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ANALYSIS OF ROLE OF VITAMIN D AT URINARY LEVEL AS A NEW BIOMARKER IN ANALYSIS OF DIABETIC NEPHROPATHY IN PAKISTAN

Zafarullah[1], Nosheen Niazi[2], Zenab İlyas Rajput[3]

[1]MO at Allergy Centre NIH Islamabad
[2]Army medical college, Rawalpindi
[3]Rawalpindi medical college

Abstract:

Introduction: *Diabetes mellitus (DM) belongs to a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Early detection of diabetic nephropathy (DN) represents a great challenge in an attempt to reduce the burden of chronic kidney diseases in diabetic patients.* ***Objectives:*** *The main objective of our study is the role of vitamin D at urinary level as a new biomarker in analysis of diabetic nephropathy in Pakistan.* ***Methodology of the study:*** *The study was conducted at Allergy Centre NIH Islamabad and Army medical college Rawalpindi with the permission of concerned department. For the purpose of study 80 patients were selected and we collect the data from these selected patients. Furthermore the analysis of Urine, creatine, Albumin and other series of test were taken place in the pathology laboratory of the hospital.* ***Results:*** *Vitamin D levels were significantly elevated in micro- and macroalbuminuria patient groups compared with those of the normoalbuminuria patient group and controls. There was significant correlation between serum and urinary levels of VDBP in total patient group.* ***Conclusion:*** *These investigations shall be helpful in assessing the biochemical alterations in the Pakistani diabetic population, which should contribute to the development of treatment plans for this disease which is one of the most widely occurring and debilitating diseases.*

Key words: *Albumin, Diabetic, nephropathy, disease, patients*

***Corresponding Author:**
Zafarullah,
MO at Allergy Centre NIH,
Islamabad

QR code

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INTRODUCTION:

Diabetes mellitus (DM) belongs to a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Early detection of diabetic nephropathy (DN) represents a great challenge in an attempt to reduce the burden of chronic kidney diseases in diabetic patients. This study aimed to investigate the potential early prediction role of urinary vitamin D-binding protein for the diagnosis of DN and to examine the possible correlation to serum VDBP, high-sensitivity C-reactive protein, and insulin resistance in these patients. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels [1]. In 2013, according to the International Diabetes Federation, an estimated 381 million people had diabetes. Its prevalence is increasing rapidly, and by 2030 this number is estimated to almost double [2].

Diabetic nephropathy (DN) is one of the most important long-term complications of diabetes. It is characterized by the development of proteinuria with a subsequent decline in glomerular filtration rate (GFR), which progresses over a long period of time, often over 10-20 years [3]. Over the past 20 years, the prevalence of DN in the USA has increased in direct proportion to the prevalence of diabetes. Although DN cases vary largely among countries, on average it develops in 30-40% of patients with diabetes [4].

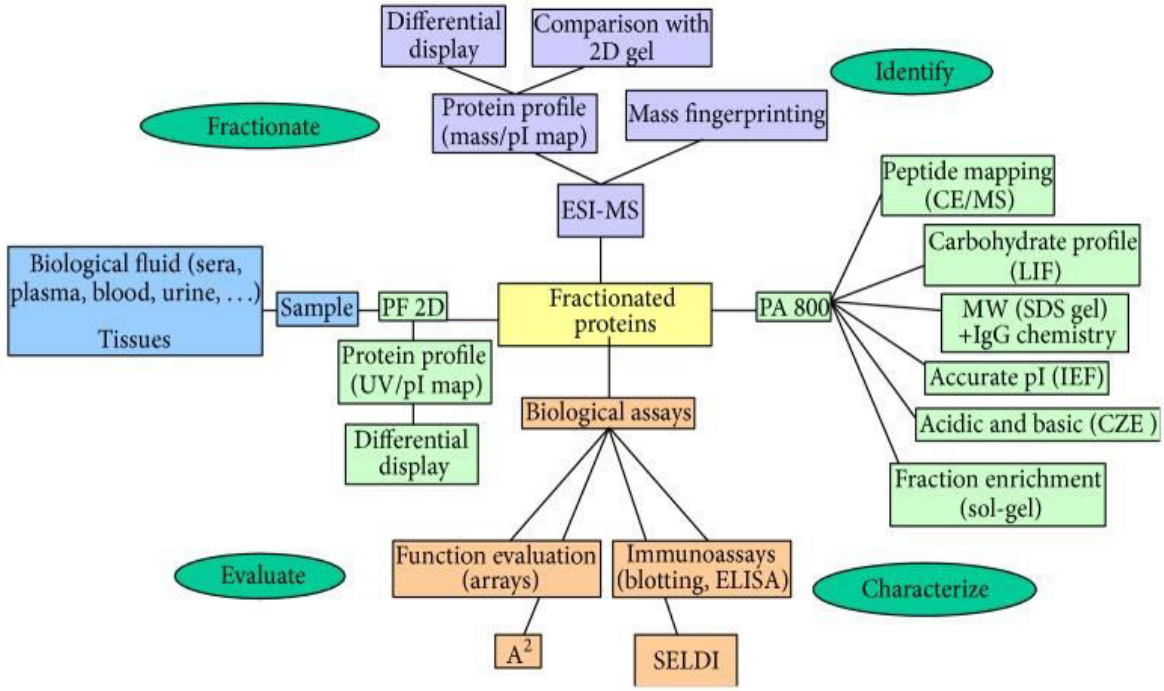

Figure shows the biomarkers for DN

In addition, it has been demonstrated that the presence of vitamin D deficiency or insufficiency in patients with diabetes is independently associated with the development of DN. Moreover, exaggerated urinary excretion of VDBP was observed in patients with type 1 diabetes, which contributed mechanistically to vitamin D deficiency in this disease [5].

Objectives

The main objective of our study is the role of vitamin D at urinary level as a new biomarker in analysis of diabetic nephropathy in Pakistan

METHODOLOGY OF THE STUDY:

The study was conducted at Allergy Centre NIH Islamabad and Army medical college Rawalpindi with the permission of concerned department. For the purpose of study 80 patients were selected and we collect the data from these selected patients. Furthermore the analysis of Urine, creatine, Albumin and other series of test were taken place in the pathology laboratory of the hospital. 5cc blood sample was taken for this purpose. Blood was further processed for the estimation of albumin and total protein. Commercially available enzymatic kits of Randox were used. Blood was centrifuged at 4000 rpm for 10 minutes and serum was separated. Blood

samples will be collected into EDTA tubes from fasting proteins. The blood will be centrifuged and indomethacin and butylated hydroxytoluene will be added into the plasma samples before they will be stored at -80°C until analysis.

Analysis of data

The economic and health status describe the level of awareness regarding disease. The collected data were analyzed using SPSS software (version 17). The results are presented as a mean with 95% confidence interval limits or standard deviations. The significant value for P <.05 was accepted as statistically significant.

RESULTS:

Table 01 shows the basic characteristics of the study group. These include blood pressure, HEI, BMI, smoking habits and some other basic things.

Table 01: Demographic characteristics of the diabetic group

Variables	Co-efficient	SE
Blood pressure	0.048	0.35
Healthy eating index (HEI)	−0.059	0.05
Smoker	0.060	0.80
Food security	0.106	0.12
Belong to rural area	0.59	0.70
BMI	0.5460.24	

Table 02 shows the lipid profile of the normal group and diabetic group. It also shows the microalbuminuria and macroalbuminuria of diabetic group. The data presented in the table shows the total protein, serum albumin, serum urea, creatinine, GFR and some inflammatory marker which is vitamin-D. It shows the elevated levels of vitamin-D in diabetic patients.

Table 02: Parameters of the study group

Variables	Control group	Diabetic groups			values
		Normal albuminuria	Microalbuminuria	Macroalbuminuria	
Lipid profile					
Total cholesterol (mmol/l)	4.8 ± 1.5	4.8 ± 0.7	4.6 ± 0.9	5.1 ± 1.4	0.289
HDL-c (mmol/l)	1.2 ± 0.4	1.2 ± 0.3	1.1 ± 0.4	0.9 ± 1.0	0.196
LDL-c (mmol/l)	6.9 ± 24.5	3.3 ± 0.6	3.4 ± 1.1	1.12 ± 0.4	0.417
Diabetic assessment					
HbA1c (%)	4.7 ± 0.4	7.2 ± 0.7[a]	7.5 ± 1.4[a]	9.4 ± 0.8[a,b,c]	<0.001
Fasting insulin (mIU/l)	9.6 ± 5.0	25.3 ± 10.4[a]	32.3 ± 14.4[a,b]	37.8 ± 16.8[a,b]	<0.001
Total protein (gm/l)	74.2 ± 10.4	73.9 ± 3.2	70.7 ± 4.2	71.9 ± 5.5	0.052
Serum albumin (gm/l)	47.7 ± 7.7	35.0 ± 3.3[a]	34.1 ± 2.4[a]	34.4 ± 2.5[a]	<0.001
Renal function tests					
Serum urea (mmol/l)	3.5 ± 1.1	4.6 ± 1.0[a]	4.5 ± 0.9[a]	4.5 ± 1.4[a]	<0.001
Serum creatinine (µmol/l)	57.7 ± 12.5	56.2 ± 16.0	59.1 ± 9.8	69.2 ± 16.6[a,b,c]	<0.001
Albumin/creatinine ratio (µg/mg)	16.7 ± 8.7	10.5 ± 7.8	77.5 ± 65.5	803.5 ± 355[a,b,c]	<0.001
eGFR (ml/min/1.73 m^2)	102.4 ± 17.6	111.2 ± 36.6	107.9 ± 17.2	113.3 ± 22.9	0.232
Inflammatory markers					
hs-CRP (mg/l)	0.12 ± 0.08	0.17 ± 0.05[a]	0.17 ± 0.04[a]	0.15 ± 0.02[a,b,c]	<0.001
VDBP analyses					
sVDBP (µg/ml)	210.3 ± 33.8	202.4 ± 43.9	248.4 ± 36.5[a,b]	299.2 ± 50.6[a,b,c]	<0.001
uVDBP/uCr (ng/mg)	127.7 ± 21.9	193.1 ± 141.0	820.4 ± 402.8[a,b]	1458.1 ± 210[a,b,c]	<0.001

DISCUSSION:

The identification of novel biomarkers of the early stages of DN is mandatory in an attempt to reduce the burden of chronic kidney diseases in diabetic patients [6]. To evaluate whether uVDBP levels could be a novel noninvasive biomarker for DN in a sample of Saudi population, the current study results demonstrated that the uVDBP levels were highly elevated in Saudi patients with DN and were correlated significantly with the severity (degree of albuminuria) of DN. Interestingly, the human VDBP gene is a member of a multigene cluster residing on chromosome 4 and coding for related albumin proteins which have structural and functional similarities [7]. In the normal kidney, VDBP as a 25-(OH) vitamin D3/VDBP complex is reabsorbed by megalin-mediated endocytosis and catabolized by epithelial cells of the proximal tubules contributing to the reduction of its urinary excretion levels. Clinically, it has been found that excessive excretion of uVDBP could indicate tubular dysfunction which was considered as one of the early hallmarks of DN.

The reasons underlying the enhanced excretion of UVDBP in patients with DN may be associated with renal tubular damage in DN patients. It has been increasingly documented that renal tubular injury plays an integral role in the pathogenesis of diabetic kidney disease. In addition, tubulointerstitial lesions were found to be the early and independent features of diabetic kidney disease [7-9]. They also indicated that damaged tubular epithelial cells in areas of tubulointerstitial fibrosis may no longer be able to handle VDBP, resulting in gross VDBP loss into the urine, and that it can be modulated by anti-proteinuric treatment in patients. Although the combination of the renin-angiotensin-aldosterone system blockade and dietary sodium restriction, an intervention considered optimal for renoprotection, considerably reduced VDBP excretion, they demonstrated that UVDBP excretion is increased early after renal injury and is associated with tubulointerstitial inflammation and fibrosis independently of albuminuria [10]. In humans, UVDBP increased with increasing severity of renal damage, and responded to renoprotective therapy. Yet, persisting UVDBP above normal suggested persistent tubular interstitial damage [11].

CONCLUSION:

These investigations shall be helpful in assessing the biochemical alterations in the Pakistani diabetic population, which should contribute to the development of treatment plans for this disease which is one of the most widely occurring and debilitating diseases. It is concluded that vitamin-D binding protein plays an important role and act as serum biomarker for the identification of diabetic nephropathy.

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