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STUDY OF BLOOD UREA NITROGEN (BUN), SERUM CREATININE IN DIABETIC AND NON-DIABETIC PATIENTS IN A TERTIARY CARE HOSPITAL

Kapil Bhatia[1], Pratibha Misra[2], Amandeep Singh[3], Bhasker Mukherjee[1], Vivek N Ambade[4]

[1]MD., Associate Professor, Department of Biochemistry, Armed Forces Medical College, Pune

[2]MD., HOD, Department of Biochemistry, Armed Forces Medical College, Pune

[3]MBBS., Junior Resident, Department of Biochemistry, Armed Forces Medical College, Pune

[4]PhD., Scientist 'F', Department of Biochemistry, Armed Forces Medical College, Pune

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Address for Correspondence: Pratibha Misra, HOD, Department of Biochemistry, Armed Forces Medical College, Pune
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Abstract

Introduction: Patients of Diabetes mellitus type 2 are known to have high levels of BUN and Serum creatinine levels as compared to non-diabetics. There is an association between the raised BUN, serum creatinine levels and poor glycemic controls, subsequently leading to complications like nephropathy in Diabetic patients.

Aim and objectives: The aim of this study is to assess the BUN, Serum creatinine levels in relation to fasting plasma glucose (FPG) and 2-hour post plasma glucose (2h-PG) status in diabetic patients as compared to non-diabetics.

Materials and methods: 215 cases of Diabetes Mellitus were recruited along with the 100 age and sex matched controls who were healthy and non-diabetic and their blood samples were analyzed for BUN and FPG and 2-h-PG after 75-gram oral glucose in National Accreditation Board for testing and calibration Laboratories (NABL) certified laboratory.

Results: In our study we have found that there is a significant association of FPG, 2h-PG, BUN and serum creatinine in diabetic cases as compared to non-diabetic controls. There also exists a significant positive correlation between mean BUN (12.3 ± 5.9mg/dL) and mean FPG (159.72 ± 71.60 mg/dL) and mean 2h-PG (222.76 ± 100.86 mg/dL) levels.

Conclusion: BUN and serum creatinine are the markers in diabetes patients to assess the diabetic nephropathy. Serum BUN may be preferred over serum creatinine in assessing early renal impairment due to positive correlation with fasting and post prandial glycemic levels.

Keywords: BUN, Nephropathy, FPG, 2h-PG, Diabetic complications.

Introduction:

Diabetes Mellitus is a condition characterized by sustained high glucose levels in the blood due to abnormal metabolism of dietary components like carbohydrates, fat and protein metabolism. The main defect involves either complete or partial deficiency of Insulin secretion or action of insulin or both (1).

Diabetes mellitus is much prevalent metabolic disorder with a global burden of around 422

million as per World Health Organization (WHO) (2), not just the developed countries but the developing countries like India have a higher prevalence of diabetes amongst the peak working age group of 40 to 65 years causing early deaths in around 43 percent of the patients. It is also anticipated that with the growing trend of shifting to sedentary life styles, lack of exercise and adoption of unhealthy diets like fast foods rich in high carbohydrates and fats (3), there is likelihood of doubling up of this figure by 2045.There were 65 million prevalent cases of diabetes in India in 2016, compared with 26 million in 1990 (4).

Diabetic nephropathy is one of the most common complication encountered amongst the diabetics in elderly age group (5). Life expectancy dips drastically with this complication due to progression to permanent renal damage (6). Diabetes may progress silently to diabetic nephropathy which is a progressive kidney disease involving damage to the capillaries in glomeruli, characterized by diffuse scarring of the glomeruli. While final diagnosis may need a biopsy, but diagnosis is usually done with measurement of BUN/ serum creatinine/ creatinine clearance/urinary albumin/Glomerular filtration rate (GFR) etc (7). Diabetic nephropathy is characterised by urinary micro albuminuria >300mg/dL and decline in the GFR and has a higher risk of cardiovascular morbidity and mortality.

There is progressive increase in the BUN and Serum creatinine with the renal disease in diabetes. As these tests are easily available and can be carried out routinely, it can help in the early detection of the kidney involvement in diabetes and can even prevent the advancement to end stage renal disease with suitable intervention. Higher level of urea may be a risk factor of increased insulin resistance and even supress insulin secretion. Even higher BUN >25mg/dL has been linked to with the increased incidence of diabetes mellitus (8).

The skeletal muscle has a fixed mass per unit of creatine and the breakdown rate of creatine to creatinine is also consistent, which is the sole reason of the constant concentration of plasma creatinine throughout and is also a direct indicative of the skeletal muscle mass (9). BUN being a small non protein bound molecule is generally freely filtered at the glomerulus of the nephron, but because of its reabsorption in the tubules of the nephrons it is not a sensitive marker of GFR. Rise in BUN usually relates to the symptoms of the uraemia as compared to creatinine whose concentration remains mostly constant and also undergoes tubular secretion, hence serum creatinine is considered a sensitive marker of the renal involvement in diabetes (10).

Considering these facts from the literature, our aim was to assess the BUN, Serum creatinine levels in relation to FPG and 2h-PG status in diabetic patients as compared to non-diabetics with objectives to study the correlation of BUN and serum creatinine in diabetic patients. We also study the levels of BUN and serum creatinine in diabetic males and females. We studied the usefulness of the BUN and Serum creatinine as a simplest tool for early diagnosis and prognosis of diabetic nephropathy in 02 age groups of ≤ 45 years and > 45 years amongst diabetic patients.

MATERIALS AND METHODS

The study was conducted in biochemistry department in a tertiary care hospital after necessary approval from institutional ethical committee.

Out of 380 screened patients, 215 known diabetic cases reporting for follow up were recruited as a study group along with 100 non-diabetic age and sex matched healthy individuals as control after the informed consent.

We further divided the diabetic group into 02 age groups of ≤ 45 years and > 45 years to compare the BUN and creatinine levels.

Inclusion Criteria: Known Diabetic cases from 22 years to 85 years of age were included as study group.

Exclusion Criteria: Patients with other kidney disease, congestive cardiac failure, urinary tract obstruction, muscular dystrophy and other myopathies and auto immune disorders were excluded.

In our NABL accredited laboratory with all the quality control procedures in place along with special emphasis to avoid pre analytical errors in sample collection , all three analytes viz plasma glucose, BUN and serum creatinine were estimated by withdrawing 5ml of Intravenous blood in the respective vacuum evacuated tubes.

Estimation of plasma sugar was done by Hexokinase method (11), BUN by Urease Glyceraldehyde dehydrogenase method (12) and serum creatinine by modified Jaffe kinetic method (13) on Siemens Dimension EXL 200 fully automated clinical chemistry system. The reference values used for various biomarkers are mentioned in Tabel 7.

The values for various statistical parameters like mean, standard deviation and coefficient of correlation 'r' were calculated using SPSS version 20.2 software. Analytical data was analysed using Fisher exact test and t test for various non parametric and parametric variables.

RESULTS

We studied 215 diabetic cases with mean age of 55.14 ± 13.44 years as compared to 100 non diabetic age and sex matched healthy controls with mean age of 50.72 ± 14.47 years. Mean of BUN & creatinine amongst Diabetic & Non Diabetic are shown in Figure 5. Our study showed significant association ($p<0.05$) of FPG and 2h-PG levels with BUN and serum creatinine values as mentioned in Table 1.

We also found that strong positive correlation between mean BUN with mean FPG and 2h-PG levels as compared to weak positive correlation of mean serum creatinine levels to the mean FPG and 2h-PG as shown in table 2 and 3. The association of BUN with FPG and 2h-PG levels was significant as compared to association of serum creatinine with FPG and 2h-PG which was not found significant in our study as represented in Figure 1-4.

Significant association in diabetic males and females to BUN and serum creatinine were seen in our study as seen in table 4. However, a greater number of males have higher values of BUN and creatinine as compared to females amongst diabetic cases. Significant association in the mean BUN as compared to serum creatinine has been found in our study amongst the two age groups as seen in table 5 and 6.

Age group >45 years shows significant higher BUN values as compared to age group ≤ 45 years while in case of serum creatinine there is narrow margin difference.

Table 1: **Mean and SD values of blood urea nitrogen, serum Creatinine and FPG and 2h-PG levels in Diabetic and Non Diabetic Controls**

Parameters (mg/dL)	Diabetic (N=215)	Non-Diabetic (N=100)	P value
FPG	158.3 ± 70.5	86.8 ± 7.9	0.00001
2h-PG after 75 gram glucose	218.2 ± 103.6	119.8 ± 13.6	0.00001
BUN	12.3 ± 5.9	11.6 ± 9.6	0.010
Serum creatinine	1.0 ± 0.5	0.8 ± 0.6	0.010

Table 2: Correlation of mean BUN and with mean FPG and 2h-PG in Diabetes

Parameter (mg/dL)	Mean BUN (12.3 ± 5.9)	R value	P value
FPG	158.3 ± 70.5	0.13	0.04
2h-PG after 75 gram Glucose	218.2 ± 103.6	0.14	0.03

Table 3: Correlation of mean serum creatinine and with mean FPG and 2h-PG in Diabetes

Parameter (mg/dL)	Mean Serum Creatinine (1.0 ± 0.5)	R value	P value
FPG	158.3 ± 70.5	0.009	0.88
2h-PG after 75 gram Glucose	218.2 ± 103.6	0.006	0.921

Table 4: Sex Distribution of BUN and Serum creatinine in Diabetes cases

	Males	Females	P value
Raised BUN (>18mg/dL)	16	7	0.01 Significant
Normal BUN (7-18mg/dL)	96	11	
Raised Serum creatinine (>1.3mg/dL)	13	4	
Normal Serum creatinine (0.3-1.3mg/dL)	91	74	

Table 5: Mean ± SD of BUN with Age in Diabetes

	≤ 45 years	> 45 years	P value
Raised BUN (>18mg/dL)	22.43±5.00	26.73±6.21	0.00
Normal BUN (7-18mg/dL)	9.83±2.75	11.21±2.72	0.00

Table 6: Mean of Serum Creatinine with Age in Diabetes

	≤ 45 years	> 45 years	P value
Raised Serum creatinine (>1.3mg/dL)	1.55±0.21	2.18±1.21	0.000
Normal Serum creatinine (0.3-1.3mg/dL)	0.88±0.27	0.92±0.18	0.000

Table 7: Various Biomarkers with the reference range

Analyte	**Normal Range**
FPG	>100 mg/dL
2h-PG after 75 gram glucose	>200 mg/dL
BUN	7-18 mg/dL
Serum creatinine	0.7 to 1.3 mg/dL

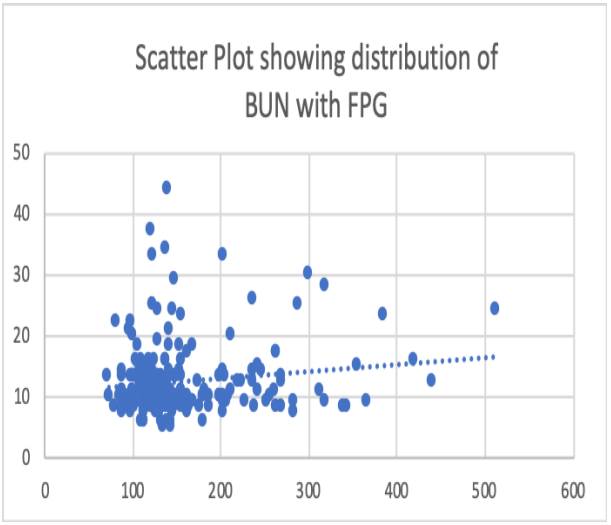
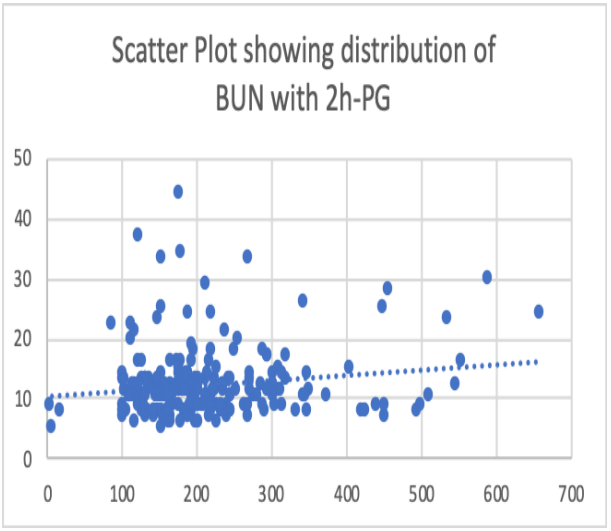


Figure 1:



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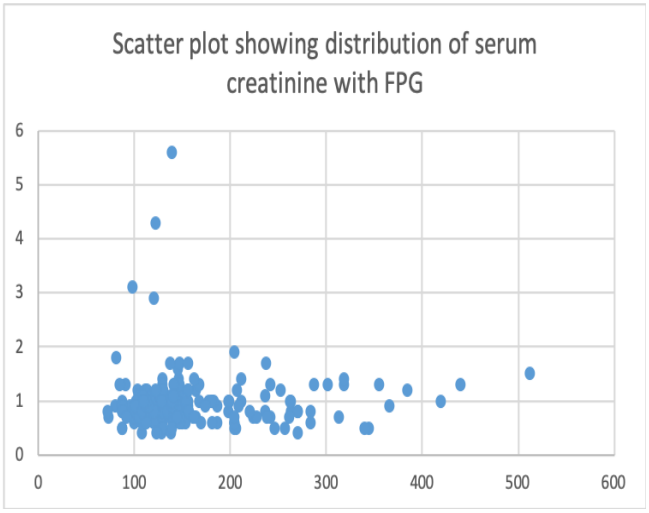

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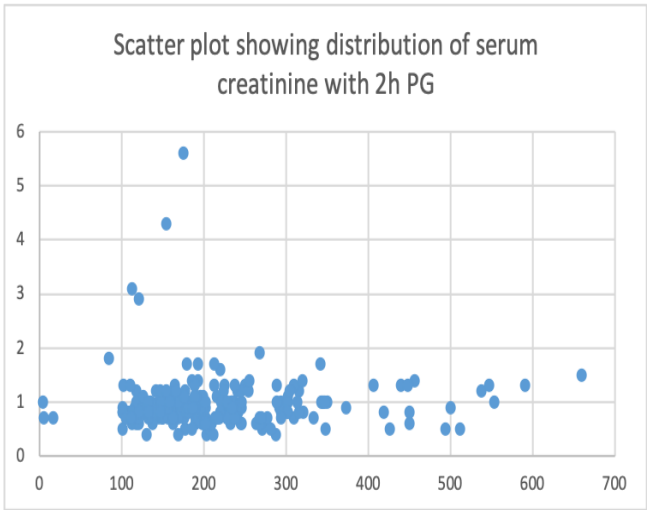

Figure 4:

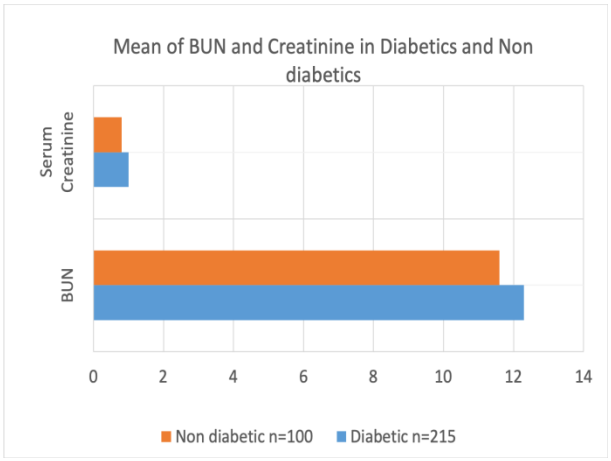

Figure 5:

DISCUSSION

Diabetes mellitus is characterized by abnormally raised blood glucose levels which is also seen in our study. High FPG and 2-h-PG levels may lead to microvascular changes via activation of non-enzymatic glycosylation of collagen and tissue proteins in kidney (14). Raised glycemic levels affects the nephrons which are the filtering units of kidney leading to renal dysfunction (15). If the kidneys are not functioning properly, the BUN and creatinine formed will not be cleared off from the kidney and will increase abnormally in the serum, the same has been found in our study and a study conducted by Mishra et al (16) and Singh et al (17).

We found a significant positive correlation of serum BUN and serum creatinine with the FPG

and 2-h-PG levels in our study, similar results were seen in the study conducted by Bamanikar et al (18). The reason for this could be BUN is earlier marker which is affected with even the minor renal dysfunction and even varies with the dietary intake of the individual in contrast to creatinine whose rate of excretion remains constant and is neither reabsorbed and not affected with the minor renal dysfunction which is usually elevated after prolonged duration of hyperglycemia especially long duration diabetes. Since our study had the limitation that about the duration of diabetes in the cases, this exact correlation cannot be commented upon.

There is a significant association with the BUN and serum creatinine values in diabetes patients. Females owing to their less muscle mass tend to have low normal serum creatinine as compared to males, in our study only 04 females as compared to 13 males were found to have raised serum creatinine. Similarly, a greater number of males were found to have raised BUN as compared to females and the same have been found in a study conducted by Wagle et al (19).

In our study there was significant difference of mean value of BUN in age >45 years as compared to ≤ 45 years of age as shown in Tabel 5 as compared to mean serum creatinine values which were less prominent as also seen in study by Verma et al (20), this may be due to lesser excretion of creatinine per kg body weight in elderly. Hence BUN may be preferred over serum creatinine as an earlier marker of renal impairment in diabetic patients of age > 45 years as compared to young diabetics ≤ 45 years of age.

CONCLUSION

Renal Parameters especially BUN and serum creatinine are the markers in diabetes patients to assess the diabetic nephropathy. From our study we conclude that serum BUN may be preferred over serum creatinine in assessing early renal impairment due to positive correlation with high FPG and 2-h-PG levels. Diabetic patients need regular monitoring with this easily available accessible test and control of glycemic levels in diabetic patients by way of therapeutic intervention and ensuring drug compliance in patients is of utmost importance to prevent complication like nephropathy which is one of the major causes of chronic renal failure.

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