

Diabetic Nephropathy and Oxidative Stress

Jyoti Dwivedi*, Dr.Purnima Dey Sarkar**

*Dept. of Biochemistry, S.S.Medical college Rewa (M.P.) India.

** Dept. of Biochemistry, N.S.C.B.Medical College Jabalpur (M.P.) India.

Summary

Nephrotic syndrome is often manifesting in progression of diabetic nephropathy. There is increasing evidence that reactive oxygen species play a major role in the development of diabetic complications. Therefore, this study was carried out to investigate oxidant and antioxidant status in diabetic nephropathy patients. The blood samples were analyzed for quantitation of malondialdehyde as index of lipid peroxide, vitamin C, total antioxidant capacity. Significantly increased levels of serum lipid peroxide and decreased levels of serum total antioxidant capacity and plasma vitamin C were noticed in the patients with diabetic nephropathy as compared to control subjects.

Key words:-Malondialdehyde (MDA), Total antioxidant capacity (TAC), vitamin C (vit C), Diabetic nephropathy (DN).

Corresponding author:

Jyoti Dwivedi

Dept. of Biochemistry,

S.S.M.C Rewa (M.P.) India.

Email ID-jyoti.bioc@rediffmail.com

Introduction

Diabetic nephropathy is a leading cause of end stage renal failure. DN has several pathways for development such as glomerular hyperfiltration, upregulation of protein kinase C, advanced glycation end products, activation of polyol pathway, increased oxidative stress and upregulation of growth factors.¹ Oxidative stress has been known to play an important role in the development and progression of diabetic nephropathy.² This is increasing evidence that reactive oxygen species (ROS) play a major role in the development of diabetic nephropathy and its complication.³ DN is characterized by excessive accumulation of extracellular matrix in the kidney reactive oxygen species (ROS) play a central role in the extracellular matrix synthesis and degradation in the glomeruli and tubulointerstitium leading to renal fibrosis.⁴ There is considerable evidence that hyperglycemia represents the main cause of complications of diabetes mellitus (DM) and oxidative stress resulting from increased generation of reactive oxygen species plays a crucial role in their pathogenesis.⁵

The objective of this study was to investigate possible associations between oxidative stress and the severity of diabetic nephropathy in nephrotic syndrome patients with the estimation of the serum TAC, MDA, plasma ascorbic acid (vit C), interrelationship of all biochemical parameters and correlate with severity of DN.

Materials and Methods

The present study was conducted at the Department of Biochemistry S.S.Medical college Rewa (M.P.) with collaboration of Department of Biochemistry N.S.C.B.Medical college Jabalpur (M.P.).

The study group:-The present study was case control study conducted on 2 groups. Each group based on 50 individuals.

Group I:-Comprised of control.

Group II:-Comprised with adult DN patients.

Age of the patients group II ranged from 30 to 80 year patients were from same geographical area and none was taking a special diet, untreated NS patients newly diagnosed by biopsies evidences of nephritis. Group Ist was judged to be free of any illness by clinical examination, DN patients were not with any other active complication medical condition or with systemic diseases. Fasting venous blood were drawn from all. Total antioxidant capacity (TAC) in serum was estimated by using spectrophotometric method described by D-Koracevic et al.⁶ MDA one of the aldehydic by product of lipid peroxidation in serum was estimated by its thiobarbituric acid reactivity, spectrophotometric method described by Hunter et al.⁷ Plasma ascorbic acid (Vit C) was measured by colorimetric method described by Roe and Kuether et al.⁸ The study protocol was approved by the ethics committee of the DAV University of M.G.M.Medical College. The mean and standard deviation were determined for each variable in all groups. All the results were expressed as mean +/-SD. Student "t" test was used to assess statistical significance of the results between group I and group II.

Results

All results of group II were compared with group I. The level of all biochemical parameters were significantly changed between groups I and II. Descriptive statics of routine diagnostic parameters in group I & group II presented in Table I. There was a statistically significant decreased level of the serum TAC, plasma vit C level and increased serum MDA, level in group II when compared to group I.

Table I- Comparison of diagnosed biochemical parameters between control (group I) and patients (group II) with DN

Parameters	Group I	Group II
n	50	50
TAC(mmol/l)	1.68 ± 0.12	0.25 ± 0.02*
MDA(nmol/ml)	0.44 ± 0.14	7.46 ± 0.29*
Vit C(mg/dl)	1.11 ± 0.25	0.15 ± 0.028*
p value		*group I compare to group II * p<0.001

(n=No. of subjects and patients). All results expressed in mean and standard deviation (SD).

Discussion

Our findings represent that DN patients have more severe oxidative stress than normal persons where oxidative stress may play an important intermediary role in the pathogenesis of diabetes complications.

The oxidative stress is increased in patients with DN compared to diabetic patients without nephropathy and this increase seems to be related to the severity of micro albuminuria levels.^{9, 10} Oxidative stresses is increased in diabetes and the overproduction of ROS in diabetes is a direct consequence of hyperglycemia. Various types of vascular cells including renal cells are able to produce ROS under hyperglycemic condition. Both NADPH oxidase and mitochondrial electron gradient play roles in hyperglycemia induced ROS generation. ROS mediate hyperglycemia induced activation of signal transduction cascades and transcription factors leading to transcriptional activation of profibrotic genes in the kidney. Conventional and catalytic antioxidants have been shown to present or delay the onset of DN. Renal lesions are associated with increased oxidative stress and decreased renal nitric oxide availability.^{11, 12, 13}

Oxidative stress occurs as a result of the imbalance between ROS production and antioxidant defenses. Sources of ROS include the mitochondria, auto-oxidation of glucose, and enzymatic pathways including nicotinamide adenine dinucleotide phosphate reductase oxidase.^{14, 15}

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References

- 1) Ohgas, shikata K, Makinoh. Nephrotic syndrome due to metabolic disease - special reference to diabetic nephropathy. *Nippon Rinsho* 2004; 62(10): 1907-1913.
- 2) Ha H, Lee HB. Oxidative stress in diabetic nephropathy: basic and clinical information. *Curr Diab Res* 2001; 1(3): 282-287.
- 3) Lee HB, Seo JY, Yum R, Uns T et al. Radical approach to diabetic nephropathy. *Kidney Int Suppl* 2007; 106: 567-570.
- 4) Hah, Lee HB. Reactive oxygen species amplify glucose signaling in renal cells cultured under high glucose and in diabetic kidney. *Nephrology (Carlton)* 2005; 10 Suppl: 57-60.
- 5) Davi G, Falco A, Patrono C. Lipid peroxidation in diabetes mellitus. *Antioxid Redox Signal* 2005; 7(1-2): 256-268.
- 6) Koracevic D, Koracevic G, Jordjevic VD et al. Method for the measurement of antioxidant activity in human fluids. *J Clin Pathol* 2001; 54: 356-361.
- 7) Hunter MI, Nlemadin BC, Davidson DL. Lipid peroxidation product and antioxidant activity protein in plasma and cerebrospinal fluid from multiple sclerosis patients." *Neurochem. Res* 1985; 10: 1645-1652 .
- 8) Roe JH, Kuether CA. Determination of vit C in whole blood and plasma by the 2, 4 dinitrophenylhydrazone method. *J Biol Chem* 1943; 147: 399.
- 9) Pan HZ, Zhang L, Guomy et al. The oxidative stress status in diabetes mellitus and diabetic nephropathy. *Acta Diabetol* 2009; 28.
- 10) Aslan M, Sabuncu T, Kocyigit A et al. Relationship between total oxidant status and severity of diabetic nephropathy in type 2 diabetic patients. *Nutr Meta Cardiovasc Dis* 2007; 17(10); 734-740.
- 11) Dave GS, Kalia K. Hyperglycemia induced oxidative stress in Type-1 and Type-2 diabetic patients with and without nephropathy. *Cell Mol Biol* 2007; 53(5):68-78.
- 12) Ha H, Hwang IA, Park JH et al. Role of reactive oxygen species in the pathogenesis of diabetic nephropathy. *Diabetes Res Clin Pract* 2008; 82 Suppl: 542-545.
- 13) Prabhakar S, Starnes J, Shi S, Lonis B, Tran R. Diabetic nephropathy is associated with oxidative stress and decreased renal nitric oxide production. *J Am Soc Nephrol* 2007; 18(11): 2945-2952.
- 14) Tan AL, Forbes TM, Cooper ME. AGE, RAGE and ROS in diabetic nephropathy. *Semin Nephrol* 2007; 27(2): 1301-1343.
- 15) Fukami K, Yamagishi S, Veda S, O Kudas. Role of AGEs in diabetic nephropathy. *Curr Pharm Des* 2008; 14(10): 946-952.