ORIGINAL ARTICLE

The Association between Retinol-Binding Protein 4, Fasting Blood Glucose and Creatinine Clearance and the Risk of Diabetic Nephropathy

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ABSTRACT

Background: Diabetic nephropathy is a syndrome typified by the occurrence of microalbuminuria, lesion of the glomeruli and reduced glomerular filtration rate in diabetic patients.
Aims: To was designed to find out the association between retinol binding protein 4, blood glucose fasting and the risk of diabetic nephropathy
Methods: 60 patients were and 20 healthy controls were taken. Patients with age range 30- 60 years suffered from Type 11 diabetes for < than five years. Levels of fasting blood glucose and of serum creatinine were analyzed by standard kits using Auto analyzer. Fasting urine samples of patients were taken for estimation of Retinol binding Protein 4 (PBP 4). Creatinine clearance was calculated.
Results: Mean age of controls and patients was 45.80 and 47.80 years respectively. Mean BMI of patients was non significantly more than of normal subjects. Levels of fasting blood sugar and of RBP 4 were high significantly in patients as compared to normal subjects. Level of serum creatinine clearance was non significantly decreased in patients in comparison of normal controls. Correlations of RBP-4 with fasting blood Glucose showed a non-significant difference whereas the a significant correlation of RBP-4 was observed with Creatinine Clearance.
Conclusion: It may be concluded that the level of urinary RBP4 is found to be increased diabetic subjects and to be link to parameters known to be related with diabetic nephropathy.
Keywords: Diabetic nephropathy, creatinine clearance, RBP-4

INTRODUCTION

With the progress of T2DM or type 2 diabetes mellitus, many complications are appeared in the patients like nephropathy, neuropathy etc[1]. The incidence of Complication of nephropathy in diabetics is 20–40 % and the indicators of nephropathy in routine are proteinuria, microalbuminuria and creatinine clearance[2,3]. Besides these indicators, Retinol binding protein 4 of urine or RBP 4 has been identified as a bio marker of proximal tubular dysfunction[4].

RBP4 is a liver protein. It may be related to resistance of insulin and T2DM and its level is increased in kidney dysfunction[5]. Its major carrier in blood is transthyretin and this complex prevents its glomerular filtration[6]. On the other hand 4 to 5% of serum RBP4 passes the barrier of glomeruli, than reabsorbed and tainted in the proximal convoluted tubule[7]. It is therefore said that RBP of urine may be a marker of dysfunction of proximal convoluted tubules[4].

Chronic diabetes may lead to impairment of renal function. The American Diabetes Association and Health Institutes advised to calculate GFR / year in diabetic people for finding the dysfunction of kidney. GFR estimates the 2 million glomeruli filter the blood plasma and remove unwanted material from it. In case of injured kidney, there is a gradual reduction of GFR, and its impairment is based on dysfunction of kidney[8]. GFR is a good measurement of function of kidney function as it accounts for sex, BMI and age. Measurement GFR is estimated by plasma clearance of a filtration indicator like serum creatinine or cystatin into the urine[9].

Factors that impair the estimation of creatinine clearance are incomplete collection of urine collection, pregnancy and energetic exercise. It also affected by some drugs like trimethoprim, cimetidine, and the drugs that can harm kidneys[10].

Creatinine clearance calculation is based on the collection of both blood and 24 hour urine sample. However, due to release of small quantity of serum creatinine is filtering tubules of kidneys; calculation of clearance of kidney is not very similar to GFR. It is thought that an overestimate of GFR is seen by calculation of creatinine clearance especially in advanced failure of kidney[11].

Estimation of kidney dysfunction is based the on the tests of microalbuminuria and creatinine clearance, however these do not give knowledge of progressive reduction in the rate of glomerular filtration and hence the loss of kidney function. Level of urinary RBP-4 may be helpful in early diagnosis of kidney problem. There is a need to compared the level of RBP4 with creatinine clearance, a conventional indicator of kidney problem and find that the better marker of kidney problem.

Therefore, a cross sectional study was planned to find out the association between RBP 4, fasting blood glucose

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and creatinine clearance and risk of developing diabetic nephropathy

MATERIAL AND METHODS

Sixty diabetic patients and 20 control subjects were involved in the study. Patients with age in between 35-45 years and have diabetes for a period of < 5 years were included in the study. Patients with diabetes for a period of > five years, with pregnancy and kidney problem or any other systemic diseases were excluded from the study. The consented patients were taken from Diabetic clinic of Sheik Zayed Hospital Lahore. Demographic findings were entered into proforma. Whole blood of patients/ controls is used for estimation of fasting blood glucose and serum sample was used for estimation of serum creatinine by standard kit methods. Fasting urine of patients was used for the estimation of RBP 4.

Statistical Analysis: Data was analyzed by SPSS 21.0. All variables were given as mean ± SD. Comparison of parameters of controls with patients was carried out by student 't' test. Correlation of RBP 4 with fasting glucose and with creatinine clearance was calculated by Spearman correlation. Value of P < 0.05 was taken as significant.

RESULTS

According to table 1 the mean age of controls and of patients and controls was 45.80 and 47.80 years respectively. Mean BMI of patients was non significantly more than of control subjects. Levels of fasting blood sugar and RBP-4 was significantly high (P<0.001) in patients in comparison with controls. Level of Creatinine Clearance was non significantly decreased in patients in comparison with controls. Correlations of RBP-4 with fasting blood Glucose showed a non significant difference whereas the a significant correlation (P<0.001) of RBP-4 was observed with Creatinine Clearance (Table 2).

Table 1: Comparison of mean age , BMI and biochemical parameters of patients with controls

Subjects	Mean age (years)	B M I (Kg /m^2)	Fasting blood sugar (mg/ dl)	Creatinine clearance (ml/min)	Retinol binding protein-4 (ng/ml)
Patients (60)	47.80±7.70	26.50±4.19	169.35±48.31**	83.53±24.40	82.90±33.07**
Controls (20)	45.80±4.31	24.84±2.80	76.10±20.29	87.1644±18.44	49.4535±35.34

** P< 0.001 = highly significant

Table 2: Correlations of RBP-4 with Glucose (F), and Creatinine Clearance

Variables	RBP4 (ng /ml)	
	Correlation coefficient (r)	p value
Fasting blood glucose(mg /dl)	0 . 148	0 .259
Creatinine clearance(ml/min)	-0 . 898	0 .001

**P<0.001 = highly significant

DISCUSSION

Diabetic nephropathy observe in both type 1 and type 2 diabetes after the problem of Pancreatitis due to prolong hyperglycemia that results in diabetic complications. Diabetic nephropathy is link with the extent of damage of the kidney and GFR[13].

According to our study, levels of fasting blood sugar and RBP-4 were significantly more in patients as compared to control subjects. We agreed with a finding that investigate the role of RBP-4 in the pathogenesis of insulin resistance and type 2 diabetes and found that kidney dysfunction is one of main complication of diabetes[14,15].

Estimation of urinary RBP 4 is an indicator of reduced function of proximal convoluted renal tubule. It is proposed that the process of endocytosis carried out by receptors of cubilin and Megalin in routine absorbs approximately 100% of protein. Defect in this process may results "tubular link proteinuria," including albumin, RBP4, and other peptides and the estimation of RBP4 in urine may be a best screening biochemical test to detect tubular proteinuria[7]. Additionally a study finds that the urinary level of RBP may be autonomously related with albuminuria in type 2 diabetes and may be a biomarker for the confirmation of diabetic nephropathy[16].

We observed that the level of creatinine clearance was non significantly decreased in patients as compared to controls. It is suggested that creatinine clearance is a cost effective parameter for finding the renal dysfunction [17]. It is proposed that for assessment of renal function before surgery can be find out by creatinine clearance. It is also a primary finding for nephrologists for management[18].

We found non-significant correlation of RBP-4 with fasting blood Glucose. Some studies also observed that increased level of RBP4 is related with altered glucose tolerance in diabetic nephropathy[19,20]. It is found that RBP4 adversely affect the function of β-cell and may disturb the signaling pathway of insulin and cause insulin resistance[21]. However a study reported no link between levels of RBP4, fasting blood glucose and function of β-cell[22].

Our study observed a significant association of RBP-4 with Creatinine clearance. Present study is in accord with some studies who found that clearance of RBP4 via kidney is may be similar to creatinine clearance and GFR[23]. It is suggested that the level of RBP4 does not alter in the initial stage of diabetic nephropathy but decline function of kidney may increased the level of RBP4 in condition of diabetic nephropathy[24,21].

Limitation of studies: Number of diabetic patients are less. Study should also include Cystatic C, a marker of kidney dysfunction.

CONCLUSION

It may be concluded that the level of urinary RBP4 is found to be increased diabetic subjects and link to parameters known to be related with diabetic nephropathy. It is therefore said that the level of urinary RBP4 may have an important role in the pathogenesis of type 2 diabetes.

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