



## Visfatin Level in Diabetic and Non-diabetic Chronic Kidney Diseases

Samer S. Zekry<sup>1</sup>, Maher A. Al Amir<sup>1</sup>, Mohamed A. Mashahit<sup>1\*</sup>,  
Hoiyda A. Abd El-Rasol<sup>2</sup> and Ehab A. Hassan<sup>1</sup>

<sup>1</sup>Department of Internal Medicine, Faculty of Medicine, Fayoum University, Egypt.

<sup>2</sup>Department of Clinical and Chemical Pathology, Faculty of Medicine, Fayoum University, Egypt.

### Authors' contributions

This work was carried out in collaboration between all authors. Author MAM designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors MAAA and EAH managed the analyses of the study. Author HAAER managed the laboratory work. Author SSZ managed the literature searches. All authors read and approved the final manuscript.

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### ABSTRACT

**Introduction:** Chronic kidney disease (CKD) has become a global public health threat. The irreversible nature of the disease, its association with significant morbidity and mortality as well as the cost of renal replacement therapy leads to a large burden for health care providers, particularly in developing countries like Egypt.

**Objective:** To find a non-invasive method to evaluate association of serum visfatin with chronic kidney disease secondary to diabetic nephropathy and compare to patients with chronic kidney disease secondary to other causes.

**Methods:** Ninety individuals including 30 healthy controls and 60 patients of CKD were included in this study. Patients with CKD were further grouped based on etiology of CKD into 30 diabetic patients and 30 non-diabetic patients. Patients with type 1 diabetes mellitus, urinary tract infection, urolithiasis, liver cirrhosis, stroke, ischemic heart disease, and rheumatoid arthritis were excluded. Measurement of serum visfatin was done through ELISA Kit (Elabscience pharmaceuticals).

\*Corresponding author: E-mail: mam22@fayoum.edu.eg;

**Results:** Visfatin concentration was significantly high in patients with CKD compared to controls ( $p < 0.001$ ). No significant difference in Visfatin concentrations between patients of CKD with and without diabetes was detected ( $p > 0.05$ ). Visfatin concentration was significantly high in patients with CKD stage 2 compared to CKD stage 1 ( $p < 0.001$ ).

**Conclusion:** The present study confirms the association of visfatin with CKD, however further studies at molecular level to check its expression within renal tissue may clarify its definitive role in CKD.

*Keywords: Visfatin; chronic kidney disease; diabetes mellitus.*

## 1. INTRODUCTION

Chronic kidney disease (CKD) has become a global public health threat. The irreversible nature of the disease, its association with significant morbidity and mortality as well as the cost of renal replacement therapy lead to a large burden for health care providers, particularly in developing countries like Egypt [1]. Diabetic nephropathy ranks top among the causes of end stage renal disease in patients older than 40 years, accounting for 44% of new cases of chronic kidney disease in United States, 20% cases of end stage renal disease in England and is the leading known cause of chronic renal failure in Egypt [2].

In Egypt, the global prevalence of diabetes mellitus in the year 2010 among adults has been estimated to be 6.4%. It is estimated that by the year 2030, Egypt will have at least 8.6 million adults with diabetes. Diabetes mellitus becomes the second most common cause of end stage renal disease in Egypt [3]. Type 2 diabetes mellitus, hypertension, obesity, and dyslipidemia are components of metabolic syndrome and are all major risk factors for cardiovascular disease. With the availability of excess food in many parts of the world, obesity is a growing problem that is increasing at an alarming rate in adults as well as in children. Obesity increases the risk for type 2 diabetes mellitus, cardiovascular disease, cancer, musculoskeletal disorders, and pulmonary disease [4].

Diabetic nephropathy, is a clinical syndrome characterized by micro-albuminuria when albumin/creatinine ratio (ACR) greater than or equal to 2.5 mg/mmol for men or 3.5 mg/mmol for women, or urinary albumin concentration greater than or equal to 20 mg/L and then overt proteinuria when ACR greater than or equal to 30 mg/mmol or urinary albumin concentration greater than or equal to 200 mg/L confirmed on at least two occasions 3-6 months apart, permanent and irreversible decrease in

glomerular filtration rate (GFR), and arterial hypertension [5].

One of the most interesting features of research done in last decade is the emergence of adipose tissue as an endocrine organ. It is no more considered as an inert site of nutrient storage but rather a metabolically active organ capable of producing different hormones and soluble factors termed adipokines and visfatin is one of them. Visfatin is a 52-kDa protein that has been cloned already years ago as pre-B cell colony-enhancing factor (PBEF). Another alternative name for visfatin/PBEF is nicotinamide phosphoribosyl transferase (Nampt) indicating a different biological property namely being a nicotinamide dinucleotide (NAD) biosynthetic enzyme, is a pro-inflammatory cytokine [6].

The Nampt gene has been implicated in the susceptibility and pathogenesis of a number of human diseases and conditions because of its pleiotropic physiological functions. As a multifunctional protein, visfatin plays an important role in immunity, metabolism, aging, inflammation, and responses to stress. Visfatin also participates in several pathophysiological processes contributing to cardio-cerebrovascular diseases, including hypertension, atherosclerosis, ischemic heart disease, and ischemic stroke [7].

Axelsson et al. in 2007 for the first time reported an increased serum level of visfatin in CKD and later on, several other studies reproduced similar relationship between visfatin and CKD. Moreover also found Visfatin to be associated with Svcam-1 (Soluble Vascular Adhesion Molecule 1) which is a biomarker of endothelial damage in chronic kidney disease [8]. Considerable progress is made in identifying association of visfatin with visceral adipose tissue, diabetes and inflammation but its role in renal damage in CKD secondary to diabetes mellitus has not been fully assessed. This study will investigate whether visfatin serum

concentration is associated with renal damage in type 2 diabetes and compare to patients with CKD secondary to causes other than diabetes.

## 2. SUBJECTS AND METHODS

The present study included 30 patients with chronic kidney disease due to diabetes mellitus (CKD stages 1 & 2) and 30 patients with chronic kidney disease due to causes other than diabetes mellitus (CKD stages 1 & 2) at Internal medicine & Nephrology clinic, Fayoum University Hospital from April 2013 to March 2015 and 30 healthy age and sex matched volunteers as a control group.

### 2.1 Inclusion Criteria

30 patients with chronic kidney disease due to diabetes mellitus (CKD stages 1 & 2) and estimated glomerular filtration rate by MDRD (Modification of Diet in renal disease) equal and above 60 ml/min/1.73 m<sup>2</sup> and 30 patients with chronic kidney disease due to causes other than diabetes mellitus (CKD stages 1 & 2) with normal fasting and 2 hours post prandial blood sugar and estimated glomerular filtration rate by MDRD (Modification of Diet in renal disease) equal and above 60 ml/min/1.73 m<sup>2</sup> and no ultrasonographic evidence of obstructive uropathy and 30 individuals of age matched controls were selected among general population of same socioeconomic group through convenient sampling, they were included if they met the following inclusion criteria, 40-70 years old having no clinical evidence of hypertension, liver disease, joint disease, acute or chronic inflammation or a recent febrile illness and on lab investigations had a FBS < 100 mg/dl and estimated GFR > 90 ml/min/1.73 m<sup>2</sup>.

### 2.2 Exclusion Criteria

Type 1 diabetes mellitus, urinary tract infection, urolithiasis, liver cirrhosis, stroke, ischaemic heart disease and rheumatoid arthritis.

The patients and the control group included in the study were subjected to the following:

- Detailed medical history for age and sex and History of diabetes mellitus and hypertension and duration of nephropathy and smoking was asked through a structured questionnaire and in diabetic group only, those populations whom

nephropathy developed 8-10 years after onset of diabetes mellitus were selected.

- General and local examination was done with emphasis on blood pressure measurement and weight and height measurement and estimation of body mass index (BMI) and was calculated as weight in kilograms divided by height in meter square.
- Laboratory tests such as blood urea and creatinine levels and creatinine clearance estimation by MDRD (Modification of Diet in renal disease) and fasting and 2 hours post prandial blood glucose and serum albumin and urine analysis and 24 hours urinary proteins and total cholesterol and triglycerides and LDL- cholesterol and serum visfatin levels.
- Imaging studies as carotid intima media thickness by B- mode carotid ultrasound (Philips clear view 370, linear probe 12 MHZ).
- Serum visfatin: Human VF (Visfatin) was performed by an enzyme linked immunosorbent assay (ELISA Kit Elabscience).
- Specimen collection: After an overnight fast, blood samples were collected from patients and normal individuals. Serum samples were separated by centrifuging at 3000 rpm for 10 minutes and were stored at -70°C until analysis.

### 2.3 Statistical Analysis

Statistical analyses were performed using the SPSS (statistical package for social science) version 17. Data were subjected to Kolmogorov-Smirnov test to determine the distribution and method of analysis. Normally distributed quantitative variables are presented as mean (SD), and the comparisons between groups were performed using Student's test (age, smoker duration, creatinine, fasting blood glucose level, postprandial blood glucose level, cholesterol, triglycerides, LDL, glomerular filtration rate and 24 hours urinary protein). Skewed data are expressed as median (range) (serum visfatin level, systolic and diastolic blood pressure, BMI, duration of nephropathy, carotid intimal thickening, serum albumin level). The comparisons between groups for skewed data were performed using Mann-Whitney test. Categorical variables are given as percentages. A chi-square test was used to compare the gender and smoker. The effect of demographic, laboratory and clinical variables on visfatin level

were determined individually using Pearson and Spearman Rank correlation coefficient (r). A P value (two-tailed) < 0.05 were considered statistically significant.

### 3. RESULTS

This study included 60 patients, 30 patients with chronic kidney disease due to diabetes mellitus (CKD stages 1 & 2) (group A) and 30 patients with chronic kidney disease due to causes other than diabetes mellitus (CKD stages 1 & 2) (group B) and 30 healthy age and sex matched control persons (group C).

**Group A:** Included 17 males (56.7%) and 13 females (43.3%) and their ages ranged from 50 to 72 years (mean  $\pm$  SD = 58.57  $\pm$  5.47 years). In these patients, total cholesterol ranged from 200 to 330 mg/dl (mean  $\pm$  SD = 249.23  $\pm$  3.8), LDL-cholesterol ranged from 70 to 150 mg/dl (mean  $\pm$  SD = 101.7  $\pm$  2.06), total triglycerides ranged from 133 to 250 mg/dl (mean  $\pm$  SD = 182.23  $\pm$  3.52) and all patients in this group were on statin therapy and 24 hours urinary proteins ranged from 156 to 810 mg/24 hours urine (mean  $\pm$  SD = 391.03  $\pm$  1.08) and body mass index (BMI) was estimated and found ranging from 23.8 to 24.9 Kg/m<sup>2</sup> (median = 25.2) and carotid intima media thickness was measured and ranged from 0.7 to 1.3 mm (median = 1.00) and normal carotid intima media thickness is from 0.4 to 0.8 mm and serum albumin ranged from 2.6 to 4.9 gm/dl (median = 3.9) and visfatin ranged from 0.5 to 15.9 ng/ml (median = 2.25).

**Group B:** Included 15 males (50%) and 15 females (50%) and their ages ranged from 39 to 67 years (mean  $\pm$  SD = 56.67  $\pm$  6.34 years) and 27 of 30 patients had CKD due to hypertension (90%) and 3 of 30 patients had CKD due to lupus nephritis (10%) and total cholesterol ranged from 169 to 453 mg/dl (mean  $\pm$  SD = 245.73  $\pm$  6.7), LDL-cholesterol ranged from 84 to 250 mg/dl (mean  $\pm$  SD = 112.87  $\pm$  3.57), total triglycerides

ranged from 125 to 350 mg/dl (mean  $\pm$  SD = 192.33  $\pm$  5.39) and 15 of 30 patients were on statin and 15 of 30 patients did not, and 24 hours urinary proteins ranged from 40 to 1300 mg/24 hours urine (mean  $\pm$  SD = 225.37  $\pm$  2.82) and body mass index (BMI) was estimated and found ranging from 22.7 to 26.8 Kg/m<sup>2</sup> (median = 25.15) and carotid intima media thickness was measured and ranged from 0.8 to 1.1 mm (median = 0.9) and serum albumin ranged from 2.6 to 4.9 gm/dl (median = 4) and visfatin ranged from 0.5 to 11.92 ng/ml (median = 1.85).

Comparison between laboratory data of study group (A) (N= 30) and control group (C) (N=30) revealed significant differences between 2 groups regarding mean total cholesterol, mean total triglycerides, mean LDL-cholesterol, which are higher in group (A) when compared to group (C) with statistically significant P value < 0.001 as shown in (Table 1).

Comparison between laboratory and imaging data of study group (A) (N= 30) and control group (C) (N=30) revealed significant differences between 2 groups regarding mean serum visfatin, mean carotid intima media thickness, which are higher in group (A) when compared to group (C), with statistically significant P value < 0.001 as shown in (Table 2). Comparison between laboratory data of study group (A) (N= 30) and control group (C) (N=30) revealed insignificant difference between 2 groups regarding mean serum albumin, with statistically insignificant P value > 0.05 as shown in (Table 2).

Comparison between laboratory data of study group (B) (N= 30) and control group (C) (N=30) revealed significant differences between 2 groups regarding mean total cholesterol, mean total triglycerides, mean LDL-cholesterol, which are higher in group (B) when compared to group (C), with statistically significant P value < 0.001 as shown in (Table 3).

**Table 1. Showing statistical comparison between lipid profile of group A and group C**

Group A & Group C	T. cholesterol mg/dl		LDL- Cholesterol mg/dl		Triglycerides mg/dl	
	Group A	Group C	Group A	Group C	Group A	Group C
Minimum	200	120	70	50	133	107
Maximum	330	200	150	90	250	142
Mean	249.23	156.03	101.7	70	182.23	121.83
Std. deviation	3.8	2.03	2.06	9.95	3.52	9.61
P – value	< 0.001		< 0.001		< 0.001	

Comparison between laboratory and imaging data of study group (B) (N= 30) and control group (C) (N=30) revealed significant differences between 2 groups regarding mean serum visfatin, mean carotid intima media thickness, which are higher in group (B) when compared to group (C), with statistically significant P value < 0.001 as shown in (Table 4). Comparison between laboratory data of study group (B) (N= 30) and control group (C) (N=30) revealed insignificant difference between 2 groups regarding mean serum albumin, with statistically insignificant P value > 0.05 as shown in (Table 4).

Comparison between laboratory and imaging data of study groups (A & B) (N= 60) and control group (C) (N=30) revealed significant differences between 2 groups regarding, mean serum visfatin, mean carotid intima media thickness,

which are higher in group (A & B) when compared to group (C), with statistically significant P value < 0.001 as shown in (Table 5). Comparison between laboratory data of study groups (A & B) (N= 60) and control group (C) (N=30) revealed insignificant difference between 2 groups regarding mean serum albumin, with statistically insignificant P value > 0.05 as shown in (Table 5).

Comparison between laboratory data of CKD 1 subjects and CKD 2 subjects in study groups (A & B) (N= 60) revealed significant differences between 2 groups regarding mean serum albumin which is lower when compared CKD 2 to CKD 1, with statistically significant P value < 0.01, and regarding serum visfatin and carotid intima media thickness, which are higher when compared CKD 2 to CKD 1 with statistically significant P value < 0.001 as shown in (Table 6).

**Table 2. Showing statistical comparison between serum albumin, serum visfatin and carotid intima media thickness of group A and group C**

Group A & Group C	S. Albumin gm/dl		S. Visfatin ng/ml		Carotid IM Thickness Mm	
	Group A	Group C	Group A	Group C	Group A	Group C
Minimum	2.6	3.7	0.5	0.4	0.7	0.7
Maximum	4.9	4.1	15.9	0.92	1.3	0.8
Median	3.9	4	2.25	0.5	1	0.75
P – value	> 0.05		< 0.001		< 0.001	

**Table 3. Showing statistical comparison between lipid profile of group B and group C**

Group B & Group C	T. cholesterol mg/dl		LDL- Cholesterol mg/dl		Triglycerides mg/dl	
	Group B	Group C	Group B	Group C	Group B	Group C
Minimum	169	120	84	50	125	107
Maximum	453	200	250	90	350	142
Mean	245.73	156.03	112.87	70	192.33	121.83
Std. deviation	6.7	2.03	3.57	9.95	5.39	9.61
P – value	< 0.001		< 0.001		< 0.001	

**Table 4. Showing statistical comparison between serum albumin, serum visfatin and carotid intima media thickness of group B and group C**

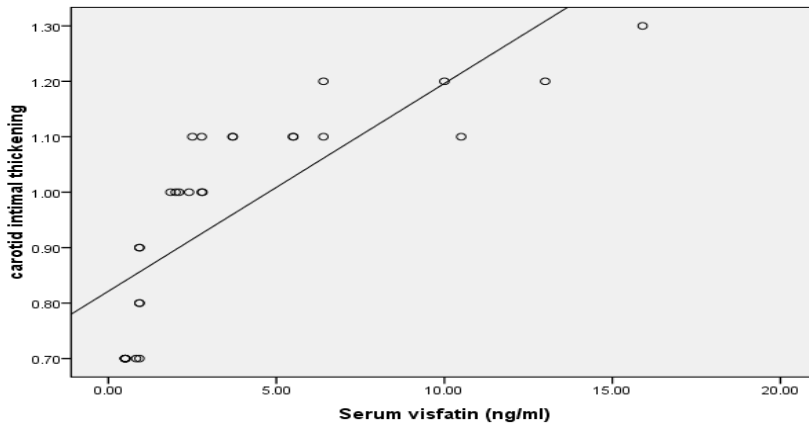
Group B & Group C	S. Albumin gm/dl		S. Visfatin ng/ml		Carotid IM Thickness Mm	
	Group B	Group C	Group B	Group C	Group B	Group C
Minimum	2.6	3.7	0.5	0.4	0.8	0.7
Maximum	4.9	4.1	11.92	0.92	1.1	0.8
Median	4	4	1.85	0.5	0.9	0.75
P – value	> 0.05		< 0.001		< 0.001	

Comparison between serum visfatin level and carotid intima media thickness for patients of study group (A) revealed positive correlation with statistically significant P value < 0.001 as shown in (Fig. 1).

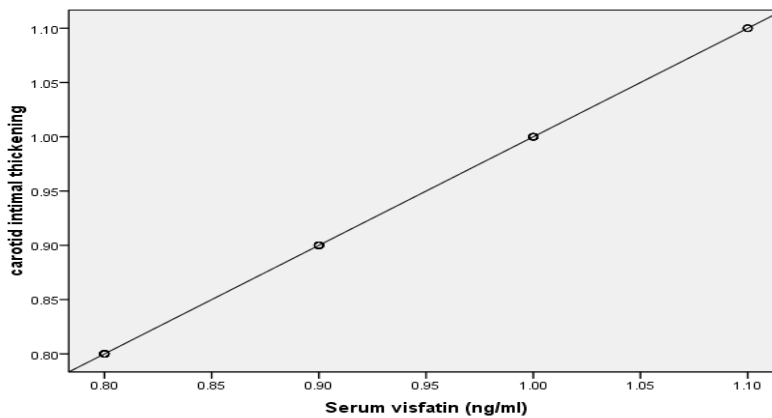
Comparison between serum visfatin level and carotid intima media thickness for patients of study group (B) on other side revealed positive correlation with statistically significant P value < 0.001 as shown in (Fig. 2).

**Table 5. Showing statistical comparison between serum albumin, serum visfatin and carotid intima media thickness of group (A & B) and group C**

Group (A & B) & Group C	S. Albumin gm/dl		S. Visfatin ng/ml		Carotid IM Thickness Mm	
	Group (A & B)	Group C	Group (A & B)	Group C	Group (A & B)	Group C
Minimum	2.60	3.7	0.50	0.4	0.7	0.7
Maximum	4.90	4.1	15.90	0.92	1.3	0.8
Median	3.9	4	2.05	0.5	0.9	0.75
P – value	> 0.05		< 0.001		< 0.001	



**Fig. 1. Correlation between serum visfatin and carotid intimal thickening among CKD subjects due to diabetes (r=0.787, P< 0.001)**



**Fig. 2. Correlation between serum visfatin and carotid intimal thickening among CKD due to other causes than diabetes (r=0.736, P< 0.001)**

**Table 6. Showing statistical comparison between serum albumin, serum visfatin and carotid intima media thickness of CKD 1 and CKD 2 subjects**

CKD 1 & CKD 2	S. Albumin gm/dl		S. Visfatin ng/ml		Carotid IM Thickness Mm	
	CKD 1	CKD 2	CKD 1	CKD 2	CKD 1	CKD 2
Minimum	3.7	2.6	0.50	1.85	0.7	0.9
Maximum	4.9	4.2	0.92	15.9	0.9	1.3
Median	4	3.9	0.50	3.45	0.8	1
P – value	< 0.01		< 0.001		< 0.001	

*P - Value is significant if < 0.05*

#### 4. DISCUSSION

Diabetes mellitus (DM) is the most frequent cause of chronic kidney disease in both developed and developing countries [9]. Adipose tissue is a specialized connective tissue. It is not simply an energy store. Adipose tissue, previously seen as an inert fat depot, is now recognized as a highly active organ with many important physiological and pathological roles [10]. Visfatin was found to be synthesized in renal mesangial cells as well as adipocytes and stimulated glucose uptake in glomerular mesangial cells mediated by glucose transporter-1 (GLUT-1). In glomerular podocytes and tubular cells as well as mesangial cells, high glucose stimulation up-regulated marked visfatin synthesis but did not increase the response to angiotensin II stimulation [11]. Our study included 90 individuals, 60 of them were CKD stages (1 & 2) and 30 healthy age and sex matched control persons then 60 patients were sub grouped into 30 patients with chronic kidney disease due to diabetes mellitus (CKD stages 1 & 2) and 30 patients with chronic kidney disease due to causes other than diabetes mellitus (CKD stages 1 & 2). The current study showed also, a statistically significant difference between CKD patients stages 1 & 2 due to diabetes mellitus (group A) and normal controls (group C) regarding serum visfatin level which was highly elevated in group (A) when compared to group (C), and that was in agreement with Chen et al. [12] who found a positive association between visfatin and the presence of T2DM, even after adjustment for BMI, age, sex, smoking status, blood pressure, and lipid profile, and this also, was in agreement with Dogru et al. [13] who found that visfatin levels were higher in the diabetic patients when compared to controls, and this is also, in agreement with Nosheen et al. [14] who studied CKD patients stages (3-5) and found that, visfatin was higher in diabetic group, and also with Gligor et al. [15] who found that, visfatin

level was higher in diabetic group when compared to normal control group, and also in agreement with Khodeer et al. [16] who showed that, mean levels of visfatin were statistically higher in group 1 (diabetics without nephropathy) and group 2 (diabetics with nephropathy) when compared to group 3 (normal healthy controls).

The current study, showed no statistically difference between CKD due to diabetes mellitus (group A) and normal controls (group C), regarding BMI and that was in agreement with Nosheen et al. [14] who studied CKD patients stages (3-5). Also, the current study showed highly significant difference in visfatin level when compare CKD (stages 1 & 2) due to causes other than diabetes mellitus (group B) and normal controls (group C) which was higher in group (B), and that was in agreement with Malyszko et al. [17] who stated that the circulating levels of visfatin in patients with chronic kidney disease (CKD) (non-diabetics) have been reported to significantly increase, moreover Nosheen et al. [14] who found that circulating level of visfatin increased in CKD (stages 3-5) patients due to causes other than diabetes mellitus when compared to normal controls, and also confirmed by Park et al. [6] who stated that, serum visfatin concentration was increased in patients with sepsis, chronic kidney disease and cancer, and Yilmaz et al. studied patients of all chronic kidney disease stages from stage 1 to 5 due to causes other than diabetes mellitus and they found a higher levels of visfatin in stages 3-5 as compared to subjects with stages 1 & 2 and to controls, but no significant difference was observed between controls and stage 1 & 2 and this difference may be due to Yilmaz et al. studied 406 individuals, 165 patients of them were CKD stages 1 & 2 and only 30 of 165 patients (18.1%) due to hypertension and 41 of 165 patients (24.8%) due to glomerulonephritis but we studied 60 patients and 30 of them were

non – diabetics and 27 of 30 patients (90%) due to hypertension and only 3 of 30 (10%) were due to lupus nephritis and so, that difference may result from small sample size or most of causes of CKD in group (B) were due to hypertension [18]. The current study showed no significant difference between CKD patients stages 1 & 2 due to causes other than diabetes mellitus (group B) and control group (group C) regarding BMI and that also was in agreement with Yilmaz et al. [18] who stated that, no significant difference between patients of CKD stage 1-5 (non-diabetics) and control group regarding to BMI.

The current study, showed a highly significant level of visfatin in patients with chronic kidney disease (stages 1 & 2) either due to diabetes mellitus (group A) or due to causes other than diabetes mellitus (group B) when compared to age and sex matched normal healthy controls (group C) which was significantly higher in groups A & B. Different researchers have studied association of visfatin with different stages of chronic kidney disease but interestingly, a positive association was observed by all suggesting a possible role of visfatin in chronic kidney disease, Nosheen et al. [14] studied CKD patients of stage 3-5 and found that visfatin was significantly higher in patients with CKD due to different causes when compared to controls, Jiao et al. [19] studied CKD patients stages 4 & 5 due to different causes and showed that, a statistically significant difference in visfatin level between CKD patients and controls, Tang et al. [20] found that, serum levels of visfatin were significantly increased in CKD patients compared with aged matched healthy control, Almaghraby et al. [21] who studied correlation of serum visfatin level with chest pain scoring as a indication of myocardial ischemia in chronic kidney disease patients and found that, serum levels of visfatin were significantly higher in CKD patients due to different causes when compared to control group.

In our study, there was no significant difference between chronic kidney disease (stages 1 & 2) either due to diabetes mellitus (group A) or due to causes other than diabetes mellitus (group B) when compared to age and sex matched normal healthy controls (group C) regarding BMI and that was in agreement with Jiao et al. [19] who studied CKD patients stages 4 & 5 due to different causes and showed that there was no significant difference between CKD patients (stages 4 & 5) and control group, and also

agreed with and Lu et al. [22] who studied association between visfatin levels and coronary artery disease with chronic kidney disease, and found that no significant difference between CKD patients stage (2-4) and control group regarding BMI.

The current study showed that, there was a highly significant positive correlation between visfatin and carotid intima media thickness (CIMT) in CKD patients stages 1 & 2 due to diabetes mellitus (group A) and that agreed with Yilmaz et al. who studied endothelial dysfunction in type 2 diabetes with early diabetic nephropathy and found that, there was a significant positive correlation between visfatin and CIMT in type 2 diabetes with early diabetic nephropathy [23]. The current study, showed a highly significant positive correlation between visfatin and proteinuria in CKD patients stages 1 & 2 either due to diabetes mellitus or due to causes other than diabetes mellitus (groups A & B) and that agreed with Nosheen et al. [14] who stated that, there was a strong association of visfatin with proteinuria irrespective of the cause of renal dysfunction.

The current study showed that, there was no significant difference between CKD patients stages 1 & 2 due to diabetes (group A) and CKD patients stages 1 & 2 due to causes other than diabetes mellitus (group B) regarding visfatin, and that was in agreement with Nosheen et al. [14] who stated that, no statistically significant difference was observed in serum visfatin level in CKD patients stages 3-5 between diabetics and non-diabetics. Also, there was a highly statistically significant differences between CKD stage 2 when compared to CKD stage 1 regarding serum creatinine, body mass index (BMI), serum visfatin level, total cholesterol, LDL-cholesterol, triglycerides and carotid intima media thickness (CIMT) which were significantly higher in CKD stage 2 when compared to CKD stage 1.

Endogenous visfatin produced from renal cells, such as mesangial cells, podocytes and tubular cells, seems to stimulate glucose uptake and intracellular metabolic abnormalities. Hyperglycemia in diabetes is associated with increased glucose uptake into cells and causes intracellular metabolic alterations, which are considered an important pathogenesis for diabetic microvascular complications. Consistently, previous studies have suggested that glucose uptake into mesangial cells



promotes mesangial extracellular matrix protein accumulation, which is characteristic of diabetic nephropathy [24]. The relation between visfatin and lipid profile may be explained in the light of cytosolic function of visfatin as a nicotinamide phosphoribosyl transferase, an enzyme involved in NAD biosynthesis, which plays an important role as energy and signal transducer. As inhibition of cholesterol esters protein increases HDL- cholesterol level and decreases LDL-cholesterol levels, it was proposed that visfatin in cholesterol homeostasis to be via inhibition of cholesteryl ester transferase protein. Proteinuria is a characteristic feature of diabetic nephropathy and an important indicator of endothelial dysfunction in CKD. Endothelial dysfunction also increases the risk of cardiovascular diseases, which is an important predictor of survival in these patients. Inflammation may be a common trigger to endothelial dysfunction in both CKD and CVD. Association of visfatin with proteinuria observed by Yilmaz et al., in 2008, and SVCAM (Soluble Vascular cell adhesion molecule 1) observed by Axelsons et al., in 2007, is a solid contribution towards possible role of visfatin in endothelial damage, as both of these are important predictors of endothelial dysfunction. Serum visfatin is considered relatively simple, cheap, fast and non-invasive method in the detection of renal damage under various conditions. Our study proved with no doubt that serum visfatin rises significantly in patients with nephropathy due to different causes with statistically significant P value < 0.001 and when we compare CKD 1 and CKD 2 patients. Using a panel of serum and urine markers including serum visfatin may potentially help to distinguish between various types of insults, establish and severity of injury, predict clinical outcome and help to monitor response to treatment in CKD patients.

## 5. CONCLUSION

We conclude that Serum visfatin is considered relatively simple, cheap, fast and non-invasive method in the detection of renal damage under various conditions. Our study proved that, there is a negative correlation between serum visfatin levels and serum albumin and also with GFR in CKD patients due to diabetes mellitus (group A), and there is positive correlation between serum visfatin levels and total cholesterol, LDL-cholesterol, total triglycerides, fasting blood sugar, 2 hours post prandial blood sugar, and 24 hours urinary proteins and carotid intima media thickness in CKD patients due to diabetes

mellitus (group A), with statistically significant P value < 0.001. And also proved that, there is a negative correlation between serum visfatin levels and serum albumin, and there is positive correlation with total cholesterol, LDL-cholesterol, total triglycerides, and carotid intima media thickness, in CKD patients due to causes other than diabetes mellitus (group B), with statistically significant P value < 0.001. Comparison between study groups (A & B) and control group (C) revealed significant differences between 2 groups regarding mean serum creatinine, mean total cholesterol, mean total triglycerides, mean LDL-cholesterol, mean creatinine clearance, mean 24 hours urinary proteins, mean serum visfatin, mean carotid intima media thickness with statistically significant P value < 0.001 for all previous laboratory and imaging data. It also showed that, comparison between serum visfatin of CKD 1 subjects and CKD 2 subjects in study groups (A & B) (N= 60) revealed significant difference, which is higher in CKD 2 when compared to CKD 1, with statistically significant P value < 0.001.

## 6. RECOMMENDATIONS

We recommend use of serum visfatin as a biomarker for early detection of endothelial damage in CKD patients as it is considered relatively simple, cheap, fast and non-invasive method in the detection and staging of chronic kidney disease under various conditions. Serum visfatin provided a very sensitive and reliable indicator of renal damage in patients with chronic kidney disease due to diabetes mellitus and other causes with statistically significant p value < 0.001 when compare to normal healthy controls. We also recommend using a panel of serum and urine markers including serum visfatin to distinguish between various types of CKD insults, establish severity of injury, predict clinical outcome and help to monitor response to treatment in CKD patients. Application of this study at larger number of patients in multi-centers in different countries dealing with patient with chronic kidney disease due to various etiologies may further promote its expression within renal tissue and may clarify its definitive role in CKD.

## CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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