



CODEN [USA]: IAJPB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.2617339>Available online at: <http://www.iajps.com>

Research Article

**RENAL TUBULAR PROTEINS AS AN INDICATION OF
TUBULO-INTERSTITIAL NEPHROSIS IN PATIENTS OF
DIABETES MELLITUS MANAGED WITH INSULIN*****Dr Satyjeet, *Dr. Sumeet Kumar, *Dr. Akash Mandhan, *Dr. Aroon Kumar**

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Article Received: January 2019**Accepted:** February 2019**Published:** March 2019**Abstract:**

Diabetic nephropathy in insulin dependent patients is believed to be characterized by glucose-induced inhibition of matrix-disrupting enzymes to contribute to matrix deposition.

Objective: The study aimed to explore renal tubular proteins that can detect an early stage of renal involvement in diabetes.

Study design: A Prospective Study.

Place and Duration: In the Nephrology department of Chandka Medical College Hospital Larkana for one year duration from July 2017 to July 2018.

Methods: The study included 42 female patients aged between 40 and 60 years with long-term diabetes and 27 male patients with insulin (18-20 units). Electrophoretic patterns of 24-hour urine proteins in diabetic patients were examined in 10% SDS gradient polyacrylamide gel electrophoresis. We estimated 24 hours urine protein from patients.

Results: The electrophoretic profile showed a proteinuria status (both high molecular weight and low molecular weight). In the urine samples, proteins with a molecular weight of 120-28 K have appeared. In normal subjects, the urinary protein range is 37-72 Kda. Among these, common proteins and control urine samples observed in patients were protein 27 molecular weight (alpha 1 microglobulin) and 42 Kda (acid glycoprotein). Gross volume (concentration) and density of these 2 proteins were observed in the urine samples of the patients.

Conclusion: Electrophoresis technique may exclude or detect tubular-interstitial nephropathies in early stages of renal complications, as in diabetes mellitus.

Key words: Type 11 diabetes, alpha-1-acid glycoprotein, SDS electrophoresis.

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Please cite this article in press Satyjeet et al., *Renal Tubular Proteins As An Indication Of Tubulo-Interstitial Nephrosis In Patients Of Diabetes Mellitus Managed With Insulin.*, Indo Am. J. P. Sci, 2019; 06(03).

INTRODUCTION:

Diabetic nephropathy is characterized by the accumulation of mesangial matrix. It is believed that glucose-induced matrix-degrading enzymes, such as collagenases, are believed to contribute to matrix accumulation [1-3]. In addition, inhibition of glucose-dependent MMP-2 (matrix metalloprotease) activity was completely blocked by neutralization of the transformed growth factor (TGF) -beta. Detection of renal tubular proteins and enzymes in urine showed a tubular compromise leading to renal complications of diabetes [3-6]. Serum and urine markers of diabetic nephropathy (both glomerular and tubular) play an important role in the early detection of kidney damage (Hong and China 1998). Glomerular and tubular markers include (1) glomerular --- transferrin, fibronectin, immunoglobulin G, Tamm-Horsfall protein, and other components of the glomerular extracellular matrix; and (2) low molecular weight tubular proteins (beta 2 microglobulin, protein, retinol, alpha 1 microglobulin and alpha-1 acid glycoprotein binding) [7]. It has been found that albumin serves as "tubular" markers, "glomerular" and alpha 1-microglobulin, measured by turbidimetry. Pathological changes in sodium dodecyl sulfate gel electrophoresis models in urine (SDS PAGE) usually precede the onset of any sign of renal involvement in diabetes⁸. The typical urine protein spectrum contains immunoglobulin G, Tamm-Horsfall protein, transferrin, albumin, beta 2-microglobulin (beta 2m), immunoglobulin light chains, retinol binding protein and alpha 1-microglobulin (alpha 1m). Low molecular weight proteinuria shows the characteristics of early stages of Balkan terminal nephropathy in diabetic patients. The experimental study showed that proteinuria in the newborn, young and adult rats is tubular, mostly

composed of low molecular weight species⁹. In contrast, late and old adult rats had a mixed glomerular structure with increased release of albumin, IgG and transferrin, as in other high molecular weight proteins.

MATERIALS AND METHODS:

This Prospective Study was held in the Nephrology department of Chandka Medical College Hospital, Larkana for one year duration from July 2017 to July 2018.

The study included 42 female patients and 27 men receiving insulin (18-20 units), age range 40-60 years, and long-term diabetic patients. 10 male and 10 female subjects of the same age without a history of diabetes were accepted as normal control. Electrophoretic patterns of 24-hour urine proteins in diabetic patients were examined in 10% SDS gradient polyacrylamide gel electrophoresis. Densitometric measurements were used to characterize patients' protein breakthrough patterns. The 24-hour urine protein was estimated using standard kit method.

RESULTS:

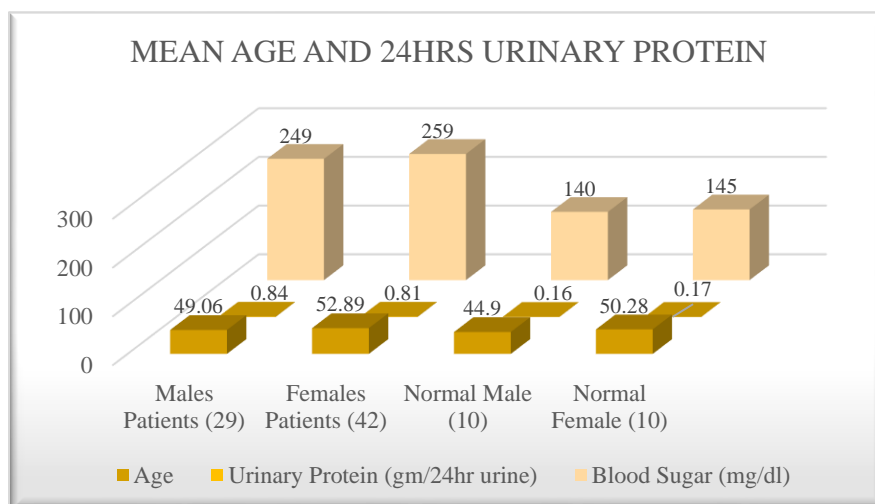
Mean age of men and women with chronic diabetes and 24-hour urine protein and blood sugar were given. The mean age of male patients with chronic diabetes was 49.06 years and female patients were 52.89 years. Urine protein levels were 0.84 and 0.81 g / 24 h urine samples in male and female patients. The urine protein level of normal male and female subjects was 0.16 and 0.17 g / 24 h urine samples, respectively. When urine protein levels of male and female patients were compared with normal male and female controls, a significant difference was observed (P <0.001).

Table No 01: Mean age and 24hrs urinary protein of males and females with chronic diabetes.

Values showed as Mean±SD

Parameters	Male Patients (29)		Female Patients (42)		Normal Male (10)		Normal Female (10)	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Age	49.06	11.83	52.89	9.04	44.9	9.1	50.28	10.8
Urinary Protein (gm/24hr urine)	0.84	0.5**	0.81	0.65**	0.16	0.12	0.17	0.56
Blood Sugar (mg/dl)	249	36.42**	259	40.42**	140	28.2	145	25.2

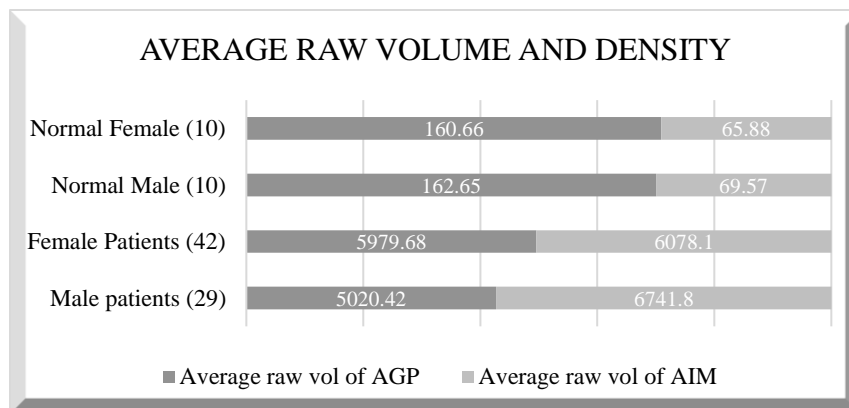
**P>0.001 = Difference is highly significant.



Blood glucose levels were 249 mg / dl and 259 mg / dl in male and female patients, respectively. Blood glucose levels of normal male and female subjects were 140.0 and 150.0 mg / dl, respectively. When the blood glucose levels of male and female patients were compared with the control subjects of normal male and female patients, a very significant difference was observed ($P < 0.001$). The electrophoretic profile of patients in both sexes showed proteins in the range of 0.004 to 0.274, with a molecular weight of 26.00 KDa to 120 KDa. In a normal subject, the protein has a molecular weight of 37.00 to 71.99 KDa in the range of 0.109 to 0.585 (data not shown).

Table No 02: Average raw volume and density of patients and normal control subjects

Parameters	Male patients (29)	Female Patients (42)	Normal Male (10)	Normal Female (10)
Average raw vol of AGP	5020.42	5979.68	162.65	160.66
Average density of AGP	0.00809	0.00664	0.25466	0.2657
Average raw vol of AIM	6741.8	6078.1	69.57	65.88
Average density of AIM	0.00428	0.00525	0.99425	0.9247



The most common proteins in patients and in normal subjects were alpha 1 acid glycoproteins and alpha 1 microglobulin, and the concentration and concentration of alpha1-acid glycoprotein and alpha 1 microglobulin were increased and compared with normal subjects.

DISCUSSION:

Urine protein patterns were found to be useful in predicting the high risk group for diabetic nephropathy in the preclinical stage. The protein model also distinguishes between nephropic glomerular or tubular origin types. It is also useful for clinicians to know the risk stage and prognosis of diabetic nephropathy. In both sexes, 24-hour urinary protein level was calculated in patients with chronic diabetes [10]. It was observed that urine protein levels of male and female patients were compared with normal male and female controls ($P < 0.001$). One study looked at additional proteins in the urine samples of patients with diabetes. The study showed that these proteins could be used as a marker for specific and definitive clinical analysis of diabetic nephropathy. It has been reported that proteinuria pattern may reflect tubular damage as well as hyperfiltration in the diabetic patient group. The electrophoretic profile of patients in both sexes showed proteins with a molecular weight of 26.00 KDa to 120 KDa [11,12]. In a normal subject the protein has a molecular weight of 37.00 to 71.99 KDa. The profile showed that in chronic diabetes, there was a proteinuria (both high molecular weight and low molecular weight) that could lead to the excretion of protein that would not normally appear in the normal protein [13]. The results support the idea that diabetic nephropathy may involve both glomerular and tubular dysfunction at an early stage. However, the precise and prognostic significance of the information provided by SDS PAGE analysis is uncertain. On the other hand, the findings of a study show the low molecular weight proteinuria of early stages of nephrology. The gross volume (concentration) and the concentration of alpha 1

glycoprotein and alpha 1 microglobulin were recorded in normal men, women and subjects. Gross volume (concentration) and alpha1 glycoprotein and alpha 1 microglobulin concentration were higher in patients than normal subjects [14]. A group of workers compared AGP levels in healthy and normal subjects and observed a high level of AGP in patients compared to normal subjects [15]. Their study shows that high levels of alpha-1 acid glycoprotein have tissue damage.

CONCLUSION:

It is therefore recommended to replace the traditional urine assay with the quantitative determination of urine proteins (SDS-PAGE). This proposed strategy may exclude or detect tubular-interstitial nephropathies in previous renal complications as in diabetes mellitus.

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