

# Estimation of Retinol Binding Protein as A Near Biomarker of Diabetic Nephropathy in type 2 Diabetic Mellitus Patients at Al-Najaf Province

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## Abstract

**Introduction:** Diabetic nephropathy is among the most important microvascular consequences of diabetes (DN). It is marked by a higher excretion rate of urine albumin, a blood pressure rising, and a deterioration in renal function, all of which contribute to end-stage renal disease. Insulin resistance and obesity have been linked to retinol binding protein (RBP), a newly identified adipocytokine. Peripheral tissues, such as the liver and adipose tissues, produce retinol binding protein. **Aim of study:** The aim of this study was to investigate the potential utility of retinol binding protein (RBP) as a biomarker for type 2 diabetic nephropathy detection. **Methodology:** Patients with long-term T2DM and healthy control subjects were recruited for this case control research. 50 patients (26 males and 24 female) selected from renal and diabetic centers in AL-Saader medical city in the period from March 2022 to May 2022. **Results:** The findings of these studies indicated a significant increase in biochemical parameters in DN patient other than healthy control. **Conclusion:** This research found that the following in persons with type 2 diabetes, RBP levels can be utilized as a biomarker for the early diagnosis of diabetic nephropathy. Further studies should be conducted to cover a larger number of patients and to approve the findings.

**Keywords:** Diabetic Mellitus, Nephropathy.

## 1. Introduction

Diabetic nephropathy is one of the most important microvascular consequences of diabetes (DN). It is marked by an increased rate of urine albumin excretion, a rise in blood rise, and a deterioration in renal function, all of which contribute to chronic kidney disease (Tonelli et al., 2012). Furthermore, these people have a high risk of developing cardiovascular disease, which gets worse as their renal function declines (Fiseha and Tamir, 2016). The prevalence of type 2 diabetes mellitus has made DN a rapidly expanding issue in developing nations (T2DM) (Miranda et al., 2016). A 2008 study found that DN, which accounts for 32.1% of cases, is the most prevalent chronic complication among Saudi Arabian people with type 2 diabetes (Alwakeel et al., 2008). Currently, alterations in albuminuria are thought to be a sign of DN start or progression. However, even if urine albumin ranks are within standard limits, some diabetic individuals experience severe renal pathological alterations and kidney function deterioration, proving that albuminuria is not a reliable marker for the early detection of DN. The morbidity and mortality of diabetic patients are impacted by diabetic nephropathy (DN) and affects 20%–40% of all people with diabetes mellitus (Korish et al., 2015). Renal function, rather than glomerular lesions, interacts better in cases of chronic diabetic nephropathy with the severity of tubule-interstitial damage., The search for tubular biomarkers should

continue to identify diabetic nephropathy patients, according to the study. (Thomas et al., 2005). Finding alternative biomarkers that could be utilized to quickly and accurately diagnose the development of diabetic nephropathy has garnered increasing interest. Several researchers have proposed biomarkers that reflect tubular damage in this regard (Tramonti and Kanwar, 2013).

Retinoid (vitamin A and its derivatives) interact with a protein termed a retinol binding protein to exert their physiological effects (RBP). Retinol is a type of vitamin A that is delivered to the tissues in a 1:1 combination. Due to their equimolar concentrations in the circulation, plasma RBP concentrations and plasma retinol have a strong correlation (El-Esawy et al., 2019).

Insulin resistance and obesity have been linked to RBP, a lately identified adipo-cytokine. Peripheral tissues, such as the liver and adipose tissues, produce retinol binding protein. (Shoji et al., 2005). Plasma RBP concentrations are highly correlated as a result of their equimolar concentrations in the circulation. We wanted to be the first to assess serum RBP levels in patients with DN in order to answer the question concerning its usefulness as a marker in this study.

## 2. Methodology

**Patient group:** 50 patients (26 males and 24 female) selected from renal and diabetic centers in in AL-Saader medical city in the period from March 2022

to May 2022.

Healthy control: These group consisted of 50 health volunteers (30 men's and 20 women's). They were same age and gender.

Inclusion criteria: In this case-control study, patients with long-term T2DM and healthy controls were both included.

Exclusion criteria: When other causes of renal illness were suspected, patients with T2DM were eliminated. Therefore, one of the exclusion requirements was the existence of:

- Hematuria.
- Renal inefficiency with unknown cause
- UTI infections
- A history of renal failure that worsened quickly.
- Glomerulo-nephritis
- renal polycystic diseases

Methods: All the biochemical tests used in this study confirmed by automated chemistry MINDRY analyzer, whereas the RBP was determined by using ELISA technique.

Statistical analysis: means, standard Deviation (SD), or frequency (number of cases) and percentage

these terms used statistically to describe the Data. P value less than 0.05 will be considered statistically significant. The statistical software package SPSS will be used for all calculations.

### 3. Result and Discussion

In a study, participants' demographics for type 2 diabetes mellitus patients (n = 50) and healthy controls (n = 50) are displayed in (Table 1). The result shows highly significant (P. <0.001) differences in body mass index, sex, and age between the patients and the controls. Patients with type II DM were dispersed as 26 males and 24 females with a usual age of 51.17 ± 10.8 (SD) year, As indicated in figure 1, healthy control subjects were split evenly between 30 men and 20 women, with an average lifespan of 32.1 12.7 (SD) years. Diabetes has a microvascular side effect known as diabetic nephropathy (DN) that manifests as an increase in urinary albumin excretion (UAE) rate and impaired renal function (Selby and Taal, 2020).

Table (1): socio-demographic characters of patient and healthy control.

Variable		Patient Mean ± SD	Control Mean ± SD	P-value
Age		51.18 ± 10.8	32.1 ± 12.7	<0.001
Sex	Male N (%)	26 (52)	30 (60)	Chi-square <0.001
	Female N (%)	24 (48)	20 (40)	
BMI(Kg/m <sup>2</sup> )		31.6 ± 7.8	26.3 ± 4.1	<0.001

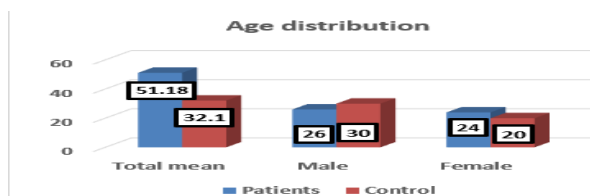


Figure 1: Age distribution among study participants.

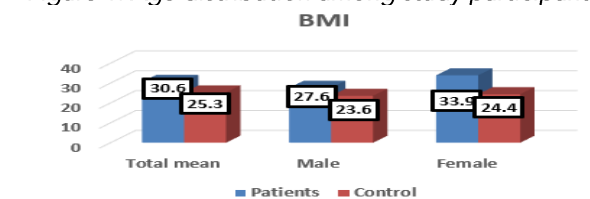


Figure 2: The body mass index (kg/m<sup>2</sup>) of the participants.

(Table 2), shows blood glucose level laboratory assessment data for the studied group. FBS, HbA1C, urea, and creatinine are all tested. In individuals with type II diabetes, all were noticeably higher than in the healthy control group. Chronic kidney disease is now most commonly caused by DN. It is also one of the most serious long-term problems for diabetic individuals in terms of morbidity and death (Papadopoulou-Marketou et al., 2015). This study aims to investigate the potential utility of serum RBP as a biomarker for the early detection of nephropathy in type 2 diabetics. In the current study, the diabetic group had significantly higher FPG, HbA1c, urea, and creatinine levels than the control group.

Table (2): The major diabetic markers among patient and healthy control.

Variable	Patients Means	Control. Means	p-value.
FBS (mg/dl).	244.5 ± 61.4	102 ± 13.8	<0.001
HbA1c (%)	9.02 ± 1.4	5.3 ± 0.89	<0.001
Urea (mg/dl)	55.6 ± 18.2	22.3 ± 8.2	<0.001
S. creatinine(mg/dl).	1.58 ± 0.82	0.74 ± 0.23	<0.001

These results are in line with other research suggesting that diabetes is the main mechanism causing DN. In diabetes, high HbA1c levels have been linked to the progress of micro-angiopathy. This could be owing to HbA1c's attraction for oxygen, which causes tissue anoxia and contributes to microangiopathy (Kundu et al., 2013). Glycemic

management issues may performance a part in the advancement of DN (Zakerkish et al., 2013). The concentrations of in our study, patients with DN had considerably higher levels of urea and creatinine than healthy control participants., as shown in table (2).

Table (3) shows the serum lipid profile in the studied population; statistically significant variations in serum

cholesterol, serum triglyceride, HDL, and LDL levels were found between healthy control subjects and type II DM patients. These findings support Bonnet and Cooper's (2000), findings that Affected lipid

metabolism is associated with DN., as seen by higher TG-rich lipoprotein, even when renal disorders are in their early stages.

**Table (3): The lipid profile among patient and healthy control.**

Variable	Patients. means	Healthy control Mean ± SD	p. value
TC (mg/dl).	222.7 ± 66.7	110 ± 30.3	<0.001
TG (mg/dl).	178.9 ± 88.2	98.4 ± 22.5	<0.001
HDL (mg/dl).	43.6 ± 10.6	32.4 ± 6.6	<0.001
LDL (mg/dl).	212.4 ± 77.4	125.3 ± 12.9	<0.001

In diabetic patients with elevated total cholesterol (TC), some studies have found a link between TC and DN (Al-Mahroos and Al-Roomi, 2007). Other investigations, on the other hand, neither a substantial alteration in serum lipid profiles nor even an inverse correlation between TG levels and DN have been seen (Song et al., 2016). Determining whether there is a link among lipid profiles and DN could lead to the development of new disease-modifying treatments. Hyperglycemia is a major cause of DN, although other factors such as dyslipidemia and alterations in insulin signaling also have a role. People with type 2 diabetes are more likely to have dyslipidemia, which has been associated to the emergence of DN. Obesity, LDL, HDL, and hypertriglyceridemia were all found to be linked with neuropathy (Callaghan et al., 2012).

Table (4) shows that patients with type II DM had a higher mean serum concentration of Retinol Binding Protein (RBP) than healthy control subjects (21.2 ± 6.7 vs. 16.3 ± 3.2). RBP (Retinol Binding Protein) is a protein family with several different activities. They are retinol-

binding carrier proteins. In health-related dietary studies, retinol binding protein is measured to estimate visceral protein mass. Retinol and retinoic acid are important regulators of gene expression and overall embryo development (Park et al., 2014). Raila et al., (2007), published a similar study. They discovered that patients with micro-albuminuria, a form of DN in its early stages, had higher serum RBP. Similarly, the amount of serum RBP increased as the clinical stage of DN progressed (Olsen and Blomhoff, 2020). In the present research, serum RBP concentration was positively correlated with TG, HbA1c, urea, and BMI as shown in table (5), which is consistent with Xu et al., (2009) findings. As demonstrated in (table 5), there were considerable inverse associations between RBP and creatinine in this study.

**Table (4): The Mean of RBP among diabetic patients and healthy control.**

Variable	Patients	Control	p. value
RBP (ng/ml)	21.2 ± 6.7	16.3 ± 3.2	<0.001
Mean ± SD			

**Table (5): Correlation between RBP and other parameters.**

Parameters	Correlation coefficient R*	P-value
RBP Vs. FBS	-.255	.116
RBP Vs. HbA1c	.162	.261
RBP Vs. Urea	.255	0.74
RBP Vs. Creatinine	-.328*	.020
RBP Vs. Cholesterol	-.144	.317
RBP Vs. TG	.176	.221
RBP Vs. HDL	-.112	.398
RBP Vs. LDL	-.114	.432
RBP Vs. BMI	.206	.151

\* The 0.05 level of significance for correlation.

The presence of impaired kidney function, rather than T2DM, is more likely to generate higher risk of renal insufficiency due to an increase in blood RBP concentration (Chu et al., 2011). As a result, circulating RBP could be a beneficial indicator of renal dysfunction in patients with T2DM. Many renal disorders have a wide range of clinical outcomes. The dearth of indicators capable of identifying and stratifying individuals with stable versus progressive disease is one of the main challenges in deciding which treatment strategy is best for a patient and in the creation of novel treatments. In comparison to other biomarkers, RBP is currently the much more sensitive functional marker of the proximal tubule. The glomerulus filters RBP before it is completely reabsorbed in the proximal tubule. RBP was also

identified as a risk element for renal impairment in people with type 2 diabetes., suggesting that it could be a useful biomarker for diagnosing kidney function before other regularly used markers.

### 4. Conclusion

This research found that the following in persons with type 2 diabetes, RBP levels can be utilized as a biomarker for the early diagnosis of diabetic nephropathy. Further studies should be conducted to cover a larger number of patients and to approve the findings.

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