

## EVALUATION OF ROLE OF URINARY ENZYMES AS A MARKER OF EARLY RENAL DAMAGE IN DIABETIC PATIENTS: AN INSTITUTIONAL BASED STUDY

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### Abstract

**Background:** Diabetes mellitus (DM) is a metabolic disease characterized by chronic hyperglycemias a consequence of defects in insulin action, secretion or both. Different intracellular pathways demonstrated a driving role in the diabetic kidney disease (DKD) process, stimulated by hyperglycemia. Hence, the present study was conducted for evaluating urinary enzymes as a marker of early renal damage in diabetic patients. **Materials & Methods:** A total of 40 diabetic patients with diabetic nephropathy and 40 diabetics without diabetic nephropathy were enrolled. Complete demographic and clinical details of all the patients were obtained. A Performa was made and detailed diabetic details of all the patients was recorded separately. Urinary samples were obtained from all the patients and auto-analyzer was used for assessment of urinary enzyme levels. **Results:** Mean urinary alkaline phosphates levels among diabetic patients without nephropathy and with nephropathy was 9.12 IU/L and 18.44 IU/L respectively. Mean urinary gamma-glutamyl transferase levels among diabetic patients without nephropathy and with nephropathy was 16.12 U/L and 41.76 U/L respectively. Mean urinary lactate dehydrogenase levels among diabetic patients without nephropathy and with nephropathy was 10.17 U/L and 20.28 U/L respectively. Significant results were obtained while comparing the urinary enzymes levels among diabetic patients with and without diabetic nephropathy. **Conclusion:** Urinary enzyme levels were significantly increased among diabetic patients with renal damage.

## INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease characterized by chronic hyperglycemias a consequence of defects in insulin action, secretion or both. DM currently affects more than 463 million people worldwide (9.3% of adults aged 20–79 years), and the number of patients with DM is estimated to rise up to 578 million by 2030, and 700 million by 2045. The World Health Organization (WHO) reported that DM is the leading cause of kidney failure globally. Specifically, diabetic kidney disease (DKD), which is defined as elevated urine albumin excretion or reduced glomerular filtration rate (GFR) or both, is a serious complication that occurs in up to 40% of all diabetic patients.<sup>[1-4]</sup> It took more than

three millennia from the first description of diabetes in 1552 BC to the recognition of an association between diabetes and kidney disease, but it took only several decades for diabetic kidney disease (DKD) to become the leading cause of ESRD (end stage renal disease) in the United States. This microvascular complication develops in approximately 30% of patients with type 1 diabetes mellitus (DM1) and approximately 40% of patients with type 2 diabetes mellitus (DM2).<sup>[5-8]</sup> Different intracellular pathways demonstrated a driving role in the DKD process, stimulated by hyperglycemia. High blood glucose stimulates protein kinase C beta type (PKC-beta) and protein kinase C delta type (PKC-delta) activation in the renal cortex.<sup>[9]</sup> Hence; the present study was conducted for evaluating urinary

enzymes as a marker of early renal damage in diabetic patients.

## MATERIALS AND METHODS

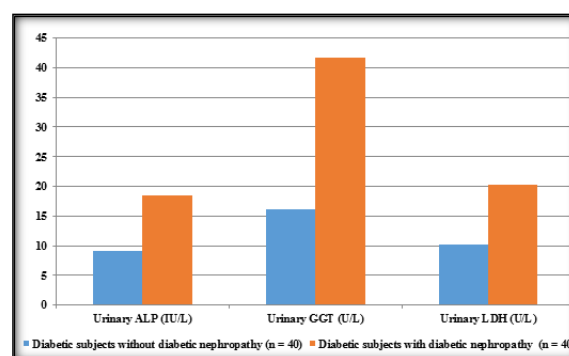
The present study was conducted for evaluating urinary enzymes as a marker of early renal damage in diabetic patients. A total of 40 diabetic patients without diabetic nephropathy and 40 diabetics with diabetic nephropathy were enrolled. Complete demographic and clinical details of all the patients were obtained. A Performa was made and detailed diabetic details of all the patients was recorded separately. Urinary samples were obtained from all the patients and auto-analyzer was used for assessment of urinary enzyme Alkaline phosphatase (ALP), Gamma-glutamyl transferase (GGT) and Lactate dehydrogenase (LDH) levels. Statistical analysis was performed using SPSS version 21.0 (IBM corporation, SPSS inc. RM 1804, Quarry Bay, Hongkong). Results were compared using the unpaired Student's *t*-test. The value of  $P < 0.01$  was considered significantly. An informed consent was obtained from each patient.

## RESULTS

Table 1 highlights the demographic data in diabetic patients without diabetic nephropathy and with diabetic nephropathy. Mean age of the diabetic patients without diabetic nephropathy and with diabetic nephropathy was 49.1 years and 47.2 years respectively. There were 22 males and 18 females among diabetic subjects without diabetic

nephropathy while there were 25 males and 15 females among diabetic subjects with diabetic nephropathy.

[Table 2] shows urinary enzymes analysis in diabetic patients without diabetic nephropathy and with diabetic nephropathy. Mean urinary alkaline phosphates levels among diabetic patients without nephropathy and with nephropathy were 9.12 IU/L and 18.44 IU/L respectively. Mean urinary gamma-glutamyl transferase levels among diabetic patients without nephropathy and with nephropathy was 16.12 U/L and 41.76 U/L respectively. Mean urinary lactate dehydrogenase levels among diabetic patients without nephropathy and with nephropathy was 10.17 U/L and 20.28 U/L respectively. Significant results were obtained while comparing the urinary enzymes levels among diabetic patients with and without diabetic nephropathy [Figure 1].



**Figure 1: Urinary enzymes analysis in diabetic patients without diabetic nephropathy and with diabetic nephropathy: ALP: Alkaline phosphatase, GGT: Gamma-glutamyl transferase and LDH: Lactate dehydrogenase.**

**Table 1: Demographic data in diabetic patients without diabetic nephropathy and with diabetic nephropathy**

Variable	Diabetic subjects without diabetic nephropathy	Diabetic subjects with diabetic nephropathy
Mean age (years)	49.1	47.2
Males (n)	22	25
Females (n)	18	15

**Table 2: Urinary enzymes analysis in diabetic patients without diabetic nephropathy and with diabetic nephropathy**

Variables	Diabetic subjects without diabetic nephropathy (n = 40)	Diabetic subjects with diabetic nephropathy (n = 40)	p-value
Urinary Alkaline phosphatase (IU/L)	9.12	18.44	< 0.001 (Significant)
Urinary gamma-glutamyl transferase (U/L)	16.12	41.76	< 0.001 (Significant)
Urinary Lactate dehydrogenase (U/L)	10.17	20.28	< 0.001 (Significant)

## DISCUSSION

In 2015, the International Diabetic Federation estimated that the prevalence of diabetes was 8.8% from ages 20 to 79 years affecting a population of approximately 440 million people. This is predicted to grow to over 550 million people by the year 2035. One of the most important clinical features of diabetes is its association with chronic tissue

complications. A short-term increase in hyperglycemia does not result in serious clinical complications. The duration and severity of hyperglycemia is the major causative factor in initiating organ damage. Early morphological signs of renal damage include nephromegaly and a modified Doppler, but the degree of damage is best ascertained from proteinuria and Glomerular filtration rate (GFR). The average incidence of diabetic nephropathy is high (3% per year) during the

first 10 to 20 years after diabetes onset.<sup>[10,11]</sup> Hence; the present study was conducted for evaluating urinary enzymes as a marker of early renal damage in diabetic patients.

Mean age of the diabetic patients without diabetic nephropathy and with diabetic nephropathy was 49.1 years and 47.2 years respectively. Mohammadi-Karakani A *et al*,<sup>[12]</sup> in a previous study compared excretion of urinary N-acetyl-beta-D-glucosaminidase (NAG), lactate dehydrogenase (LDH), alkaline phosphatase (ALP) activities, urea, creatinine and albumin, with levels of serum glucose and creatinine and whole blood glycosylated hemoglobin (HbA1c) in diabetes mellitus patients with healthy subjects. They reported that urinary NAG, ALP, LDH excretion and microalbuminuria in the diabetic patients group were significantly increased compared to control patients. They also showed that the urinary NAG excretion had the highest sensitivity and specificity (100% and 87.5%, respectively) compared to other markers.<sup>12</sup> Previously, we provided evidence supporting that dyslipidaemia and Cystatin C levels as a predictive marker of chronic kidney disease in Type 2 Diabetes Mellitus patients.<sup>[13]</sup> In that study we suggested that cystatin C estimation in serum is a useful, early detection marker, practical, noninvasive tool for the evaluation of renal disease in the course of diabetes patients. We also showed that significant lipoprotein abnormalities in CKDs and Type 2 diabetic patients when compared with control subjects.

In the present study, a mean urinary alkaline phosphates level among diabetic patients without nephropathy and with nephropathy was 9.12 IU/L and 18.44 IU/L respectively. Mean urinary gamma-glutamyl transferase levels among diabetic patients without nephropathy and with nephropathy was 16.12 U/L and 41.76 U/L respectively. Mean urinary lactate dehydrogenase levels among diabetic patients without nephropathy and with nephropathy was 10.17 U/L and 20.28 U/L respectively. Significant results were obtained while comparing the urinary enzymes levels among diabetic patients with and without diabetic nephropathy. In another study conducted by Pallavi K *et al*, authors assessed the role of urinary enzymes as early diagnostic marker for diabetic nephropathy. They measured fasting blood sugar, random blood sugar, urea, creatinine, and cystatin c in serum and ALP, LDH, GGT in urine. Their correlation studies of urinary enzyme levels with albumin-creatinine ratio (urine) and cystatin C (serum) levels didn't show any strong association among the enzyme's levels with established markers of diabetic nephropathy.<sup>[14]</sup>

## CONCLUSION

Our study suggests that evaluating urinary enzymes as a marker of early renal damage in diabetic patients. Our study has particularly highlighted the significant differences in urinary enzyme levels among diabetic patients with renal damage. Urinary alkaline phosphates, gamma-glutamyl transferase and lactate dehydrogenase levels are significantly increased in diabetic patients with nephropathy.

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