ORIGINAL RESEARCH ARTICLE

Correlation of Renal Artery Resistive Index with Albuminuria and Other Risk Factors in Type 2 Diabetes Mellitus Patients

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A B S T R A C T

Introduction: Diabetes mellitus is one of the most common non communicable disease globally. Diabetic nephropathy is the most frequent microvascular complication in diabetic patients that occur in ~30% of diabetics. Microalbuminuria is considered risk factor for development of macroalbuminuria and overt nephropathy in later stages of disease. Resistive index was recognized to be noninvasive diagnostic procedure, which strongly indicated outcome of renal function in type 2 diabetic patients.

Material and methods: Cross sectional study was conducted with sample size of 80 patients. All patients who are diagnosed as type 2 diabetes mellitus according to American diabetes association with age group of 18-70 years were included. Patients with chronic kidney disease secondary to other causes were excluded. Relevant biochemical investigations obtained. Renal artery RI was recorded using USG Philips affinity G. The statistical program SPSS used for data analysis. *P*- value <0.01 considered statistically significant.

Results: Clinical and biochemical data of study patients were summarized. In the patients with diabetes mellitus, mean RI was significantly higher in patients with albuminuria, compared with patients without albuminuria. RI had significant associations with duration of disease (, *P* < 0.01), eGFR (*P* < 0.01), and serum creatinine (*P* < 0.01).

Conclusion: Many factors are included in development of small vessel abnormalities of kidney as part of vascular damage in type 2 diabetes. The consequence of these abnormalities can be elevation of renal RI, which can be used as indirect marker in diagnosing severity of renal disease in diabetic patients.

Keywords: Renal Resistive Index, Diabetes Milletus 2, Albuminuria

INTRODUCTION

Diabetes mellitus is now one of the most common non communicable disease globally. Diabetes is known as group of heterogeneous disorders with common element of hyperglycemia and glucose intolerance due to insulin deficiency, impaired effectiveness of insulin or both. Diabetic nephropathy is the most frequent micro vascular complication in diabetic patients that occur in ~30% of diabetic patients.[1] Microalbuminuria (excretion of albumin 30-300mg/day) is considered to be risk factor for development of macroalbuminuria and leading to overt nephropathy in later stages of disease.[2] Hemodynamic changes, including intraglomerular hypertension, raised renal vascular resistance, and ischemic nephropathy are responsible for the development of various stages of diabetic nephropathy. Resistivity index (RI) of renal arteries was found to correlate significantly with effective renal plasma flow, renal vascular resistance, and the filtration fraction in patients with chronic renal failure. In patients with renal dysfunction secondary to type 2 diabetes mellitus, RI was significantly increased compared with patients with non diabetic renal disease.[3] RI was found to be a noninvasive diagnostic procedure, which strongly predicted the outcome of renal function in type 2 diabetic patients, even when glomerular filtration rate patterns were still within normal limits. RI was significantly higher in patients with type 2 diabetes with albuminuria than in patients without albuminuria

Study aimed at assessment of correlation between intrarenal artery resistive index with 24 hr albumin excretion, duration of illness, eGFR, serum creatinine and serum cholesterol in diabetes mellitus type 2.

MATERIAL AND METHODS

This is a cross sectional study conducted in the Department of Radio diagnosis, Bangalore medical college and research institute, Karnataka from June 2017 to December 2017

Inclusion criteria: Study sample of 80 patients who are diagnosed as type 2 diabetes mellitus according to American diabetes association with age group of 18-70 years were selected

Exclusion criteria: Patients with renal artery stenosis, chronic kidney disease secondary to other causes were excluded.

Participating patients well informed consent taken. The initial evaluation consisted of detailed clinical history and biochemical investigations. Urinalysis was done. 24hrs urine albumin excretion was measured. The albuminuria status was defined and classified according to the standards of medical care of the American Diabetes Association as normal (<30 µg/mg), microalbuminuria (30–299 µg/mg) or macroalbuminuria (≥300 µg/mg).[4]

Blood investigations were done. Serum creatinine, serum total cholestrerol was measured and eGFR was calculated using Cockcroft –gault formula

eGFR (male) (ml/min per 1.73m^2) = $0.741 \times 175 \times Age^{-0.203} \times Cr^{-1.154}$
[if female : eGFR (male) × 0.742]

Patient was subjected to ultrasound and doppler assessment. Renal artery RI was recorded using single Philips affinity G ultrasound machine. A curved array transducer (2-5Hz) was used to record intra renal resistive index. Color and spectral Doppler was used to measure RI. The resistive index was measured using PSV and EDV values [RI: (peak systolic velocity – end diastolic velocity)/ peak systolic velocity at segmental arteries in kidney] automatically by the equipment. The average of right RI and left RI was taken.

Eighty patients complete data were enrolled for statistical analysis The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs.

RESULTS

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max). Multiple regression was applied to analyze the relationship between dependent variable RI and other analyzed variables (24hrs albumin excretion, diabetes duration, lipid values, creatinine, and eGFR) as independent variables. Significance is assessed at 5% level of significance. *P*- value <0.01 was considered statistically significant.

Student t test (two tailed, independent) is used to find significance of study parameters on continuous scale between two groups on metric parameters.
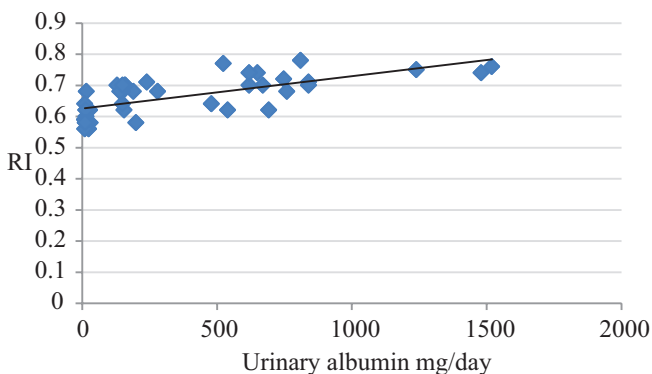

Figure-1: Scatter diagram showing correlation between RI and 24 hr urinary albumin (mg/day)
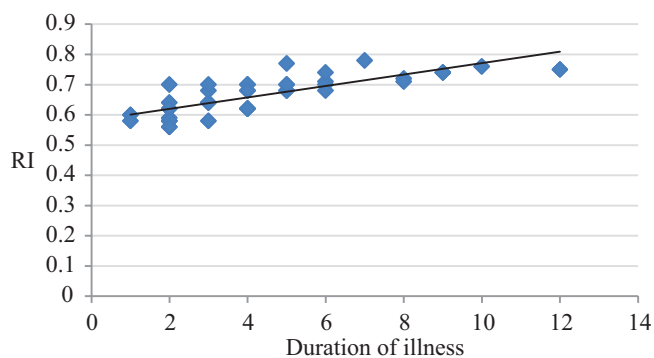

Figure-2: Scatter diagram showing correlation between RI and duration of illness in years
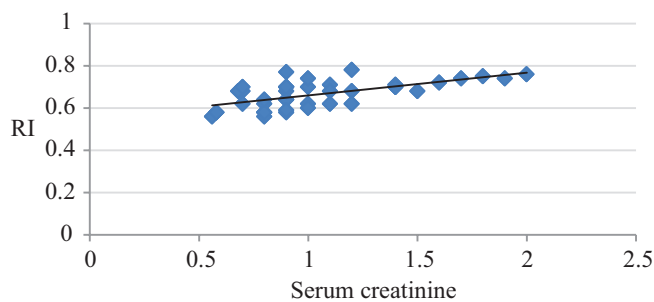

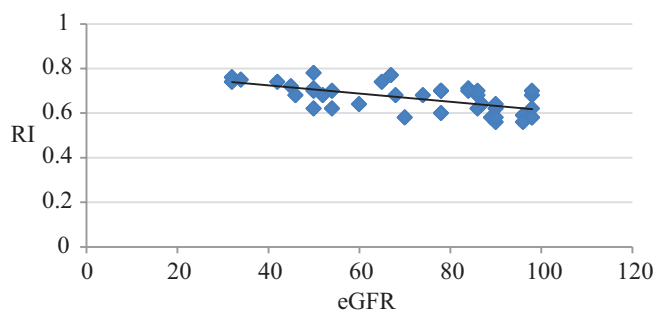**Figure-3:** Scatter diagram showing correlation between RI and Serum creatinine(mg/dl)

Figure-4: Scatter diagram showing correlation between RI and eGFR(ml/min/1.73m^2)

Chi-square/ Fisher Exact test is been used to find the significance of study parameters on categorical scale between two or more groups, non-parametric setting for Qualitative data analysis.

Eighty diabetic patients were included in the study. Out of 80 patients, 55 patients (69%) were males and 25 subjects (31%) were females. Mean age of patients included in the study was 52.58±8.13 years.

Albumin excretion and RI

The study group of 80 patients consisted of 24 normoalbuminuric patients and 32 microalbuminuric patients and 24 macroalbuminuric patients. A statistically significant difference in RI was found between the groups of normoalbuminuric patients and albuminuric patients (0.60±0.04 vs. 0.69±0.05; *P*<0.01).

A positive correlation was noted between RI and levels of 24 hr urinary albumin concentration when normoalbuminuric, microalbuminuric and macroalbuminuric patients were compared. Among RI of these three groups, RI was found to

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be highest in macroalbuminuric patients and the difference among these 3 groups was statistically significant (P<0.01) (0.60±0.04 vs0.67±0.04 vs0.71±0.05) (Figure-1).

Duration of illness and RI

Out of 80 patients, this study group consisted of 44 subjects of 0-5yrs duration, 36 patients of >5 year duration. A statistically significant difference in RI was found between the groups of 0-5years patients and >5years patients (0.64±0.05 vs. 0.732±0.03; P<0.01) (Figure-2).

Serum creatinine and RI

Out of 80 patients, this study group consisted of 66 subjects with creatinine level <1.2mg/dl, and 14 patients with creatinine level of >1.2mg/dl. A statistically significant difference in RI was found between the groups of <1.2mg/dl patients and >1.2mg/dl patients (0.64±0.06vs. 0.72±0.04; P<0.01) (figure-3).

eGFR and RI

Out of 80 patients, this study group consisted of 54 subjects of stage 1and 2 with eGFR >60 ml/min/1.73m^2 and 26 patients of stage 3,4 and 5 with eGFR <60 ml/min/1.73m^2. A statistically significant difference in RI was found between above two groups (0.65±0.61 vs. 0.71±0.05; P<0.01) (figure-4).

Serum cholesterol and RI

Out of 80 patients, this study group consisted of 30 subjects of total cholesterol >240mg/dl and 50 subjects with total cholesterol <240mg/dl. No significant difference in RI was found between above two groups (0.67±0.01 vs. 0.68±0.06; P>0.05).

DISCUSSION

Microalbuminuria is one of the earliest predictor of onset of diabetic nephropathy and its progression.[7] In renal diseases, diagnosis is based on the patient's clinical history, physical examination, laboratory tests, diagnostic imaging, scintigraphy, and histopathology. Early diabetic nephropathy is been identified by persistent microalbuminuria defined as an albumin excretion rate of 20–200 μg/min or 30–300 mg/24 h, or a spot urine albumin to creatinine ratio of 30–300 mg/g (3.5–3 5 mg/mmol) in males and 20–2 00 mg/g (2.5–2 5 mg/mmol) in females. Overt DN is marked by proteinuria >500 mg/24 h or albuminuria >300 mg/24 h. Decreased estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m2 may be another manifestation of overt DN. Color and power Doppler is able to provide an definite morphological and functional evaluation of the intraparenchymal vascularity. Intrarenal resistive index is a more sensitive parameter measured on the renal parenchymal arteries, which provides pathophysiological information about nephropathy. Increased intra-renal artery RI indicates renal impairment, with being RI≥0.7 can predict decreasing renal function in diabetic patients suffering from micro or macroalbuminuria.

This study evaluated the relationship between intrarenal RI with albuminuria, duration of illness, serum creatinine, eGFR and serum cholesterol in type II diabetic mellitus patients. Resistive index as measured in parenchymal vessels of diabetic patients, showed values ranging from 0.6 to 0.9

having mean of 0.65 among 80 subjects. Mean RI values in diabetic patients without albuminuria was 0.60 and patients with albuminuria was 0.69, these findings were consistent with studies which showed diabetic patients with renal dysfunction have higher RI value and is emerging as a useful marker of diabetic nephropathy as few studies showed raised RI values even before appearance of microalbuminuria, which is considered early biochemical marker in diabetic nephropathy. The study showed significantly higher RI in patients with macroalbuminuria, which shows that severity of diabetic nephropathy has positive correlation with RI values.

Spomenka et al.[8] found that Doppler can be useful in early diagnosis of diabetic nephropathy by measuring intra-renal artery RI and found significant positive correlation between intra-renal RI and diabetic nephropathy which was consistent with our study. Nejad et al.[9] showed that RI can be used to estimate 24-hour urine protein especially in those patients who are not suitable for 24 hour urine collection. However in some cases up to 20%, albuminuria was found to be absent in diabetics throughout life in spite of renal dysfunction.

Regardless of the status of albuminuria, glomerular filtration rate is considered to be a risk factor for diabetic nephropathy and it was also reported to be correlated with RI. In our study correlation between GFR and RI was indirect as patients with decreased eGFR (<60mg/ml/1.73m^2) showed increased mean RI value of 0.71 with statistically significant P value <0.01 when compared with mean RI value in patients with eGFR>60mg/ml/1.73m^2 which was found to be consistent with previous studies.

Previous studies have shown significant correlation between RI and serum creatinine and clearance creatinine values in patients with microalbuminuria and clinically evident proteinuria. Soldo et al.[10] also showed a correlation between RI and serum creatinine. Our study showed consistent results with previous studies in patients with increased serum creatinine levels >1.2mg/dl showed higher RI of mean 0.72 in comparison with patients with serum creatinine levels <1.2mg/dl with statistically significant P value.

Other risk factors affecting progression of kidney disease include age, duration of illness, serum cholesterol, glycemic control and blood pressure. In the studies by Mostbeck et al.[11] diabetes duration was established as a statistically significant covariable which affected renal RI of diabetic patients. Similar correlation was seen in this study, diabetics with duration of illness >5yrs showed statistically significant higher RI values when compared with diabetic patients with <5 years duration.

Cholesterol and LDL-cholesterol levels are considered to be good predictors for the development of atherosclerotic changes in diabetes. However serum cholesterol did not show statistically significant correlation with RI

Many factors are included in the development of small vessel abnormalities of the kidney as part of the widespread vascular damage in type 2 diabetes. The consequence of these abnormalities can be the elevation of intrarenal resistive index. Most studies showed value of RI in diabetic patients to be between 0.65-0.72. RI was found to have significant positive correlation with albuminuria, duration of illness,

eGFR and creatinine which were consistent with our study. However in our study serum cholesterol did not show significant correlation with RI ($P>0.01$) in type II diabetes mellitus patients.

In this study, elevated RI is observed in type 2 diabetic patients with diabetic nephropathy with albuminuria. Duration of illness, eGFR and serum creatinine were shown to be statistically significant covariables influencing RI unlike serum cholesterol.

CONCLUSION

Microalbuminuria is earliest appearing established marker of diabetic nephropathy having both predictive and prognostic values. This study shows strong association between albuminuria and renal RI as risk factor for diabetic nephropathy and progression of renal insufficiency. Since microalbuminuria has been inferred as a reliable and earliest appearing marker of diabetic nephropathy by various studies and renal resistive index is well correlated with albuminuria and also with other established risk factors of diabetic nephropathy, it can be used as surrogate marker in place of albuminuria. Thus renal resistive index can be declared as reliable and early marker of diabetic nephropathy as well as other cardiovascular risk associated with type II diabetes mellitus. Since increased RI is associated with adverse renal outcomes, decreasing albuminuria with ACE inhibitor or ARB therapy, can lead to improved outcomes. Other variables such as duration of illness, eGFR and serum creatinine has shown poor outcome in diabetic nephropathy which shows significant correlation with increased RI.

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