Study of Serum Sialic Acid and Malondialdehyde Levels in Chronic Renal Failure Patients: A Hospital Based Study in Government General Hospital, Anantapur, Andhrapradesh

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Abstract

Background: Chronic renal failure (CRF) is a progressive and irreversible destruction of kidney tissue. Renal failure is the cause of death in uncontrolled diabetes especially in the case of early onset insulin dependent diabetes. Serum sialic acid, a marker of acute phase response is related to the presence of diabetic micro and macro vascular complications. Malondialdehyde (MDA) is a highly toxic product formed by lipid peroxidation by free radicals. The concentration of MDA is high in diabetic patients.

Aim: The aim of the Present study is estimation of serum sialic acid, serum malon dialdehyde (MDA), in Chronic Renal failure patients (CRF) and also to study the correlation between serum sialic acid, serum MDA and plasma glucose and serum creatinine levels.

Materials and Methods: Present study was done in the Govt General Hospital, Anantapur; Andhra Pradesh. 100 subjects were taken for the study. Among them 50 was chronic renal failure patients, remaining 50 were taken as healthy controls. The study was divided in to 2 groups. Group -1: Chronic renal failure patients, Group-2: healthy controls. The parameters plasma glucose, serum creatinine, blood urea, total protein was estimated in clinical biochemistry lab GGH by using semi-auto analyzer. Serum sialic acid was estimated by modified thiobarbituric acid method of Warren, serum malondialdehyde (MDA) was estimated by thiobarbituric acid (TBA) method.

Results: The mean value of plasma glucose, blood urea, serum creatinine, serum sialic acid, serum malondialdehyde (MDA) is high in CRF patients when compared to controls. The mean value of serum total protein was low in CRF patients when compared to controls. There is a positive correlation between serum sialic acid and serum MDA(r=0.1859), serum sialic acid &

serum creatinine(r=0.1462) and also a positive correlation between serum MDA and plasma glucose(r=0.164). A negative correlation was absorbed between serum sialic acid and serum total protein(r=-0.1015).

Conclusion: Serum sialic acid is a marker for assessment of micro and macro vascular complications in diabetic patients. Malondialdehyde (MDA) is a biochemical marker to asses' oxidative stress and free radical damage to the body. Screening for earliest stages of renal damage can have a significant impact on prevention and progression of diabetic nephropathy.

Keywords: Chronic renal failure (CRF), serum sialic acid, serum malondialdehyde (MDA), Diabetes mellitus, oxidative stress

Introduction

Chronic renal failure (CRF) is a progressive and irreversible destruction of kidney tissue. The major adverse effects of chronic renal failure are due to the significant loss of functioning nephrons. In CRF due to impaired ability to regulate water balance, patients my become fluid overloaded or fluid depleted quite easily. Renal tubules of these patients lose their ability to dilute and concentrate urine [1]. The major cause of CRF include chronic glomerulo nephritis, progressive Nephrotic syndrome, Diabetes Mellitus, chronic Hypertension, long standing polycystic kidney and chronic pyelo nephritis [2]. Chronic renal failure develops insidiously, often over many years and is irreversible, leading eventually to end stage renal failure [1]. Diabetes mellitus is a group of metabolic disorder with one common manifestation: hyperglycemia. Chronic hyperglycemia causes damage to the eyes, kidney, nerves, heart, and blood vessels. In India 25-30 million persons do not know that they are diabetic. India would have around 57 million diabetic patients by the year 2025.The prevalence of diabetes is about 10-12 percent in urban population, while in rural area the percentage is about3-4 percent [3]. Renal failure is the cause of death in uncontrolled diabetes mellitus, especially in the case of early onset insulin dependent diabetes [1]. The N or O-substituted derivatives of neuraminic acid are collectively known as sialic acid, which are constituents of both glycoprotein's and gangliosides. Glycophorin is a major integral membrane glycoprotein of human erythrocytes. G lycophorins are rich in sialic acid, which gives the red cells a very hydrophilic charged coat. This enables them to circulate without adhering to other cells or vessel walls [3]. Sialic acid contributes to the maintenance of the negative charge of renal glomerular basement membrane, one of the regulators of membrane permeability. Sialic acid is a constituent of acute phase reactants which have been associated with micro vascular squeal in diabetes mellitus [4]. Malondialdehyde (MDA) is a highly toxic product formed by lipid per oxidation by free radicals. The concentration of MDA is high in diabetes mellitus which correlates well with poor glycemic control. The membrane lipids are more liable to attack by free radicals and produce damage to the integrity of the membranes [4]. The estimation serum MDA often used to assess oxidative stress, and free radical damage to the body [5]. Present study aimed to find out the correlation between serum sialic acid and serum malondialdehyde (MDA) and plasma glucose.

Materials and Methods

A total of 100 subjects were taken for this study. Out of 100subjects, 50 (32 males and 18females) clinical diagnosed chronic renal

failure cases, and 50(32 male and 18 females) age and sex matched were taken as healthy controls. The age group included individuals from 35 to 60years.

Exclusion criteria include know case of ischemic heart disease, preeclampsia patients, metabolic conditions like ketoacidosis, cerebrovascular accidents, smoking, alcohol intake, malignancy or any inflammatory disorders are excluded from this study.

Ethics: The study of approved by institutional ethical committee. The subjects of the study were divided into 2 groups. Group-1: Chronic renal failure patients, Group-2: Healthy controls.

Sample Collection

Blood samples were collected in the medicine department at Govt general hospital, Anantapur, Andhra Pradesh. 5ml of venous blood sample was collected in plain tube in the morning after an overnight fast. After collection, the samples were centrifuged, and serum was analyzed for estimation of sialic acid, malondialdehyde (MDA), serum creatinine, fasting blood sugar (FBS), postprandial blood sugar (PPBS), Serum total protein. Blood sugar was estimated by Glucose oxidize –peroxides (GOD-POD)

method [6]. Serum sialic acid was estimated by modified Thiobarbituric acid method of warren [7]. Serum malondialdehyde (MDA)estimated by Thiobarbituric acid method (TBA method) [8], Blood urea was estimated by Diacetyl monoxime (DAM) method [9]. serum creatinine estimated by Jaffes method [10]. Total protein by Biuret method [11].

Statisticial Analysis

In data analysis, a comparison of parameters between the two groups was made by using an unpaired t-test. The data was entered and complied in an excel sheet. The data was analyzed and consolidated as mean and standard deviation (SD). To analyze the statistical significance; the student t-test was performed utilizing Graph pad software. The test of the probability of less than $0.05(P<0.05)$ was significant.

Results

In present study, the age of the subjects varied from 35-60 years. The mean age in controls was 48.7 ±6.8 and 49.7 ±6.7 in CRF patients. Among the 50 CRF patients, 32 were males, 18 were females and 43 patients had diabetes mellitus. The subject's characteristics of age and sex are shown in table- 1

Table 1: Base Line Characteristics

Parameter	Chronic renal failure (group 1)	Controls (group 2)
No of participants	50	50
Age(years)Mean ±SD	49.7±6.7	48.7±6.8
Sex: male/Female	32/18	32/18
No of diabetics	43	0

The mean value of blood urea, serum creatinine, serum sialic acid and serum MDA are significantly elevated in group-1 compared to group- 2 and the mean value of serum total protein was decreased in Group-1 compared to Group-2 are shown in table-2.

Table 2: Parameters of both groups

Biochemical parameter	Chronic renal failure Cases (Group-1) N=50	Healthy Controls (Group2) N=50	t-value	P value
Fasting plasma glucose (mg/dl)	166.2±28.2	86.9±7.1	18.84	<0.0001

Post prandial plasma glucose (mg/dl)	212.9±35.8	118.0±5.2	18.54	<0.0001
Blood urea (mg/dl)	79.6±9.0	30.0±5.3	33.57	<0.0001
Serum creatinine(mg/dl)	3.4±0.6	1.2±1.7		<0.0001
Serum total protein(g/dl)	5.1±0.3	6.6±0.3	21.10	<0.0001
Serum sialic acid(mol/l)	3.2±0.3	1.5±0.2	27.42	<0.0001
Serum malondialdehyde (nmol/ml)	4.1±0.5	1.6±0.1	29.11	<0.0001

There is a positive correlation between serum sialic acid & serum MDA, serum sialic acid & serum creatinine, serum MDA & plasma glucose, MDA & plasma glucose and negative correlation between serum sialic and serum total protein, as shown in table-3.

Table 3: Malondialdehyde (MDA), Sialic acid, plasma glucose, creatinine with t –value & p-value

	r-value	t-value	p-value
Sialic acid vs. malondialdehyde (MDA)	0.1859	9.73	<0.0001
Sialic acid vs. creatinine	0.1462	2.108	P=0.0377
Sialic acid vs. total protein	-0.1015	2.032	P=0.0449
Sialic acid vs. plasma glucose	0.1663	39.87	P<0.0001
MDA vs. plasma glucose	0.1641	39.5	P<0.0001

Discussion

Chronic kidney disease is becoming a significant health problem and is rapidly assuming importance of epidemic proportions globally. India has the highest number of diabetics globally, with a prevalence of 3.8% in rural and 11.8% in urban. It is associated with unfavorable outcomes in all stages of chronic kidney diseases [12]. Chronic renal failure develops insidiously, often over many years and is irreversible, leading eventually to end stage renal failure [1].

In the present study the mean value of plasma glucose (fasting and post prandial plasma glucose) was high when compared to healthy controls(p<0.0001). Our study findings are consistent with previous study by Rajeswari A *et al* [4], Neelofer KM *et al* [12]. Diabetes is established as a metabolic disease that causes multi organ failure and renal failure increases or decreases the requirement of insulin in diabetic patients. The accumulation of toxins due to uremia leads to increased levels of parathyroid hormone in chronic renal failure patients, increase in insulin resistance in cells and tissues, usually of skeletal muscle tissues. This is attributed to the damage in the process after insulin binding to its receptors, which alters glucose metabolism and glycogen production. Secretion of insulin is also seen to be reduced in patients with CRF and appears to be due to metabolic acidosis and decreased levels of vitamins [13]. In the present study the mean blood urea value s were high when compared to controls (p< 0.0001) our study findings consistent with previous studies by pandya D*et al* [13], kamal A [14].

Measurement of blood urea is used to assess the renal function. The mean serum creatinine values are high in CRF patients when compared to controls (p<0.0001). The obtained results were consistent with previous studies by Pandya D *et al* [13], Kamal A [14]. High blood sugar levels damage millions of nephrons resulting in inability of kidneys to maintain fluid and electrolyte homeostasis.

Creatinine is filtered by glomerulus and thus, serum creatinine level is considered as an indirect measure of glomerular filtration. Diminishing of glomerular filtration rate results in rise of plasma concentrations of serum creatinine and urea.

This rise indicates progression of kidney disease and thus serum creatinine has greater prognostic ability compared with urea for predicting the adverse outcomes. Thus, serum creatinine is used for monitoring disease progression [13]. The mean value of serum total protein was low in CRF patients when compared to controls(p<0.0001). Our study findings consistent with previous studies by Lasisi T J et al [15], Gatua Wk et al [16].

Alpha and beta globulins as well as plasma albumin are some of the proteins manufactured by the liver. One of major function of the kidney in the body is pressure proteins. A dysfunctional kidney loses the ability to filter proteins and a lot of it is subsequently lost through the urine with resultant reduction in the levels of proteins in plasma in patients with chronic kidney disease (CKD) [16].

In the present study the mean value of serum sialic acid is high when compared with health controls(p<0.0001). our study finding consistent with previous studies by Rajeswari A et al [4], Shahvali S et al [17]. Serum sialic acid is marker to assess micro and macro vascular complications in diabetic patients. Sialic acid regulates vascular permeability.

Diabetic vascular complications stimulate local cytokine secretion from macrophages and endothelium which induces an acute phase response and involves the release of acute phase glycoprotein's with sialic acid from liver in to the general circulation leading to increased serum sialic acid concentration. The micro vascular damage associated with diabetes results in its shedding into the circulation. This leads to an increase in vascular permeability and increased serum sialic acid concentration [4]. In our study the mean serum malondialdehyde (MDA) was significantly elevated in Chronic renal failure patients when compared with controls (p<0.0001). Our study results consistent with previous study results by Rajeswari et al [4], Shahvali S et al [17].

CRF is a pro-oxidant state that the degree of intra cellular and extra cellular oxidative stress is mostly related to the severity of the renal failure. The oxidative stress is plays an essential role in chronic kidney disease. The oxidative state is thought to be a state of alteration between the generation of free radicals and their degradation by antioxidant systems, if not balanced, this leads to increased accumulation of the radicals, is known to occur in patients chronic kidney disease and further contributes to inflammation, endothelial dysfunction, risk of atherosclerosis and progression of chronic kidney disease.

Several pro-oxidant factors, including advanced age, diabetes, renal hypertension, low levels of antioxidant vitamins, uremia related factors and dialysis related factors contribute to the oxidative stress in chronic kidney disease patients [18]. Malondialdehyde (MDA), a three-carbon compound and is a low molecular weight aldehyde produced as a result of free radical attack on poly unsaturated fatty acids (PUFA) [19]. Free radical induced per oxidation of membrane lipids occurs in three stages-initiation, propagation and termination.

Most of products of lipid peroxidation are unstable eg. carbonyls, esters, alkenes, 2-alkenal,2,4-alkadienal,malondialdehyde (MDA). Of these, MDA is most extensively studied, and is used as a biomarker for the assessment of lipid peroxidation. MDA and other aldehydes react with thiobarbituric acid produce red–colored products namely thiobarbituric acid reactive substances (TBARS) [5]. MDA levels increase with the progression of kidney dysfunction [13]. MDA

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is used as a biochemical marker for the assessment of oxidative stress and free radical damage to the body [5].

Conclusion

Serum sialic acid is a marker to assess micro and macro vascular complications in diabetic patients. Malondialdehyde (MDA) is used as a biochemical marker for the assessment of lipid peroxidation. Blood urea & serum creatinine are mostly accepted parameters to assess chronic kidney disease status as well as to assess renal status in susceptible diabetics. Screening for earliest stages of renal damage can have a significant impact on prevention and progression of diabetic nephropathy.

Acknowledgements

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