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Accuracy of Fetuin-A in Predicting Hemodialysis in Diabetic and Non-Diabetic Patients

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ABSTRACT
Background: Diabetes mellitus (DM) has routinely been described as a metabolic disorder characterized by hyperglycemia that develops because of defects in insulin secretion, insulin action, or both
Aim: To explore the accuracy of fetuin in predicting hemodialysis in diabetic and non-diabetic patient.
Patients and methods: This case-control control trial was performed at the Internal Medicine Department, Minia University Hospital during the period from June 2024 to February 2025. The study included a total of 45 subjects who were classified to group (I) included 15 healthy subjects (non-diabetic and not on hemodialysis) served as control group (Control group), group (II), included 15 non-diabetic patients on hemodialysis (HD group) and group (III) included 15 diabetic patients on hemodialysis (DM+HD group).
Results: The sensitivity of using Fetuin-A to predict hemodialysis was 93.3%, specificity was 72%, positive predictive value was 66.7%, negative predictive value was 94.7% and accuracy was 80%. The sensitivity of using Fetuin-A to predict hemodialysis among patients with diabetes was 93.3%, specificity was 73.3%, positive predictive value was 77.8%, negative predictive value was 91.7% and accuracy was 83.3%
Conclusion: Fetuin-A was significantly higher in diabetic patients on hemodialysis compared to non-diabetic patients on hemodialysis and the normal healthy subjects, Furthermore, fetuin-A is reliable and accurate biomarker in predicting hemodialysis in diabetic and non-diabetic patients.

Keywords: Fetuin-A, Hemodialysis, Diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) has routinely been described as a metabolic disorder characterized by hyperglycemia that develops because of defects in insulin secretion, insulin action, or both. Type 2 diabetes mellitus (T2DM) encompasses individuals who have insulin resistance (IR) and usually relative (rather than absolute) insulin deficiency (1). T2DM has emerged as amajor worldwide public health problem; according to Diabetes Atlas (7th ed.), the global prevalence of diabetes is estimated at 415 million (8.8%), which is predicted to increase to 642 million in the next 25 years (2).

Diabetic kidney disease occurs in diabetic patients and reduced kidney function that can be from many diverse causes and it has been estimated that about 10-30% of type 1 DM and 15- 40% of type 2 DM patients suffer from diabetic kidney disease (3).

Biochemical markers have a vital role in accurate diagnosis and also for assessing risk and adopting therapy that improve clinical outcome. Fetuin-A is a hepatically synthesized 62-kDa glycoprotein belongs to the cystatin family of the proteinase inhibitors, it inhibits insulin receptor tyrosine kinase activity and it is directly associated with insulin resistance and dyslipidaemia (4).

Fetuin-A [also referred to as α-2 Heremans Schmid glycoprotein (AHSG)] is a multifunctional glycoprotein which is exclusively secreted from the hepatocytes in human (5). For a long time, fetuin-A has been considered to play a critical role in the safety from vascular calcification by solubilizing calcium and phosphorus in serum (6). It also became pronounced that fetuin-A could inhibit insulin receptor substrate-1 and stimulated a lower-grade inflammation, which led to IR (7). Epidemiological research confirmed that serum fetuin-A became associated with IR and its comorbidities, including metabolic syndrome (MetS) and T2DM (8).

This study attempts to explore the accuracy of fetuin in predicting hemodialysis in diabetic and non-diabetic patient.

PATIENTS AND METHODS

This case-control control trial was performed at the Internal Medicine Department, Minia University Hospital during the period from June 2024 to February 2025. The study included a total of 45 subjects who were classified to group (I) included 15 healthy subjects (non-diabetic and not on hemodialysis) served as control group (Control group), group (II), included 15 non-diabetic patients on hemodialysis (HD group) and group (III) included 15 diabetic patients on hemodialysis (DM+HD group).

Inclusion criteria: Adult subjects (Age 20-60 year) of both genders were included.

Exclusion criteria were; patients with chronic liver diseases, autoimmune diseases and those who receive drugs that increase blood sugar eg. corticosteroids.

All participants were subjected to the following:

Full medical history included age, sex, body mass index (BMI), comorbidities, current medications (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, other antihypertensives, corticosteroids and other immunosuppressants). Full clinical examination; anthropometric measurement including waist and hip circumference in cm, weight in kg, and height in cm; BMI calculated asweightin kilograms divided by square of height in meters Estimation of biochemical variables (fasting and postprandial glucose, total cholesterol, triglycerides, low-density lipoprotein-cholesterol (LDL-c), highdensity lipoprotein-cholesterol (HDL-c), urea, creatinine clearance, and 24-h urinary protein) after an overnight fasting of at least 10 h. Concerning laboratory investigations, random blood sugar, HbA1C, urine analysis, blood urea and creatinine and lipid profile were determined using commercial kits. Serum Fetuin-A was measured in samples by Sandwich ELISA Detection method using the kits of SinoGeneClon Biotech Company LTS (HangZhou, China). Serum Fetuin-A was measured before and after hemodialysis for group II and III. Homeostasis model assessment for IR (HOMA-IR) values were calculated based on fasting value of plasma glucose and insulin according HOMA model formula: HOMA-IR=fasting insulin (mlU/l) ×fasting glucose (mg/dl)/405. IR was arbitrarily considered altered when it wasmore than

Ethical considerations: The study protocol and all procedures were approved by the ethical committee of the Minia Faculty of medicine. A verbal consent was taken from patients before getting them involved in study. The steps, the aims, the potential benefits and hazards, all were discussed with the patients

Statistical analysis

Statistical Package for Social Science (SPSS) version 21 was used. Results are expressed as means ± SD for quantitative data and by No. (%) for qualitative data. Analyses were done for quantitative variables using one-way ANOVA test for comparison between three groups and post Hoc Duncan's correction between each two groups. However, Chi square test was used for qualitative data between groups. Correlation between two quantitative variables was done by using Pearson's correlation coefficient and for non-parametric variables using Spearman's rho correlation test. Probability level (P. value) was assumed significant if < 0.05 and highly significant if < 0.01.

RESULTS

Table 1: Comparison between the studied groups as regards personal data

	Group A (n=30)	**Group B (n=30)**	**Group C (n=20)**	**Test**	**p**
Age				F= 1.651	0.199
Range	30 – 60	29 – 61	32 – 61		
Mean ± SD	44.63 ± 8.38	47.87 ± 9.57	43.45 ± 9.49		
Sex				χ^2= 1.418	0.492
Female	14 (46.7%)	17 (56.7%)	8 (40%)		
Male	16 (53.3%)	13 (43.3%)	12 (60%)		

SD: Standard deviation, χ^2: Chi-square test, F: one-way ANOVA test, p: p-value for comparing between different groups, *: Statistically significant at $p \leq 0.05$

There was no statistically significant difference between the studied groups regarding age as shown in Table **1**

Table 2: Receiver operating characteristic curve for Fetuin-A to predict hemodialysis (n=80)

	AUC	**p**	**Cut-off value**	**Sensitivity**	**Specificity**	**+PV**	**-PV**	**Accuracy**
Fetuin-A	0.881	<0.001*	77.0	93.3	72.0	66.7	94.7	80.0

AUC: area under curve, +PV: positive predictive value, -PV: negative predictive value
The sensitivity of using Fetuin-A to predict hemodialysis was 93.3%, specificity was 72%, positive predictive value was 66.7%, negative predictive value was 94.7% and accuracy was 80% as shown in **Table** .

Table 3: Receiver operating characteristic curve for Fetuin-A to predict hemodialysis among patients with diabetes (n=60)

	AUC	p	Cut-off value	Sensitivity	Specificity	+PV	-PV	Accuracy
Fetuin-A	0.842	0.001*	77.0	93.3	73.3	77.8	91.7	83.3

AUC: area under curve, +PV: positive predictive value, -PV: negative predictive value
The sensitivity of using Fetuin-A to predict hemodialysis among patients with diabetes was 93.3%, specificity was 73.3%, positive predictive value was 77.8%, negative predictive value was 91.7% and accuracy was 83.3% as shown in
Table .

DISCUSSION

In our study, there was no statistically significant difference between the study groups regarding age
However, **Al Akad et al.** foundsignificant differences were noticed among groups regarding age <0.01, and no significant sex (p=0.70), BMI (p=0.98) and duration of dialysis (p=0.92) (**9).**
In our study, the sensitivity of using Fetuin-A to predict hemodialysis was 93.3%, specificity was 72%, positive predictive value was 66.7%, negative predictive value was 94.7% and accuracy was 80%
In our study, the sensitivity of using Fetuin-A to predict hemodialysis among patients with diabetes was 93.3%, specificity was 73.3%, positive predictive value was 77.8%, negative predictive value was 91.7% and accuracy was 83.3%
To our knowledge, our paper is the first one to measure sensitivity, specificity, positive predictive value, negative predictive value and accuracy in literature.
In the study of **Al Akad et al.,** there were significant differences among the three studied groups in Fetuin-A (the highest level was in DM+HD group followed by HD group however the lowest level was noticed in the control group, p< 0.01). Also, patients group (group II and group III) had significantly higher Fetuin-A level compared to the control group (p< 0.01) (**9).**
In line with those findings, increased fetuin-A in pre-diabetic patients is associated with increased progression to diabetes and decreased reversal to normoglycemia and is also used as a predictor of adverse glycemic outcomes in prediabetes **(10).**
Furthermore, a recent study by **Perez-Sotelo et al.,** found that Fetuin-A can be considered as a biomarker of nutritional status, and malnutrition in CKD patients **(11).**
El-Batch et al. found a significant increase in serum fetuin-A levels in microalbuminuric patients compared to normoalbuminuric patients and to control groups. These results may be explained by the role of fetuin-A in mediating insulin resistance, lipid profile abnormalities and endothelial dysfunction which underlie the association between fetuin-A and abnormal albuminuria (**12).**
Lorant et al. investigated Fetuin-A Levels in Patients with Type 2 diabetes and peripheral arterial disease and found Type 2 diabetes–Peripheral arterial disease PAD subjects (399 ± 155 μg/ml) had significantly higher fetuin-A levels than type 2 diabetes–non-PAD subjects (247 ± 42; P < 0.001). In NGM-PAD subjects (376 ± 144), fetuin-A was significantly higher than in type 2 diabetes–non-PAD subjects (P < 0.001) **(13).**

CONCLUSION

Fetuin-A was significantly higher in diabetic patients on hemodialysis compared to non-diabetic patients on hemodialysis and the normal healthy subjects, Furthermore, fetuin-A is reliable and accurate biomarker in predicting hemodialysis in diabetic and non-diabetic patients.

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