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Research Article

THE ROLE OF OXIDATIVE STRESS AND MICROALBUMINURIA THE EARLIEST MARKER OF DIABETIC NEPHROPATHY

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ABSTRACT

Aim &Objectives: To study the role of oxidative stress causing nephropathy in diabetes mellitus. The earliest indication of nephropathy is microalbuminuria.
Materials & Methods: The study included 25 healthy controls, 50 diabetic patients with no nephropathy, serum glutathione and glutathione peroxidase as oxidant and antioxidant is estimated. FBS, PPBS & creatinine is estimated by kit method. Microalbuminuria in the urine sample is estimated by using turbidometric method
Results: Lowered glutathione values and elevated glutathione peroxidase values were consistently observed in all the cases indicating the association of oxidative stress in all diabetic patients. Microalbuminuria is observed in all the patients irrespective of the duration of the illness, indicating subclinical damage of microvasculature, probably due to oxidative stress.
Conclusions: Thus the study indicates the valuable role of estimating microalbumin excretion values in all diabetic patients periodically right from the earliest stage, so that remedial measures can be instituted to prevent renal failure.

INTRODUCTION

The prevalence of diabetes is increasing worldwide, mainly due to the increase in type 2 diabetes. Diabetic kidney disease (DKD) is the leading cause of chronic kidney disease in developed countries. Several factors are involved in the development and progression of DKD including hyperglycaemia, obesity, hypertension, smoking, hereditary and advanced age.(1) It is well known that diabetic patients are two to four times more likely to suffer from these macrovascular complications. Of note here is also the fact that the atherosclerosis develops at an early stage and progresses more rapidly compared to non-diabetic patients; which translates into a poor prognosis with high morbidity and mortality in diabetic patients [2]. Besides these macrovascular complications, added microvascular injury further compounds the quality of life in such patients. The microvascular injury mainly targets two major organs, *i.e.*, eye and kidney. Its common manifestations include diabetic retinopathy and nephropathy, which incidentally are the leading cause of blindness and end stage renal disease (ESRD). Diabetic nephropathy accounts for about 40% of ESRD (End Stage Renal Disease). [3, 4, 5]The earliest clinical evidence of progressive diabetic nephropathy is repeated appearance of low but above normal levels of albumin in urine. Such a condition is referred as microalbuminuria. Diabetic nephropathy progresses gradually. In early stages of diabetic nephropathy, there are no clinical signs and symptoms of glomerular changes. The onset of diabetic nephropathy can be diagnosed only by screening the suspected patient for microalbuminuria. Oxidative stress is becoming increasingly recognized as an important causative factor. An imbalance between oxidation and antioxidation is thought to precede the development of renal lesions, and thereafter the degree of oxidation gradually increases in parallel with the progression of the disease. The emergence of microalbuminuria not only indicates the early stage of diabetic nephropathy (DN), but may also be the consequence of extensive damage of systemic endothelial cells. Previous studies confirmed that although microalbuminuria was currently the best predictor of early stage of DN, advanced changes in renal structure may have already developed when microalbuminuria is first seen. It has also been shown that reducing urinary protein excretion is of therapeutic benefit to patients with clinically significant microalbuminuria. However,

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the normal values for microalbuminuria currently used to diagnose DN may be too high, and the range of microalbuminuria values is probably too wide [6]. In the present study, we determined the association between levels of oxidant and antioxidant markers and different degrees of microalbuminuria in patients with type 2 diabetes (T2D) and an early stage of nephropathy. This information would help to the prevention and treatment of DN.

MATERIALS AND METHODS

The study was conducted over a period of six months. The study was done using microalbuminuria test and oxidative stress parameters among the subjects having diabetes. The study includes 50 diabetic subjects admitted in medicine department in RIMS Hospital, Srikakulam, Andhra Pradesh, India, having diabetic duration of below 10 years. They were in the age group of 30 to 60 years. The data on family history and personal history of diabetes, smoking habits, alcohol consumption and hypertension and treatment history for diabetes were collected through standard questionnaire. The study was approved by the Institutional Human Ethical Committee (IHEC). Informed verbal consent was obtained from all subjects. The objectives of the study were explained and a written concept was taken from each subject. Statistical Analysis: All data were expressed as mean ± S.D. The 'P' value was used to compare mean values of patients and controls. Blood samples were collected after 12 hours of fasting for estimation of FBS and analyzed and blood is collected in heparin bottles for the estimation of glutathione and glutathione peroxidase respectively. PPBS sample was collected after two hours of ingestion of food and analyzed. Fasting urine sample is collected in sterilized. Microalbuminuria in the urine sample is estimated by using turbidometric method [7]. Estimation of creatinine by the jaffe's method[8]. Determination of glutathione by nitrobenzoic acid (DTNB)[9]. estimation of glucose by glucose oxidase and peroxidase method [10].

RESULTS

Table showing the comparable values of Patients and Control with statistical analysis

Sl. No	Parameter	PATIENTS		CONTROLS		p VALUE
		Mean	S.D.	Mean	S.D.	
1	Microalbuminuria	120.2	45.4	10.53	4.63	0.01
2	Creatinine	2.02	0.53	0.96	0.35	0.01
3	Glutathione	2.4	0.92	6.98	0.56	0.01
4	Glutathione Peroxidase	130.1	50.2	36.1	4.6	0.01
5	PPBS	252.9	41.9	102	11.7	0.01
6	FBS	220.8	40.8	90.8	9.33	0.01

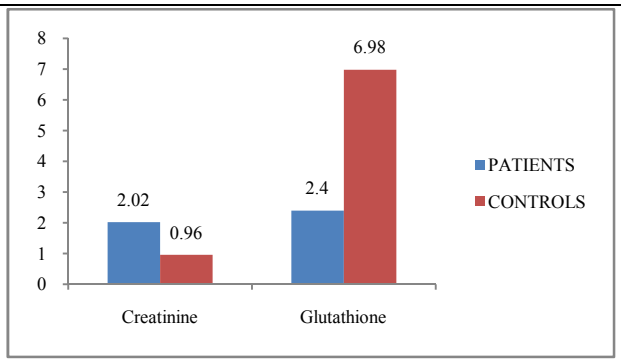

Fig 1 Comparison of mean values of Patients and Control

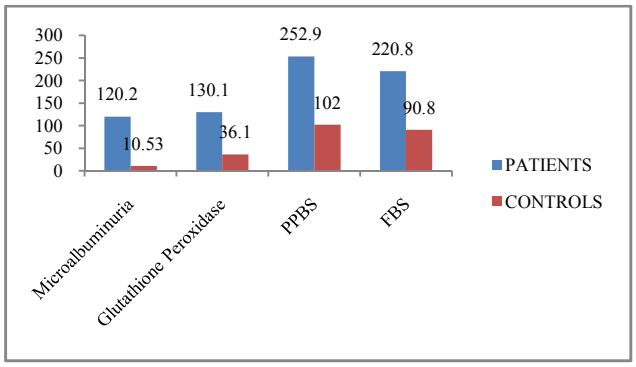

Fig 2 Comparison of mean values of Patients and Control

DISCUSSION

The present study was undertaken to assess the role of oxidative stress causing nephropathy in diabetes mellitus. The earliest indication of nephropathy is microalbuminuria.

As diabetes advances, especially in illtreated patients, it leads to microvascular damage causing various complications, one of them being nephropathy. In the present study the patients were suffering from DM for the past 5 to 15 years. None of them had clinical manifestations of well developed nephropathy. But almost all of them have shown microalbuminuria varying from 40 to 200 mg/dL (120.2 ± 45.4). It indicates that mild vascular damage starts right from the beginning of diabetes mellitus. As many authors pointed out vascular damage starts with the hyperglycemia and hence it is essential that the patients should be subjected to periodical assessment of renal functions, the best is to test for albumin in urine (microalbuminuria).

Thus it, is concluded that albumin is excreted in micro quantities in all diabetes patients to some extent. Hence it is a valuable parameter to screen all the diabetic patients periodically for microalbuminuria so that renal damage at the earliest stage can be detected and remedial measures can be instituted.

In all the cases studied serum creatinine values were not classically elevated to the extent to diagnose renal failure. Though they are elevated in most of the cases to the upper part of normal range, they are not significant as markers for renal function at subclinical stage.

Reduced glutathione and glutathione peroxidase enzyme activities were measured as markers of oxidative stress. Glutathione is an important antioxidant and its values were reported to be low in diabetes patients with oxidative stress. Reduced glutathione is a tripeptide with free –SH group and hence it is an antioxidant. In the present study glutathione values were substantially reduced (2.4 ± 0.9).

Glutathione peroxidase was elevated (130.1±50.2) in all the patients of diabetes mellitus studied. It is the enzyme which is glutathione dependant and splits H_2O_2, being the oxidant molecule, to H_2O and oxygen. The elevation of the enzyme is highly significant compared to controls (36.1 ± 4.6). It also correlates well with decreased glutathione values. Probably its elevation can be explained by the induction of the activity to combat the effect of oxidative stress caused as evidenced by decreased RBC glutathione levels.

Thus the present study supports the following the effect of oxidative stress is a damage on vascular endothelium which effects kidney and causes renal failure which is a life threatening complication. The damage of vascular endothelium causes albuminuria. Hence test for microalbuminuria periodically in diabetes patients helps to prevent chronic renal failure, if attended at the earliest stage.

It is advisable to have screening for multiple parameters with glutathione, glutathione peroxidase and microalbuminuria periodically in all diabetics along with serum creatinine, so that there can be effective monitoring of renal functions.

Thus the study indicates the valuable role of estimating microalbumin excretion in all diabetic patients periodically right from the earliest stage, so that remedial measures can be instituted to prevent renal failure.

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