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# ANALYSIS OF VITAMIN D AS A NEW BIOMARKER OF NEPHROPATHY IN DIABETIC PATIENTS OF PAKISTAN

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**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. 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.*

***Objectives:*** *The main objective of our study is to find the role of vitamin-D as a biomarker in investigation of nephropathy in diabetic patients in Pakistan.*

***Methodology of the study:*** *This cross sectional study was conducted in District Headquarter Hospital Lodhran during January 2019 to July 2019. For this purpose we collected the data of 100 patients that were selected for further analysis. Those who selected for study were further goes for the analysis of Urine, creatine, Albumin and other series of test.* ***Results:*** *Lipid profile of the normal group and diabetic group 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.* ***Conclusion:*** *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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## INTRODUCTION:

Diabetes mellitus (DM) belongs to a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. 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. Over the past 20 years, the prevalence of DN in the USA has increased in direct proportion to the prevalence of diabetes [3]. Although DN cases vary largely among countries, on average it develops in 30-40% of patients with diabetes.

D-binding protein (DBP), a multifunctional and highly polymorphic plasma protein synthesized primarily in the liver, was identified about half a century ago and characterized as able to bind various forms of vitamin D [4]. DBP (also referred to as Gc-globulin) is a member of the albumin gene family. Vitamin D circulate bound to vitamin D-binding protein (VDBP) (85-90%) and albumin (10-15%), with less than 1% of circulating hormone in its free form. VDBP prolongs the serum half-life of 25-hydroxyvitamin D and protects against vitamin D deficiency by serving as a vitamin D reservoir [5].

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 [6].

**Objectives:**

The main objective of our study is to find the role of vitamin-D as a biomarker in investigation of nephropathy in diabetic patients.

**Methodology of the study:**

This cross sectional study was conducted in District Headquarter Hospital Lodhran during January 2019 to July 2019. For this purpose we collected the data of 100 patients that were selected for further analysis.

**Data collection:**

Those who selected for study were further goes for the analysis of Urine, creatine, Albumin and other series of test. 5cc blood sample was taken from vein. Blood was further processed for the estimation of albumin and 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**.**

**Statistical analysis:**

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:

The data was collected from 100 patients. The mean age was 45±6.67 years. 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 |
| Drinker | -0.343 | 0.08 |
| Belong to city area | 0.057 | 0.01 |
| 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 | |
| | | N=50 | N=50 | N=50 | |
| 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 |

## 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. 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 [8].

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 [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].

## CONCLUSION:

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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