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PATIENTS OF DIABETES MELLITUS MAINTAINED ON ORAL HYPOGLYCEMIC DRUGS THE IMPORTANCE OF URINARY IgG AS A DIAGNOSTIC FACTOR FOR DIABETIC NEPHROPATHY

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Abstract
Objective: *In patients on oral hypoglycemic drug type II aim to conclude urine IgG in diabetes as marker for early stages of diabetic nephropathy.*
Study Design: *A Retrospective Study.*
Place and Duration: *In the Nephrology Department of Mayo Hospital, Lahore for one-year duration from July 2017 to July 2018.*
Methods: *The study included 42 female patients and 27 male patients, age range 40-60 and long-term diabetic patients. Patients receiving oral hypoglycemic agents were taken from the internal and external medicine OPD. Electrophoretic models of 24-hour urine proteins in diabetic patients were investigated in polyacrylamide gel electrophoresis with a 10% SDS gradient. The 24-hour urine proteins of the patients were estimated.*
Results: *Electrophoretic profile showed proteinuria status (both high molecular weight and low molecular weight). There was a significant increase in the volume (concentration) and IgG density in the patient's urine.*
Conclusion: *Urinary excretion of IgG is an important prognostic factor in idiopathic membranous nephropathy. Therefore, it is suggested that early recognition of IgG level is indicative of renal changes that may increase the likelihood of preventing the development of diabetic nephropathy.*
Key words: *Type II diabetes, IgG, SDS electrophoresis.*

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INTRODUCTION:

The toxicity of glucose in patients with diabetic nephropathy is an important cause of glomerular injury. Prolonged increase in blood glucose levels results in the formation of the latest glycation products that interfere with the normal collagen cycle and accelerate the formation of vascular permeability, matrix accumulation and adhesion molecules. Prolonged inappropriate increases in angiotensin-II lead to a reduction in renal blood flow and glomerular filtration rate, and in the release of cytokines and growth factors. An important glomerular result of these multiple activations of cytokines is destruction; this is difficult to change when podocytes are lost (such as neurons). (Townsend, R., 2010) Changes in renal tubules are important for the development of progressive diabetic kidney disease. Tubular hypertrophy, reduction of organic ions and other tubular changes usually develop before the onset of diabetic proteinuria. In addition, increased tubulo-glomerular feedback and defective uptake may contribute independently to hyperfiltration and protein loss in urine. (Townsend, R., 2012). Recent studies have shown that albumin and other proteins concentrate on the possibility of glomerular patency due to light dysfunction of proximal tubular cells, which is a direct cause of tubular cell damage. Some proteins that are cytotoxic are transferrin / iron, lipoproteins and complement components, all of which appear in urine under proteinuric conditions. The absorption of high molecular weight proteins stimulates cells of the proximal tubules to produce matrix proteins, cytokines, chemical attractants and vasoactive mediators that can cause inflammation and scarring. (R Townsend, 2007) The excess of tubular cells with filtered proteins can play an important role in the progression of diabetic nephropathy by translating the inflammation of the cellular signal (Townsend R.2008) of the glomerular protein leak. Different patterns of nephropometry are involved in patients with nephropathy diabetes: normoalbuminurica with a nephropathic hyperfiltration, with newborn (microalbuminurica) and overt nephropathy (macroalbuminurica). IgG excretion in urine was significantly increased only in patients with macroalbuminuric diabetes. Thus, this marker may characterize the stage of the manifested nephropathy (Solerte SB, Severgnini S, Locateli M, 2007). IgG antibodies consist of two types of polypeptides (heavy and light chains) held together by disulfide bonds and non-covalent bonds. Two heavy (H) and light (L) with partial reduction of IgG, HG and L chains in each molecule of IgG taking into account the molecular weights ~ 50kD for H and ~ 25kD However, the weight of the intact IgG has shown that the weight is ~ 150kD (Khurshid R., 2000)

MATERIALS AND METHODS:

This Retrospective Study was held in the Nephrology Department of Mayo Hospital, Lahore for one year duration from July 2017 to July 2018. The study included 46 female patients and 27 male patients with long-term diabetes of 40-60 years. All patients had old diabetes, renal failure, and open proteinuria. The diabetic patient and control electrophoretic 24-hour urine protein (Laemmli, UK, 1970) were examined for 10% of the gradient SDS gel electrophoresis polyacrylamide. Densitometric measurements were used to separate the protein breakthrough patterns. The 24-hour urine proteins of the patients were estimated using the standard kit method.

RESULTS:

The mean age and 24-hour urine protein and blood glucose levels were tabulated in male and female patients with chronic diabetes (Table 1).

Table1: Mean age and 24 hr urinary protein of male and female patients with chronic diabetes Values expressed as mean±SD.

Parameter	Male (29)	Female (42)	Normal Male (10)	Normal Female (10)
Age (yr)	49.06±11.83	52.89±9.04	44.90±9.10	50.28±10.8
Urinary Protein (gm/24 hr urine)	0.84±0.50**	0.81±0.65**	0.16±0.12	0.17±0.56
Blood sugar (mg/dl)	249.00±36.42**	259.00±40.42**	140.00±28.2	145.00±25.2

**P>0.001= Highly significant difference

The mean age of male patients with chronic diabetes was 49.06 years and female patients were 52.89 years. Urinary protein levels were 0.84 and 0.81 g / 24h urine samples in male and female patients. In

normal male and female subjects, the urine protein level of urine samples is 0.16 and 0.17 g / 24 h, respectively. When urine protein levels of male and female patients were compared with diabetes in normal men and women (in the past), a significant difference was observed (P <0.001). In male and female patients the blood glucose level was 259 mg / dl 259 mg / dl. Normal male and female blood glucose levels were 140.0 and 150.0 mg / dl, respectively. The blood glucose levels of male and female patients showed a significant difference when compared with normal women and men (without history) diabetes (P <0.001). The electrophoretic profile of patients in both sexes showed proteins with a molecular weight range of 32.00 KDa to 80 KDa and a density range of 0.00525 to 0.01771. However, in a normal subject, the protein had a molecular weight range from 41.77 to 71.99 KDa with a density range of 0.109 to 0.585 (data not shown). We observed gross volume (concentration) and IgG density in males, females and normal subjects. Gross volume (concentration) and IgG density in women were significantly decreased in male patients. However, IgG levels in women increased compared to normal subjects and showed a significant difference (P <0.001).

Table 2:Raw volume (concentration) and density of IgG in patients of both sexes.

Sample	Raw volume	Density
Male	6896.23±985**	0.00740±0.002**
Female	6784.68±1011**	0.00664±0.001**
Normal	182.83±110	0.43308±0.002

**P<0.001= highly significant difference

DISCUSSION:

Urinary protein patterns were found to be useful in predicting the high-risk group of diabetic nephropathy in the preclinical period. The protein pattern also distinguishes the nephropic-type glomerular or tubular origin. They are also useful for clinicians to recognize the risk and prognosis of diabetic nephropathy (Hiratsuka N, Shiba K, 1997). The mean age of male patients with chronic diabetes was 49.06 and 52.89 for female patients. One study has demonstrated that glomerular changes in early diabetes reinforce diabetes as an accelerated form of aging, similar to those with age (Acevedo LM, Londono I, Oubaha M, 2008). A 24-hour urine protein level was estimated in patients with chronic diabetes in both sexes. It was observed that urine protein levels of male and female patients were compared with normal men and women with diabetes and this difference was significantly different (P <0.001). One study looked at additional proteins in urine samples from patients with diabetes. The study has shown that these proteins can be used as markers for specific and definitive clinical analysis of diabetic nephropathy (Jain S, Rajput A, Kumar Y, Uppuluri N, 2005). Proteinuria pattern in a group of diabetic patients has been reported to reflect tubular injury as well as hyperfiltration (Woo KT, 1997). This study used sodium dodecyl sulfate gel electrophoresis (SDS PAGE) technique to analyze the protein model of chronic diabetes samples of normal subjects and patients of both sexes. The profile showed that chronic diabetes was proteinuria (both high molecular weight and low molecular weight) which could lead to the excretion of normally not visible protein in the normal protein. The study concludes with studies using the SDS-PAGE technique (Koliakos G, Papachristou F, 2001) to examine pathological changes in the protein pattern in urine. On the other hand, the findings of a group of workers (Raicevic S, Trnacevic S, 1991) show low molecular weight proteinuria in the early stages of nephrology. We observed gross volume (concentration) and IgG density in males, females and normal subjects. It was observed that gross volume (concentration) and IgG density were lower in females compared to male patients, but when these levels were compared with normal subjects, it was observed that the IgG level increased significantly in women. On the other hand, the human gross volume (concentration) and IgG density were higher in female patients and normal subjects than in the density and density of this protein, and this showed a significant difference (P <0.001). Our study was consistent with the higher number of IgG observed studies (Calzada-Garcia JA, 1996). The increase in the excretion of high molecular weight proteins is considered to be a mixed glomerular model (García). This showed that the membranes of proximal tubules and kidney glomeruli were damaged early in the course of the period of subclinical diabetic nephropathy. In another study, it was found that high molecular weight IgG protein correctly predicted kidney outcomes in patients with idiopathic membranous nephropathy (Reichert LJ, Koene RA, 1997). Recently, it has been

reported that IgG nephropathy is one of the most described glomerulopathies in patients with kidney problems (Lim BJ, Hong SW, 2009).

CONCLUSION:

It was concluded that urinary IgG excretion is an important prognostic factor in idiopathic membranous nephropathy. Therefore, it is suggested that early recognition of IgG level is indicative of renal changes that may increase the likelihood of preventing the development of diabetic nephropathy.

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