Assessment of Visfatin and Risk Factors in Relation with Diabetic Mellitus Type II

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Abstract: This study was conducted on randomly selected 68 type 2 diabetic patients (27 Males and 41 Females) attending the diabetes mellitus center in Al-Sadder Teaching City in Al-Najaf province, Iraq and a group of 20 apparently healthy subjects (10 Males and 10 Females) were included as a control group. The study was carried out from February 2013 to July 2013. The age of patients and control groups were range of 35-65y. The concentration of fasting blood glucose, cholesterol, triglyceride, LDL, VLDL, HDL, Visfatin and BMI were estimated in patients and control groups. The results show significant increase ($P<0.05$) in fasting blood glucose, cholesterol, triglyceride, LDL, VLDL and Visfatin levels in patients compared with control groups. The results revealed that Visfatin not significant difference ($p>0.05$) in patients and control groups at different ages. The results also revealed that Visfatin level increase significantly ($P<0.05$) in males than females in both patients and control groups. The results also revealed that significant increase ($P<0.05$) in BMI in patients compared with control groups. The results also show that Visfatin concentration increase significantly ($P<0.05$) with increasing BMI in males than females compared with control groups. The results have been shown significant positive correlation ($P<0.05$) between Visfatin, FBG, cholesterol, triglyceride, LDL and VLDL in patients (males and females), while the results have been shown significant negative correlation ($P<0.05$) between Visfatin and HDL in patients (males and females). The present study concluded that Visfatin level was a marker for detection and diagnosis of diabetic patients type 2.
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Keywords: Visfatin, Diabetic Mellitus Type II, Al-Najaf province and Lipid profile.

1. Introduction

Diabetes Mellitus is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces (Gadsby, 2002). There are mainly three types of diabetes; Type 1 diabetes is immune-mediated and requires daily administration of insulin. The other common type is type 2 diabetes and characterized by insulin resistance or relative insulin deficiency (Gadsby, 2002; Diamond, 2003). The gestational diabetes occurs in pregnant women who have never suffered from diabetes, but gestational hyperglycemia, which might be develop after the pregnancy into type 2 diabetes mellitus. Other more rarely types of this disease such as neonatal diabetes, congenital diabetes, cystic fibrosis-related diabetes and steroid diabetes (Malecki and Maciej, 2005).

Type 2 diabetes is the most common form and comprises of 90% of people with diabetes around the world. The prevalence of type 2 diabetes rates continue to increase with increasing number of patients at risk of serious diabetes-related complications. Having type 2 diabetes increase the risk of a myocardial infarction two times and the risk of suffering a stroke two to four times. It is also a leading cause of blindness, limb amputation and kidney failure (Stumvoll et al., 2005; Cubbon et al., 2007).

Visfatin, an adipokine that is highly enriched in the visceral fat, has increased expression level in plasma during the development of obesity, implying its important role in obesity. Visfatin is expressed primarily in bone marrow, muscle and liver tissue but can also be detected in placenta, lung, kidney and heart tissue. In addition to its role in obesity, visfatin also has other biological functions. Visfatin has also been reported to be a cytokine that promotes B-cell maturation and inhibits neutrophil apoptosis (Hug and Lodish, 2005).

2. Material and Methods

The study was conducted on randomly selected 68 type 2 diabetic patients (27 Males and 41Females) and a group of 20 apparently control subjects (10 Males and 10 Females) were included as a healthy group.

Diabetes Mellitus was diagnosed by consultant doctors. The information of patients were obtained through a questionnaire consisted of the name, sex, age, weight, height. Patients with renal dysfunction, heart diseases, who were on drugs affect oxidative stress, i.e: antioxidants, antihyperlipidemic agents were excluded from the current investigation.

Five milliliters of venous blood samples were drown using a disposable needle and plastic syringes from each patients and controls subject. Blood was left at room temperature for 10 minutes for clotting, centrifuged 6000 rpm for 10 minutes, and then serum

was separated and transported into new disposable tubes.

Visfatin ELISA Kit for quantitative determination of visfatin in human serum was supplied by RayBiotech, Inc.

3. Results

3.1 Fasting blood glucose and serum Lipid profile level

The results of table (1) indicate a significant increase (P<0.05) in fasting blood glucose (FBG) level in diabetic patients (274.29 ± 59.20 mg/dI) in comparing with control group (102.05 ± 9.66 mg/dI). Also the results show that there is a significant increase (P<0.05) in serum Cholesterol, Triglycerides, LDL-C and VLDL-C level in diabetic patients (5.46 ± 0.12, 3.06 ± 0.06, 3.17 ± 0.04 and 1.37 ± 0.11 mmol/L) respectively comparing with control group (4.12 ± 0.06, 1.65 ± 0.11, 2.36 ± 0.06 and 0.79 ± 0.07 mmol/L) respectively, and a significant decrease (P<0.05) in HDL-C level in diabetic patients (0.86 ± 0.08 mmol/L) in comparing with control group (1.28 ± 0.14 mmol/L).

Table 1. Serum level of FBG and lipid profile components in patients and control groups

Groups W Groups / Parameters	Mean ± S.D	
	Control	Patients
	n = 20	n = 68
FBG (mg/dI)	102.05 ± 9.66	274.29 ± 59.20 *
Cholesterol (mmol/L)	4.12 ± 0.06	5.46 ± 0.12 *
Triglyceride (mmol/L)	1.65 ± 0.11	3.06 ± 0.06 *
LDL-C (mmol/L)	2.36 ± 0.06	3.17 ± 0.04 *
VLDL-C (mmol/L)	0.79 ± 0.07	1.37 ± 0.11 *
HDL-C (mmol/L)	1.28 ± 0.14	0.86 ± 0.08 *

* means significant difference at (P<0.05)

3.2 Visfatin level

The results in figure (2) show a significant increase (P<0.05) in visfatin level in diabetic patients (244.62 ± 16.47 ng/ml) in comparing with control group (176.77 ± 5.79 ng/ml).

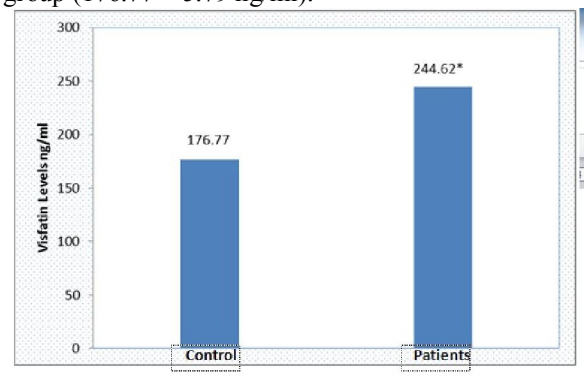

Figure 1. Visfatin level in diabetic patients and control groups

* means significant difference at (P<0.05)

3.3 Comparison Visfatin level between diabetes and control groups according to age

The results of table (2) show a significant increase (p<0.05) in serum visfatin level in patients at different ages, while serum visfatin level is highly significant increase (p<0.05) in patients at different ages in comparing with control groups. Also the results show that there is no significant difference (p>0.05) in serum visfatin in patients at different ages.

Table 2. Visfatin level of patients and control groups in different age

Age	Mean ± S.D	
	Visfatin	
	Control	Patients
	n = 20	n = 68
35 -45	177.06 ± 5.19 a	240.85 ± 21.58 b
46 – 55	167.01± 6.76 a	243.02 ± 23.40 b
56 – 63	178.43 ± 7.13 a	246.86 ± 27.45b

a,b means significant difference at (P<0.05), between patients and control groups .

3.4 Comparison Visfatin level between diabetes and control groups according to gender

The results of table (3) reveal a significant increase (p<0.05) in serum visfatin level in males than females in both patients and control groups, while serum visfatin level are highly significant increase (p<0.05) in both males and females in patients in comparing with control groups.

Table 3. Biomarkers level in both gender of patients and control groups

Marker	Mean ± S.D			
	Control		Patients	
	n = 20		n = 68	
	Male	Female	Male	Female
	n =10	n =10	n =27	n =41
Visfatin ng/ml	177.05 ± 6.32*	166.48 ±5.27	294.39 ± 14.53*#	244.85± 10.41#

* means significant difference at (P<0.05), different gender at the same group

means significant difference at (P<0.05), at the same gender in different group

3.5 Comparison Visfatin level between diabetes and control groups according to BMI

The figures (3),(4),(5) show a significant increase (P<0.05) in visfatin level in all groups normal weight, over weight and obese weight in comparing with control groups. Also the same figures show a significant increase (P<0.05) in visfatin level in all groups normal weight, over weight and obese weight in males (240.45, 263.88, 252.47 kg/m^2) in comparing with females (211.76, 229.92 , 236.89 kg/m^2).

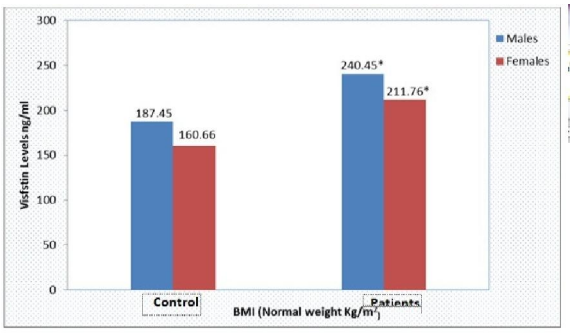

Figure 2. Visfatin concentrations of patients and control groups in normal weight
* means significant difference at (P<0.05)

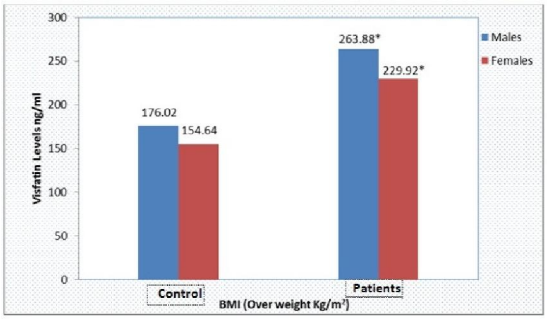

Figure (3):Visfatin concentrations of patients and control groups in over weight
* means significant difference at (P<0.05)

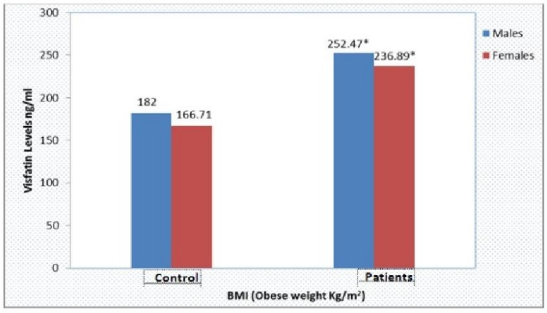

Figure 4. Visfatin concentrations of patients and control groups in obese weight
* means significant difference at (P<0.05).

3.6 Relationship between Visfatin and fasting blood glucose levels

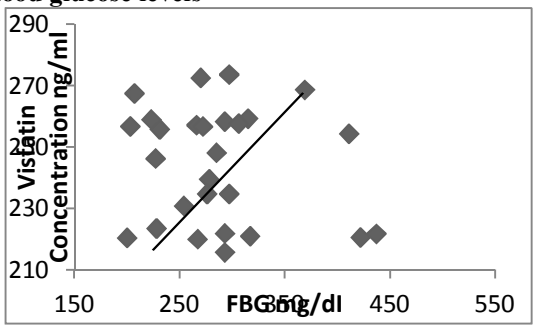

Figure 5. Correlation between Visfatin and FBG in males of Diabetic Mellitus patients

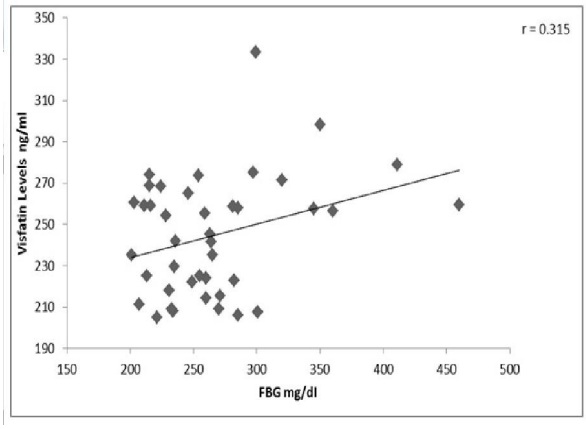

Figure 6. Correlation between Visfatin and FBG in females of Diabetic Mellitus patients

3.7 Relationship between Apelin and lipid profile levels

A. Cholesterol

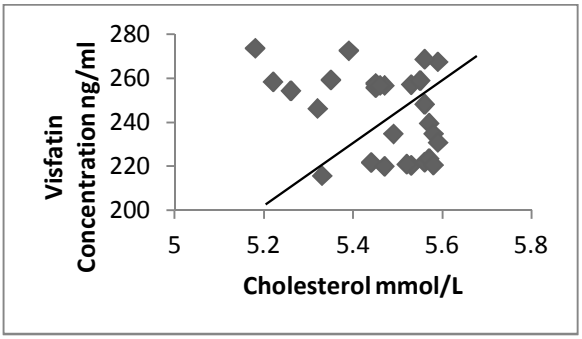

Figure 7. Correlation between Visfatin and cholesterol in males of Diabetic Mellitus patients.

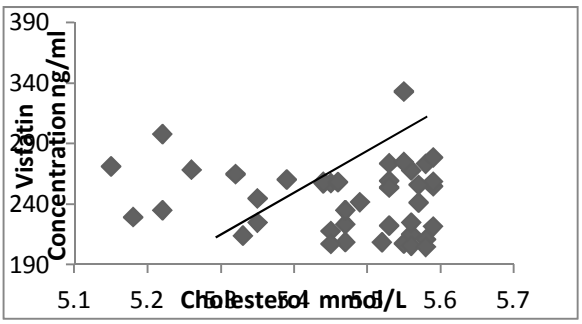

Figure 8. Correlation between Visfatin and cholesterol in females of Diabetic Mellitus patients

B. Triglycerides

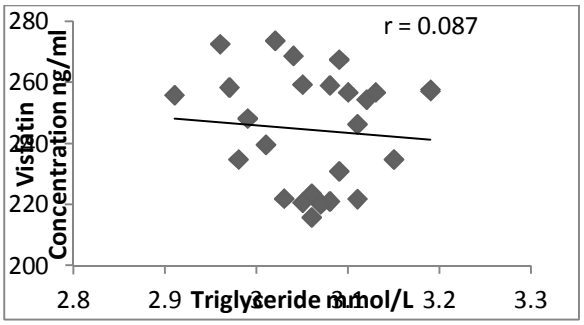

Figure 9. Correlation between Visfatin and triglycerides in males of Diabetic Mellitus patients.

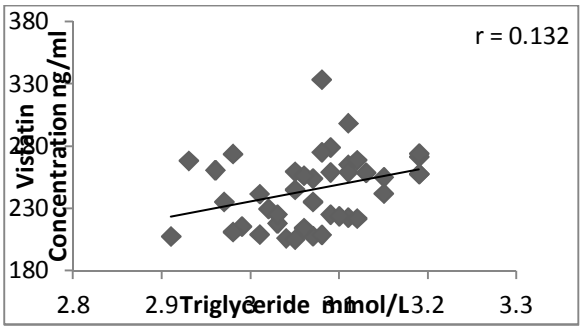

Figure 10. Correlation between Visfatin and triglyceride in females of Diabetic Mellitus patients

C. LDL-C

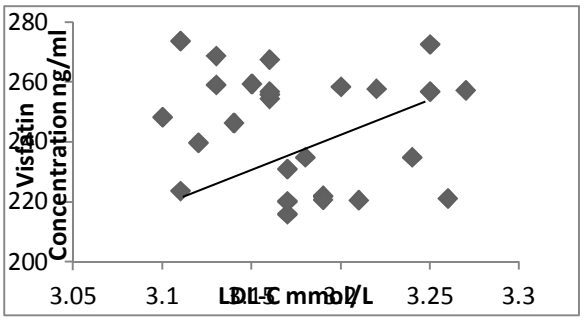

Figure 11. Correlation between Visfatin and LDL in males of Diabetic Mellitus patients.

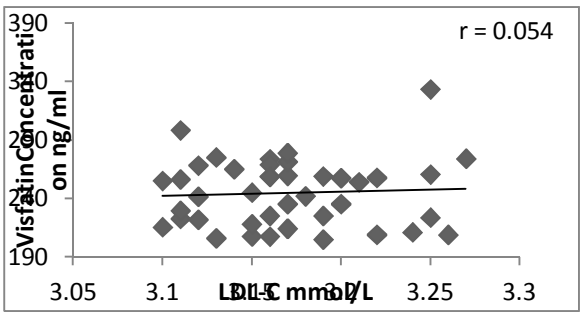

Figure 12. Correlation between Visfatin and LDL in females of Diabetic Mellitus patients

D. VLDL-C

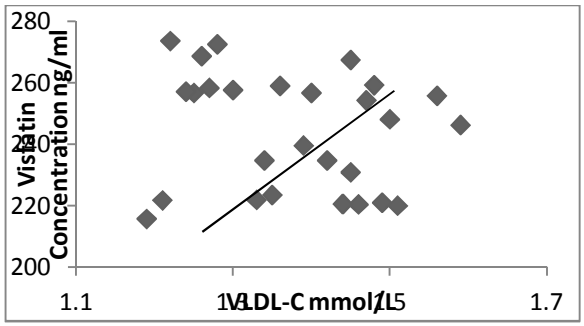

Figure 13. Correlation between Visfatin and VLDL in males of Diabetic Mellitus patients.

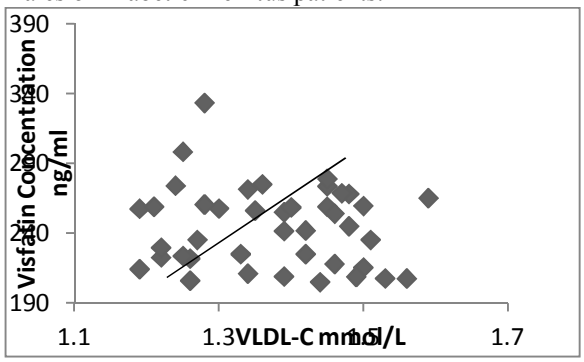

Figure 14. Correlation between Visfatin and VLDL in females of Diabetic Mellitus patients

E. HDL-C

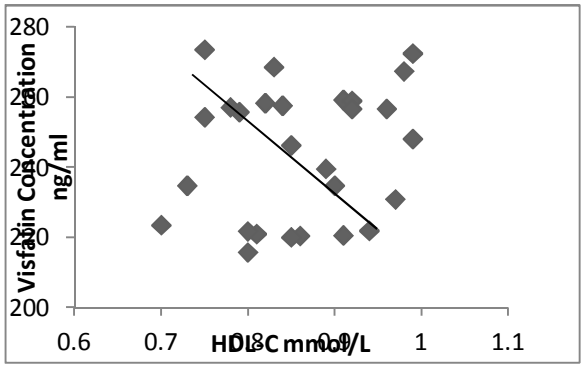

Figure 15. Correlation between Visfatin and HDL in males of Diabetic Mellitus patients

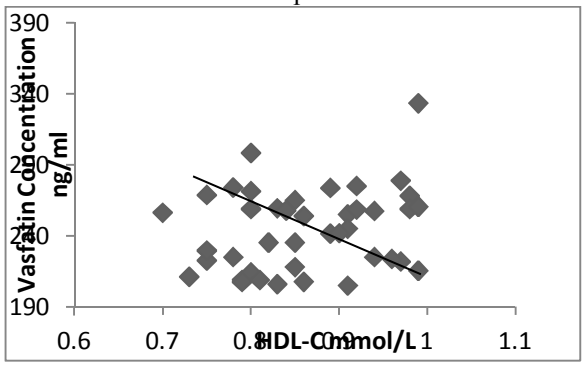

Figure 16. Correlation between Visfatin and HDL in females of Diabetic Mellitus patients

4. Discussions

The study revealed a significant elevation in fasting blood glucose in patients comparing with control group as presented in table (1). These results are expected due to the fact that the main characteristic feature of DM is hyperglycemia. Blood glucose is tightly controlled by two key processes: insulin secretion by pancreatic ß-cells in response to a nutrient and insulin action on major target organs, i.e., skeletal muscle, liver and adipose tissue. T2DM, is often associated with obesity and results from insufficient insulin production/secretion and IR (Paz *et al*., 2006).

The results show that there is a significant increase in serum cholesterol, triglycerides, LDL-C and VLDL-C and decrease HDL-C in patients comparing with control group as presented in table (1). The dyslipidemia noticed in the patients group are common in diabetic patients and has different explanations (Garg, 1992; Keys *et al*., 1995; Cui *et al*., 2001; Keith and Jackson, 2006; Pietilainen *et al*., 2007).

The presented study of figure (1) indicated a significant increase in visfatin level in T2DM patients in comparing with control groups.

Revollo *et al* (2007) provided several line of evidence that visfatin mediated a systemic nicotin amide adenine dinucleotide (NAD). Biosynthesis is critical for Beta-cell function and alteration in NAD level could alter the enzymatic activity of NAD-dependent decyclase and that are essential regulation of glucose-stimulated insulin secretion in pancreatic Beta-cell.

Many studies proved that insulin level does not influence visfatin synthesis in adipocyte and there is no difference in serum visfatin between type 2 diabetes mellitus treated with insulin or hypoglycemia agent (Kralisch *et al*., 2005; Chen *et al*., 2006; Haider *et al*., 2006). Recent studies indicated that glucose level but not insulin may be a key role in the elevation of visfatin level in type 2 diabetic patients (Takebayashi *et al*., 2007; Kadoglou *et al*., 2010). Some phenomena may be also involved an increase of visfatin level may be as a result of beta-cell deterioration which is consider as a newly diagnosed T2DM (Lopez-Bermejo *et al*., 2006; Wajchenberg, 2010). There are growing evidence the role of visfatin in inflammatory process, therefore it can be also possible to consider increase glucocorticoids enhance Visfatin release from adipocyte (Kralisch *et al*., 2005; Bruehl *et al*., 2007).

Visfatin is an adipocytokine and a marker of inflammation and have a role in in pathogenesis of insulin resistance and diabetes mellitus (Yılmaz *et al*., 2009; Kang *et al*., 2010). Visfatin was an effective as insulin in reducing hyperglycemia in insulin deficient diabetic mice and also bound to activated insulin receptors causing receptor phosphorylation and activation of the downstream signaling molecule (Fukuhara *et al*., 2005; Adeghate, 2008).

Chen *et al* (2006) reported that plasma visfatin level elevated in patients with T2DM compared with those of healthy subjects and negatively correlated with Adiponectin. Previous study suggested that increase circulation of visfatin level may be by up-regulation of visfatin secretion by adipocyte in response to hyperglycemi (Stadler *et al*., 2010).

Study of (Van der Veer *et al*., 2005) suggested that increase circulating of mRNA expression of visfatin in diabetic subject may be related to increase adipose tissue mass. Recent study proved the correlation between RBP-4 factor derived from fat cells and visceral obesity by impaired signaling in skeletal muscle through reduction in insulin-stimulated tyrosine phosphorylation of insulin receptor substrate-1 (IR-1) thus RBP-4 could lead to insulin resistance which is followed by hyper secretion of visfatin (Schindler *et al*., 2006).Another studies found a significant positive correlation between external eating and serum visfatin suggestion that psychological reactivity and eating behavior in T2DM patients may consequently affect serum visfatin by inducing adipose tissue metabolism and higher visfatin level are associated with visceral fat (Hida *et al*., 2005; Lim *et al*., 2008; Ohman *et al*., 2009).

The results of present study of table (3) showed a significant increase in males than females in diabetic patients. Study of De Luis *et al* (2010) suggested that visfatin level was shown in males more than in females which stimulate the production of cytokines (TNF-α) and C-reactive protein (CRP) and in turn exaggerate insulin resistance. Another previous study showed that visfatin level was greater in males compared to females because a food craving was greater in males compared with females and also caloric intake and nutritional status were different between sexes (Burton *et al*., 2007). The high level of visfatin in males may be as a result of testosterone hormone while estrogen in females have a preventive role in expression of mRNA visfatin into adipocytes.

The results of figures (2), (3), (4) indicated a significant increase in visfatin level in normal weight, over weight and obese weight of T2DM patients in comparing with control groups.

Conflicting results have been reported the relationship between visfatin and body fats accumulation (Fukuhara *et al*., 2005). Visfatin secreted by visceral fat cells and increased in obesity and this is considered to reflect an impairment of visfatin signaling or dysregulation in its biosynthesis (Fukuhara *et al*., 2005; Kralisch *et al*., 2005).

Study of (Berndt *et al*., 2005) indicated the correlation between visfatin level and visceral fat or visceral adipose tissue and any rise in visfatin could indicate an increase visceral fat. The present study in agreement with other authors that indicated a higher visfatin level in over weight of both sexes and concluded that visfatin correlated positively with BMI (Choi *et al*., 2007; Zahorska-Markiewicz *et al*., 2007; Chang *et al*., 2011). Some previous studies showed that increased visfatin level that have a role in progressive increase of visceral fat and total abdominal fat and lead to increase in pro-inflammatory markers TNF- α and IL-6 gene expression in adipose tissue and CRP is produced in higher level by the liver also is another reason of increased inflammation and insulin resistance in type 2 diabetic patients (Festa *et al*., 2000; Shah *et al*., 2008).

Visfatin is only a biomarker elevated in type 2 diabetic patients regradness of obesity by positively correlated with visceral but not subcutaneous fat.

The present study showed a significant positive correlation in visfatin level in the fasting blood glucose in both males and females in type 2 diabetic patients and negative correlation between omentin level in the fasting blood glucose in males only.

Recent study reported that elevation of visfatin level reflected a higher blood glucose and demonstrated that fasting blood glucose as an predictor of serum visfatin level (Haider *et al*., 2006).

Previous findings prevent that fasting blood glucose not insulin resistance play a key role in elevation of visfatin level (Kallen and Lazar, 1996). In view of reported role of visfatin in glucose metabolism suggested that visfatin correlated with serum parameters of glucose metabolism and significantly related with fasting blood glucose (Fukuhara *et al*., 2005; Revollo *et al*., 2007). Many of studies have been reported on the potential link between visfatin level and insulin resistance and no correlation between visfatin and insulin sensitivity was found (Berndt *et al*., 2005; Jian *et al*., 2006; Pagano *et al*., 2006; Dogru *et al*., 2007).

The results of current study indicate a significant positive correlation between visfatin level and cholesterol and VLDL-C in males and females and only with triglycerides in females and positively with LDL-C in males and negatively with HDL-C in males and females.

Raji *et al* (2001) have shown that an increase in visfatin level lead to increase in pro-inflammatory cytokines (TNF-α and hs-CRP) also oxidative stress which have an important role in increment of cholesterol and OX-LDL-C.

The increase in the visfatin level and inflammatory markers should be associated with visceral fat and oxidative stress in the diabetic states associated with insulin resistance, dyslipidemia and hypercholesterolemia and increase cardiovascular disease (Holvoet, 2008; Shah *et al*., 2008; Sam *et al*., 2009). Georgia *et al* (2009) was found a significant positive correlation between visfatin and cholesterol and triglycerides and positively correlated with LDL-C and Apolipopretien and association with diabetes (Filippatos *et al*., 2007; Ingelsson *et al*., 2007), while Wang *et al* (2007) demonstrated negative correlation between visfatin level and triglyceride, a few studies reported that visfatin have a role in pathogenesis of hyperlipidemia and obesity (Yılmaz *et al*., 2009; Kang *et al*., 2010).

Serum visfatin level were significantly correlated with cholesterol, triglyceride and LDL-C. It was suggested that visfatin induced free fatty acids flux to the liver drive very low density lipoprotein production leading to elevated cholesterol and triglycerides (Chang *et al*., 2010). In contrast negative correlation were reported between visfatin and cholesterol, triglyceride and HDL-C (Wang *et al*., 2007). Visfatin may participate in cardiovascular disease and may lead to hypercholesterolemia and hypertriglyceridemia.

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