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Assessment of VEGF and microalbuminuria in early diabetic nephropathy

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ABSTRACT

Background: Diabetes is a disease assuming epidemic proportions, and the number of people developing the disease is growing every year. The present study was conducted to assess VEGF and microalbuminuria in early diabetic nephropathy.

Materials & Methods: 70 patients diagnosed with diabetic nephropathy of both genders underwent routine hematological profile, blood sugar levels, urinalysis, blood urea and creatinine, serum electrolytes, and ultrasound imaging of the kidney. The concentration of VEGF 165 isoform was donenn urine and plasma using enzyme-linked immunosorbent assay (ELISA) by using a kit for human VEGF.

Results: Out of 70 patients, males were 40 and females were 30. The mean BUN (mg/dl) was 15.4 and 23.9, creatinine (mg/dl) was 0.79 and 0.80, albumin (g/dl) was 4.25 and 4.08, 24 hours proteinuria (mg/dl) was 294.2 and 512.6, microalbuminuria (mg/dl) was 12.5 and 10.6.2, plasma VEGF (pg/mL) was 924.5 and 852.6 and urine VEGF (pg/mL) was 61.4 and 126.4 in patients with normal albuminuria and microalbuminuria respectively. The difference was significant ($P< 0.05$).

Conclusion: Increased levels of GA and microalbuminuria reflected a quicker response to short – term changes in diabetes treatment and best glycaemic index in uncontrolled diabetes mellitus.

Key words: sugar levels, diabetic nephropathy, blood urea

INTRODUCTION

Diabetes is a disease assuming epidemic proportions, and the number of people developing the disease is growing every year. The kidney is affected in ~40% of diabetic patients, and diabetic nephropathy (DN) is the chief cause of end-stage renal disease (ESRD).[1] Projections from Indian Council of Medical Research–India Diabetes study have shown that India possibly has 62.4 million people with diabetes, making DN an important cause of renal failure.[2]

Microalbuminuria is a marker of DN, and it is regarded as the non-invasive indicator of early DN. Nevertheless, currently no technique can estimate who develops DN, before any damage ensues.[3] Quantification of pathological kidney injury is difficult with the available clinical and laboratory investigations.[4] Vascular endothelial growth factor (VEGF) A is highly expressed by podocytes in the glomerulus and provides essential maintenance signals for GEnC, including those for survival and regeneration, maintenance of fenestrations, and regulation of solute flux and protein passage. Systemic and glomerular vessels become more “leaky” in pathological conditions where VEGFA bioavailability is increased, such as cancer, retinal disease and early DN.[5]

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The metabolic and hemodynamic variations in diabetes disturb the glomerular filtration barrier, causing ultrastructural alterations of the glomeruli. Variations seen are fusion and detachment of podocyte foot processes, thickening of glomerular basement membrane (GBM), reduced endothelial cell glycocalyx, and accumulation of extracellular matrix in the mesangium and glomerulosclerosis, finally progressing to albuminuria and ESRD.[6] The present study was conducted to assess VEGF and microalbuminuria in early diabetic nephropathy.

MATERIALS & METHODS

The present study comprised of 70 patients diagnosed with diabetic nephropathy of both genders. They were included in the study with their written consent.

Demographic data such as name, age, gender etc. was recorded. All underwent routine hematological profile, blood sugar levels, urinalysis, blood urea and creatinine, serum electrolytes, and ultrasound imaging of the kidney. The concentration of VEGF 165 isoform was donenn urine and plasma using enzyme-linked immunosorbent assay (ELISA) by using a kit for human VEGF. The linear range of detection was 5 - 1500 pg / ml for the assay. Results were studied using chi- square test. P value less than 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Gender	Males	Females
Number	40	30

Table I shows that out of 70 patients, males were 40 and females were 30.

Table II Comparison of parameters

Parameters	Normal albuminuria	Microalbuminuria	P value
BUN (mg/dl)	15.4	23.9	0.02
Creatinine (mg/dl)	0.79	0.80	0.94
Albumin (g/dl)	4.25	4.08	0.81
24 hours proteinuria (mg/dl)	294.2	512.6	0.01
Microalbuminuria (mg/dl)	12.5	10.6.2	0.01
Plasma VEGF (pg/mL)	924.5	852.6	0.04
Urine VEGF (pg/mL)	61.4	126.4	0.02

Table II, graph I shows that mean BUN (mg/dl) was 15.4 and 23.9, creatinine (mg/dl) was 0.79 and 0.80, albumin (g/dl) was 4.25 and 4.08, 24 hours proteinuria (mg/dl) was 294.2 and 512.6, microalbuminuria (mg/dl) was 12.5 and 10.6.2, plasma VEGF (pg/mL) was 924.5 and 852.6 and urine VEGF (pg/mL) was 61.4 and 126.4 in patients with normal albuminuria and microalbuminuria respectively. The difference was significant ($P< 0.05$).

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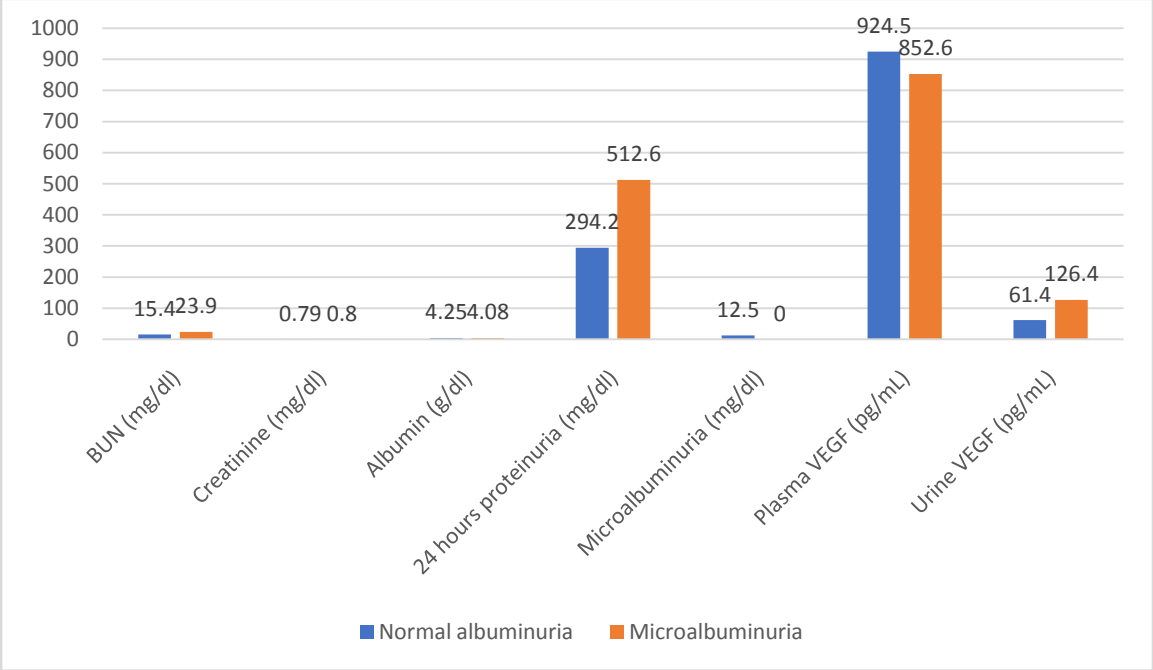
Graph I Comparison of parameters



DISCUSSION

Systemic endothelial dysfunction is an initiating step in the development of vascular damage in diabetes and is associated with microalbuminuria (urinary albumin secretion 30–300 mg/day). It is widely accepted that microalbuminuria indicates disruption of the glomerulus and is the earliest clinically detectable indicator of incipient diabetic nephropathy (DN).[7] Glomerular endothelial cells (GEnCs) restrict the passage of protein across the highly specialized glomerular capillary wall via the luminal facing endothelial glycocalyx (eGLX), which consists of proteoglycans, glycosaminoglycans (GAGs), glycoproteins, and trapped soluble plasma proteins.[8] GEnCs have transcellular fenestrations that form in attenuated areas of GEnC cytoplasm, which constitute 20–50% of the entire endothelial cell surface. Fenestrae are necessary for the high permeability of the glomerulus to water and small solutes. However, fenestrae are covered by eGLX, which is known to regulate vascular permeability by limiting the passage of charged macromolecules.[9] The present study was conducted to assess VEGF and microalbuminuria in early diabetic nephropathy.

In present study, out of 70 patients, males were 40 and females were 30. Dudhat et al[10] included 30 patients with 36 eyes scheduled for intraocular surgery. 19 patients were males and 11 were females. The mean age of the patients was 62.32+12.04 years. 24 hours before the surgery, blood samples were taken from the patients for the evaluation of blood glucose, HbA1c, and C-reactive protein (CRP). Out of 30 patients, 21 patients were diabetic whereas 9 patients were non-diabetic. The subjects of the patients were grouped into two groups, Group A (diabetic patients) and Group B (non-diabetic patients). Group A consisted of 21 patients with 25 eyes in consideration for the study. Group B consisted of 9 with 10 eyes in consideration for the study. The samples of aqueous humor were collected just before the intraocular surgery under sterile conditions in the operating theatre. Results: The mean age of subjects in Group A was 63.21 + 14.12 years and Group B was 65.23 + 12.61 years. The level of Aqueous VEGF in aqueous humor in Group A was 212.3+52.3 pg/ml and in Group B was 68.12+31.2 pg/ml. The HnA1c

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level in the blood in Group A was 10.7 + 3.1 % and Group B was 5.1 + 1.3 %. The fasting glucose level in the blood of Group A was 182 + 48.21mg/dL and Group B was 98.21 + 7.2 mg/dl. The results with respect to aqueous VEGF, HbA1c, and fasting Glucose were statistically significant.

We observed that mean BUN (mg/dl) was 15.4 and 23.9, creatinine (mg/dl) was 0.79 and 0.80, albumin (g/dl) was 4.25 and 4.08, 24 hours proteinuria (mg/dl) was 294.2 and 512.6, microalbuminuria (mg/dl) was 12.5 and 10.6.2, plasma VEGF (pg/mL) was 924.5 and 852.6 and urine VEGF (pg/mL) was 61.4 and 126.4 in patients with normal albuminuria and microalbuminuria respectively. Cha et al[11] investigated the effect of high glucose on the signaling and production of VEGF in rat mesangial cells in culture and measures the urinary VEGF level in patients with different stages of diabetic nephropathy. A high ambient glucose concentration in the culture medium increased VEGF mRNA expression and protein production within 3 h in a concentration-dependent manner. A protein kinase C (PKC) inhibitor and PKC down-regulation inhibited glucose-induced increases in VEGF production. Urinary excretion of VEGF significantly increased according to the degree of proteinuria in patients with diabetes. A weak but significant correlation was found between urinary VEGF excretion and the levels of serum creatinine, creatinine clearance, microalbuminuria, and proteinuria. Immunohistochemistry revealed marked differences in the extent of mesangial VEGF staining between diabetic and control kidneys. Pronounced up-regulation of VEGF was observed in the glomerular epithelial cell in the early phase of diabetic kidney disease, whereas widespread expression of VEGF was found in the tubular segments, especially the proximal segment, in advanced diabetic nephropathy.

Kondaveeti et al[12] randomly selected Uncontrolled Type 2DM (n = 75), controlled Type 2DM (n = 75) and healthy controls (n = 75). Their fasting venous blood samples were obtained for GA and serum creatinine, while their morning urine samples were obtained for detection of microalbuminuria. The mean GA, microalbuminuria and serum creatinine were the highest in Uncontrolled DM as compared to those in Controlled DM respectively. Microalbuminuria and GA had a significant correlation with the duration of diabetes.

CONCLUSION

Authors found that increased levels of GA and microalbuminuria reflected a quicker response to short – term changes in diabetes treatment and best glycaemic index in uncontrolled diabetes mellitus.

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