ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 04 | April - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EVALUTION OF ROLE OF RBP4 IN DIABETIC NEPHROPATHY SUBJECTS AT TERTIARY CARE HOSPITAL, BIKANER

Medical Biochemistry

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ABSTRACT

Diabetic Nephropathy (DN) has been characterized as a condition caused by metabolic and hemodynamic variables, rather than an immune-driven illness. It progresses in a much unexpected way, frequently developing gradually over several years. The aim of the study to estimate RBP4 level in Diabetic nephropathy and healthy control groups and its role in progression of DN. It was an observational cross sectional study, carried out in Department of Biochemistry, Sardar Patel Medical College and Department of Nephrology & associated groups of PBM Hospital, Bikaner and Rajasthan. 90 participants with diabetic nephropathy and 90 as healthy controls were enrolled. In this study, an analysis of blood Urea, serum Creatinine and serum RBP4 was done in both the groups. We found that the mean blood urea, serum Creatinine, serum RBP4 level were higher in participants with DN as compare to healthy control 135.31mg/dlvs33.77mg/dl, 3.45mg/dlvs0.96mg/dl, and 4.59µg/mlvs0.63µg/ml respectively and all the parameters were statistically significant ($p<0.001$). The correlation between RBP4 and Creatinine was found to be 0.549. We conclude that, the serum RBP4 can be used to understand the advancement in nephropathy in diabetic mellitus subjects and early diagnosis of diabetic nephropathy.

KEYWORDS

RBP4, Rrtinol Binding Protein, Diabetic Nephropathy, Diabetic Kidney Disease, Renal marker, Urea, Creatinine.

INTRODUCTION

Diabetic Nephropathy (DN) has been characterized as a condition caused by metabolic and hemodynamic variables, rather than an immune-driven illness[1]. It progresses in a much unexpected way, frequently developing gradually over several years. Renal biopsy is infrequently done on diabetic individuals in many countries. In order for physicians to ascertain whether there is another kidney issue or comorbidities, it is only looked at when there is a notable rise in albuminuria or severe decline in renal function (1, 2, 9). As a result, renal biopsies are often carried out after DN has progressed. This has made it very difficult for researchers to understand how the immune system contributes to the development of DN. In both clinical trials and experimental DN models, macrophages are often seen within the glomeruli as well as interstitium throughout all phases of the disease[2,3]. Increased levels of CD4+ T lymphocytes in the kidney and blood and T cell activation are correlated with the evolution of diabetic nephropathy[4]. Retinol binding protein 4 belongs to lipocalin family and is a carrier protein for vitamin A. It transports retinol from liver to peripheral tissues. RBP4 may trigger subclinical inflammation leading to cardiovascular disease. RBP4 metabolized mainly in kidney as it is filtered by glomeruli and reabsorbed by proximal tubules, which makes it renal function parameter. Its level in serum increases in renal dysfunction. Retinol-binding protein 4 was reported as an adipokine that impairs insulin sensitivity[5] and also seen elevated in subjects with insulin resistance, impaired glucose tolerance and type 2 DM[6,7]

METHODS

Study Design:- It is an observational cross sectional study.
Study Place:- This study was carried out in Department of Biochemistry, Sardar Patel Medical College and Department of Nephrology & associated groups of PBM Hospital, Bikaner and Rajasthan.
Study Population:- Subjects with diabetic nephropathy and healthy controls.
Sampling Technique:- Purposive Sampling Technique
Sample Size:-90 Diabetic nephropathy cases and 90 healthy controls were included in this study.

Inclusive Criteria

- Clinically diagnosed with Type 2 Diabetes mellitus based on Fasting blood glucose level ≥126 mg/dl after 8 hour fasting or 2 hr PP glucose ≥200 mg/dl as per the criteria by ADA 2021[8].
- All had ≥ 30 mg/ml albumin in urine.
- Age between 45-70 years.

Exclusive Criteria

- Patients with previous history of liver disease, pulmonary disease, malignancy, pregnancy, coagulation abnormalities.
- Alcohol addiction and smoking habit.
- Type 1 diabetes
- Pregnant women.

Data Collection

Ethical approval certificate has been taken from institutional ethical committee. An informed consent was obtained from all participants those are diagnosed with diabetic nephropathy and healthy controls. From each participant following data was collected: Age, gender, other profile and Biochemical parameters, including complete physical examination of each participant were done very carefully.

Sample Collection and Processing

Blood sample was collected by venupuncture using aseptic technique and subjected to the following assays:-

- Serum RBP 4 :- Estimated by ELISA.
- Serum urea and Serum Creatinine:- Estimated by enzymatic method using fully auto analyzer.

Statisitcal Analysis

Data is entered in MS Office Excel work sheet in the form of master chart and analysis is performed with IBM SPSS. These data are classified and analyzed as per aims and objectives. Quantitative data is expressed in the form of Mean±SD. To compare categorical variables, the χ^2 test or t test are performed. Inference is drawn with the use of appropriate test of significance. Correlation of parameters is done using Pearson's correlation test. Result is considered as statistically significant if $p<0.05$.

Observation Tables and Graphs:-

Table 1: Comparison of Mean Urea, Creatinine and RBP4 Between Diabetic Nephropathy Group and Healthy Control Group

Subjects / Parameters	Controls (n=90) Mean±SD	Case (n=90) Mean±SD	P value
Urea (mg/dl)	33.77±12.61	135.31±35.16	<0.001*
Creatinine (mg/dl)	0.96±0.30	3.45±1.82	<0.001*
RBP4 (µg/ml)	21.09±8.15	34.10±17.5	<0.001*

*Highly significant

Descriptive Statistics and Independent Sample t test for equality of mean is applied

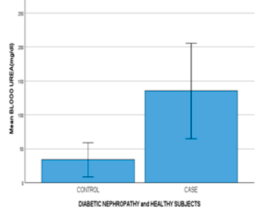

Figure 1:- Showing Comparison of Mean Urea Level Between Diabetic Nephropathy Group and Healthy Control Group

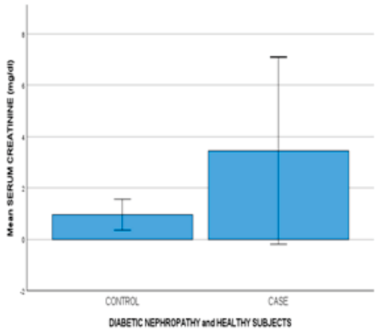

Figure 2:- Showing Comparison of Mean Creatinine Level Between Diabetic Nephropathy Group and Healthy Control Group

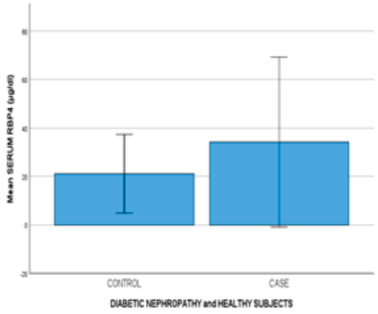

Figure 3:- Showing Comparison of Mean RBP4 Level Between Diabetic Nephropathy Group and Healthy Control Group

Table 2: Correlation of CREATININE with CYSTATIN C in Diabetic Nephropathy

PARAMETER	CREATININE	p-value
RBP4	0.549	0.001

Pearson's correlation is employed.

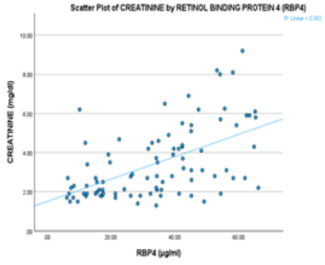

Figure 4:- Correlation of CREATININE with CYSTATIN C in Diabetic Nephropathy Subjects.

RESULTS

Mean Urea level between Case and Control group was observed in table 1 and figure 1. 135.31±35.16 mg/dl and 33.77±12.61mg/dl was mean Urea concentration in case and control groups, respectively. Its concentration is significantly higher in case group ($p<0.001$). These findings are in close agreement with the previous studies Akpinar[9] et al and Sun[10] et al which have suggested that impairment of urea level is because of reduction in kidney function in diabetic patients due to hyperglycemia induced damage led to become diabetic nephropathy.

In the same table (figure 2), mean creatinine level was shown to be higher in DN group (3.45±1.82 mg/dl) in contrast to healthy group (0.96±0.30 mg/dl) which is statistically significant ($p<0.001$). In light of our results, there is a positive association between serum creatinine and DN which explains that there is insufficient filtration or incapability of kidney's to filter blood, and this has a similarity with other research articles of Takir[11] et al, Dejenie[12] et al and Mussap[13] et al.

Comparison of serum RBP4 in subjects of case and control group was stated in table 1 (figure 3). The mean value of RBP4 was 34.10±17.5 µg/ml in case group and 21.09±8.15 µg/ml in control group. There is a significant elevation of RBP4 in DN group ($p<0.001$). Amin[14] et al, Thawnashomi[15] et al and Assi[16] et al had an outcome similar to our study. Thus, it suggests that RBP4 as an adipokines is a link between inflammation and diabetic nephropathy.

An analysis on correlation of RBP4 and creatinine in DN subjects was depicted in table 2 and figure 4. As per the table, creatinine is positively correlated with RBP4 and r value for this is 0.526 ($p<0.001$).

DISCUSSION

Diabetic nephropathy is an under-recognised disesae as a worldwide burden of disease, the prevalence of DN is rising steadily in low to middle income countries with uneven growth. It has extended epidemic proportions worldwide. In early kidney dysfunction, renal cells become hypertrophied and leads to hyperfiltration but in this stage serum level of creatinine is not markedly elevates so diabetic nephropathy remains unidentified.

Analysis of mean urea level was found considerably higher in DN subjects than healthy subjects ($p<0.001$), which indicates increased protein breakdown of tissues during kidney damage. Determination of mean serum creatinine was relatively elevated in DN subjects than healthy subjects ($p<0.001$). Thus, there is insufficient filtration or incapability of kidney's to filter blood in diseased state. Mean RBP4 concentration was significantly increased in case group as compare to control group ($p<0.001$). It was indicated that enhanced level of RBP4 may indicate inflammatory mechanism behind the progression of Diabetic nephropathy.

As per my study, RBP4 can be used to understand the prognosis of diabetic nephropathy from the early stages of the disease and it can also be used to diagnose Diabetic nephropathy as a subsitute of creatinine.

REFERENCES

1. Tesch GH. Diabetic nephropathy- is this an immune disorder? Clinical Science. 2017; 131 (16): 2183-99.
2. Guiteras R, Sola A, Flaquer M, Manonelles A, Hotter G, Cruzado JM. Exploring macrophage cell therapy on diabetic kidney disease. Journal of Cell Molecular Medicine. 2019; 23 (2): 841-51.
3. Chow F, Ozols E, Nikolic-Pterson DJ, Atkins RC, Tesch GH. Macrophages in mouse type2 diabetic nephropathy: Correlation with diabetic state and progressive renal injury. Kidney International. 2004; 65 (1): 116-28.
4. Kong L, Andrikopoulos S, MacIssac RJ, Mackay LK, Nikolic-Pateerson DJ, Torkamani N. Role of the adaptive immune system diabetic kidney disease. Journal Diabettes Investigation. 2022; 13(2): 213-26.
5. Yang Q, Graham TE, Mody N, Preitner F, Peroni OD, Zabolotny JM. Serum retinol binding protein 4 contributes to insulin resistance in obesity and type 2 diabetes. Nature. 2005; 436: 356-62.
6. Lee DC, Lee JW, Im JA. Association of serum retinol binding protein 4 and insulin resistance in apparently healthy adolescents. Metabolism. 2007; 56: 327-31.
7. Graham TE, Yang Q, Bluher M, Hammarstedt A, Ciaraldi TP, Henry RR. Retinol vinding protein 4 and insulin resistance in lean, obese and diabetic subkects, New England Journal of Medicine. 2006; 354: 2552-63.
8. American Diabetes Association: Nephropathy in diabetes. Diabetes Care. 2004; 27 (1): S79–S83.
9. Akpınar K, Aslan D, Fenkçi SM. Assessment of estimated glomerular filtration rate based on cystatin C in diabetic nephropathy. Brazilian Journal of Nephrology. 2021 July; 43 (3): 340-348.
10. Sun J, Liu C. Correlation of vascular endothelial function and coagulation factors with renal function and inflammatory factors in patients with diabetic nephropathy. Experimental and Therapeutic Medicine. 2018 Nov; 16 (5): 4167-4171.
11. Takir M, Unal AD, Kostek O, Bayraktar N, Demirag NG. Cystatin-C and TGF-β levels in patients with diabetic nephropathy. Nephrologia. 2016 Nov-Dec; 36 (6): 653-659.
12. Dejenie TA, Abebe EC, Mengstie MA, Seid MA, Gebeyehu NA, Adella GA. Dyslipidemia and serum cystatin C levels as biomarker of diabetic nephropathy in patients with type 2 diabetes mellitus. Front Endocrinology. 2023 April; 14:1124367.
13. Mussap M, Vestra MD, Fioretto P, Saller A, Varagnolo M, Nosadini R. Cystatin C is a more sensitive marker than creatinine for the estimation of GFR in type 2 diabetic patients. Kidney international. 2002; 61(4): 1453-61.
14. Amin EM, Saad EM, Allam HM, Zidan AA. Serum levels of adipocyte fatty acid binding protein 4 and retinol binding protein 4 as biomarkers for early detection of diabetic nephropathy in type 2 diabetes. Zagazig University Medical Journal. 2014; 20: 1-12.
15. Thawnashom K, Tungtrongchitr R, Chanchay S, Tungtrongchitr A, Raila J, Henze A. Association between retinol-binding protein and renal function among Asian subjects with type 2 diabetes mellitus: a cross-sectional study. Southeast Asian Journal of Tropical Medicine and Public Health. 2011 Jul; 42 (4): 936-45.
16. Assi MA, Mohammed MH. Estimation of retinol binding protein as a near biomarker of diabetic mellitus patients at Al-Najaf Province. HIV Nursing. 2022; 22 (2): 3056-59.