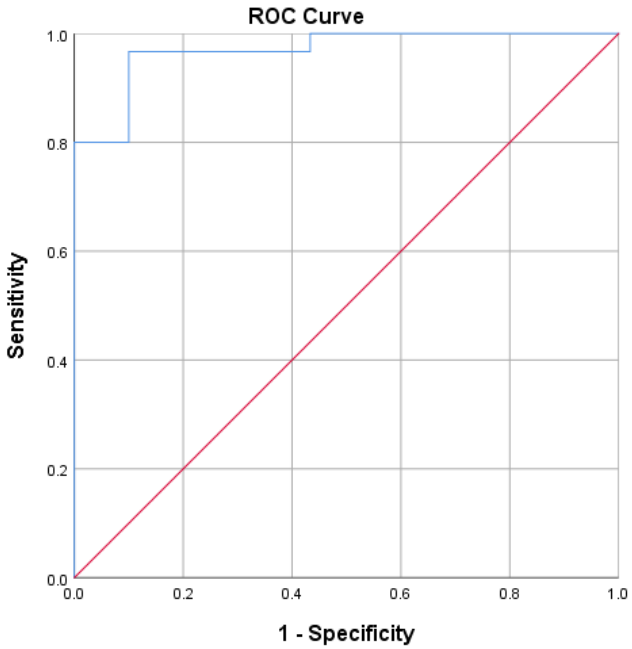

Figure 4: ROC curve showing the diagnostic value of S. FABP1 to detect diabetic nephropathy

ROC: Receiver Operating Characteristic curve, S.FABP1: serum fatty acid-binding protein 1.

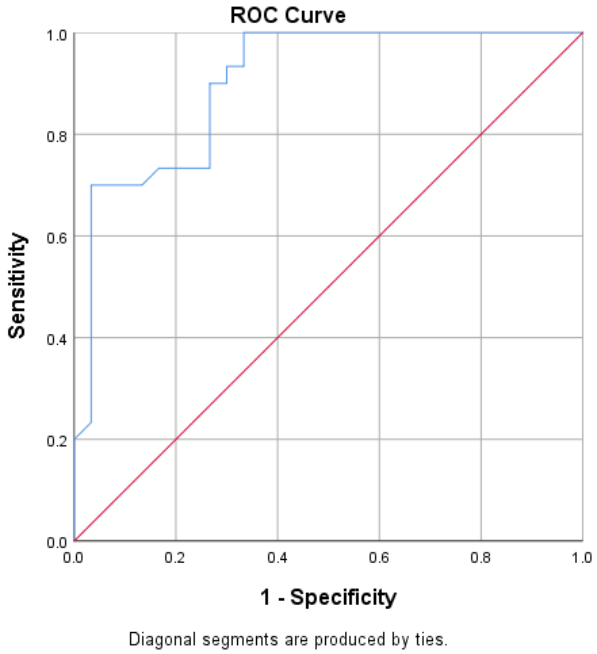

Figure 5: ROC curve showing the diagnostic value of U. FABP1 to detect diabetic nephropathy

ROC: Receiver Operating Characteristic curve, U.FABP1: urinary fatty acid-binding protein 1.

Discussion

This case control study was conducted to assess the correlation of the serum and urinary levels of FABP1 to diabetic nephropathy in type II diabetic patients aiming to discover novel biomarkers that help to follow up the progression of the disease.

In the present study the 3 groups were age-matched. They were comparable to each other in gender as well. In contrast to the duration of diabetes mellitus that showed an evident statistical significance among the diabetic groups, denoting the increased risk of developing renal insult with longer duration of type 2 diabetes mellitus. This came along with Rabie et al. who found that the duration of diabetes in diabetic patients with macroalbuminuria was longer than in micro-albuminuric diabetic patients with a statistically significant difference. Similarly, Kondaveeti et al. noticed that there was a direct correlation between the duration of diabetes and the development of microalbuminuria, as a result of prolonged exposure to hyperglycemia as well as deposition of advanced glycated end products [10, 11].

The current study showed that the glycemic markers had no statistical significance among the diabetic groups. However, the renal biomarkers were notably higher in the DN group than the normo-albuminuric DM group and control group with the eGFR progressively declining in the DN group than the other groups. On the contrary, Tsai et al. found that the patients with overt nephropathy had higher HbA1c. Hassaan et al. also reported that fasting blood glucose levels and HbA1c had higher mean values among diabetic nephropathy patients than control group and diabetic group without diabetic nephropathy, and Rabie et al. noticed that the fasting blood glucose and HbA1c were significantly higher in patients with DN (micro-albuminuric and macro-albuminuric diabetic patients) compared with normo-albuminuric diabetic patients and the control group. This may be attributed to their larger study groups with more macro-albuminuric patients. However, these studies agreed with the current study in regards to the renal biomarkers [10, 12, 13].

Serum and urinary levels of fatty acid-binding protein 1 were significantly higher in the DN group compared to the other groups. which denoted that they can be considered as biomarkers for renal insult among diabetic patients. This coincided with Tsai et al, who found that the mean plasma FABP1 level increased parallel to the severity of nephropathy. Furthermore, Kare et al. affirmed the significant elevation of U. FABP1 in the micro- and macro-albuminuric group compared to the normo-albuminuric groups. Kamijo-Ikemori A et al., also reported that urinary FABP1 levels were progressively increased in subjects with micro- or macro-albuminuria [13-15].

In the present study, serum and urinary FABP1 levels were negatively correlated with eGFR. Serum FABP1 level showed positive significant correlation to the duration of diabetes, serum creatinine and UACR. On the other hand, there was no significant correlation to neither the RBS nor HbA1c.

These results came in agreement with Tsai et al., who revealed that plasma FABP1 level was positively correlated with serum creatinine, and negatively correlated with eGFR. In disagreement with our results, Hassaan et al. stated that there was significant positive correlation between FABP1 and the glycemic markers, most probably due to their larger macro-albuminuric DN group. However, they

agreed with our study in regards to the positive correlation between S. FABP1 level, serum creatinine, UACR and diabetes duration [12, 13].

Urinary FABP1 level showed positive correlation to the duration of diabetes, serum creatinine, and UACR. But there was no significant correlation with the glycemic markers.

Like our study, Rabie et al. reported that there was a positive correlation between U. FABP1 and markers of DN such as UACR. Also, Kare et al. stated that there was a statistically significant positive correlation between U. FABP1 levels and duration of diabetes, serum creatinine and urinary UACR and a negative correlation with eGFR. This correlation between U. FABP1 and eGFR supports the use of U. FABP1 as a marker of degree of renal damage as estimated by GFR [10, 14].

When assessing the role of serum and urinary FABP1 concentrations as predictors for the presence of DN, both S. FABP1 and U. FABP1 concentrations were significantly associated with diabetic nephropathy and increasing levels of S. FABP1 and U. FABP1 were independently associated with diabetic nephropathy.

This came in agreement with Tsai et al., that reported that the increasing levels plasma FABP1 showed a significant linear trend and was independently associated with diabetic nephropathy. Hassaan et al., reported that the multivariate analysis for predictors of diabetic nephropathy showed significant difference between the study groups regarding FABP1, thus it was considered a statistically significant predictor for diabetic nephropathy among diabetic patients [12, 13].

Concerning the effectiveness of FABP1 as a diagnostic biomarker for diabetic nephropathy, S. FABP1 had a sensitivity of 93% and specificity of 90% at a cut-off value >243 ng/L with an area under the curve (AUC) 0.97. On the other hand, U. FABP1 had 90% sensitivity and a 73% specificity at a cut-off value >155.67 ng/L and AUC 0.90.

These results were supported by the findings of Thi et al., that showed that the AUC of U. FABP1 was significantly higher than the AUC of UACR. Also, Rabie et al., reported that U. FABP1 exhibited 87% sensitivity and 83% specificity in prediction of incidence of diabetic nephropathy. Tsai et al. documented the usefulness of plasma FABP1 as a marker for diabetic kidney disease with a sensitivity of 75.3% and specificity of 75.6%. While Hassan et al., stated that serum FABP1 exhibited 87% sensitivity and 83% specificity in prediction of incidence of diabetic nephropathy [10, 12, 16].

Lastly, serum and urinary levels of FABP1 showed a significant increase in the DN group than the normo-albuminuric groups reflecting the progression of diabetic nephropathy, thus they can be used as diagnostic biomarkers with significant sensitivity and specificity.

Conclusion

Serum and urinary levels of fatty acid - binding protein 1 (FABP1) observed in patients with diabetic nephropathy were higher compared to the normo-albuminuric groups making them good diagnostic biomarkers with significant sensitivity and specificity. They accurately reflected the progression of diabetic nephropathy in type 2 diabetes, as well.

Serum and urinary FABP1 are advisable novel biomarkers for follow up of diabetic nephropathy progression.

List of abbreviation:

DM: Diabetes mellitus

DN: Diabetic nephropathy
FABP1: Fatty acid-binding protein 1
T2DM: type 2 diabetes mellitus
CKD: chronic kidney diseases
ESRD: end-stage renal disease
eGFR: estimated glomerular filtration rate
UACR: urinary albumin to creatinine ratio

References

1. Aldukhayel A. Prevalence of diabetic nephropathy among Type 2 diabetic patients in some of the Arab countries. International journal of health sciences. 2017;11(1):1.
2. Baynes H. Classification, pathophysiology, diagnosis and management of diabetes mellitus. J diabetes metab. 2015;6(5):1-9.
3. Lerma EV. Diagnosis 101: diabetic kidney disease. Oxford University Press; 2022. p. 1797-9.
4. Selby NM, Taal MW. An updated overview of diabetic nephropathy: Diagnosis, prognosis, treatment goals and latest guidelines. Diabetes, Obesity and Metabolism. 2020;22:3-15.
5. Campion CG, Sanchez-Ferras O, Batchu SN. Potential role of serum and urinary biomarkers in diagnosis and prognosis of diabetic nephropathy. Canadian journal of kidney health and disease. 2017;4:2054358117705371.
6. Kimura I, Ichimura A, Ohue-Kitano R, Igarashi M. Free fatty acid receptors in health and disease. Physiological reviews. 2019.
7. Schrezenmeier E, Barasch J, Budde K, Westhoff T, Schmidt-Ott K. Biomarkers in acute kidney injury–pathophysiological basis and clinical performance. Acta physiologica. 2017;219(3):556-74.
8. Kashani K, Cheungpasitporn W, Ronco C. Biomarkers of acute kidney injury: the pathway from discovery to clinical adoption. Clinical Chemistry and Laboratory Medicine (CCLM). 2017;55(8):1074-89.
9. Teo SH, Endre ZH. Biomarkers in acute kidney injury (AKI). Best practice & research Clinical anaesthesiology. 2017;31(3):331-44.
10. Rabie AA, Ragheb AT, Serag SA, Mohammed WF. Liver-type fatty acid-binding protein as an early biomarker of nephropathy in type-2 diabetes. Menoufia Medical Journal. 2020;33(3):760-5.
11. Kondaveeti SB, Kumaraswamy D, Mishra S, Kumar A, Shaker IA. Evaluation of glycated albumin and microalbuminuria as early risk markers of nephropathy in type 2 diabetes mellitus. Journal of clinical and diagnostic research: JCDR. 2013;7(7):1280.
12. Hassaan MMM, Elsayed AME, Deraz HA, Hussein AG. Fatty Acid Binding Protein (1 & 2) as Markers of Diabetic Nephropathy in Elderly Patients with Type 2 Diabetes Mellitus. The Egyptian Journal of Hospital Medicine. 2022;89(1):5778-83.
13. Tsai I-T, Wu C-C, Hung W-C, Lee T-L, Hsuan C-F, Wei C-T, et al. FABP1 and FABP2 as markers of diabetic nephropathy. International journal of medical sciences. 2020;17(15):2338.
14. Kare PK, Garg M. Assessment of Urinary Liver-Type Fatty Acid Binding Protein (LFABP) Levels in Type 2 Diabetes Mellitus Patients with Nephropathy. Journal of Clinical & Diagnostic Research. 2019;13(1).
15. Kamijo-Ikemori A, Sugaya T, Ichikawa D, Hoshino S, Matsui K, Yokoyama T, et al. Urinary liver type fatty acid binding protein in diabetic nephropathy. Clinica Chimica Acta. 2013;424:104-8.
16. Thi TND, Gia BN, Le Thi HL, Thi TNC, Thanh HP. Evaluation of urinary L-FABP as an early marker for diabetic nephropathy in type 2 diabetic patients. Journal of Medical Biochemistry. 2020;39(2):224.