

# Study the Interferon $\gamma$ , C- reactive Protein and Lipid Profile in Iraqi Diabetic Patients With and Without Hypertension

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## Abstract:

Diabetes mellitus is a major challenge for global public health, and it is characterized by elevated glucose. The current study aimed to research the association between serum lipid profile and cytokines in type 2 diabetes mellitus patients with hypertension and without hypertension. The study population comprised of (80) type 2 diabetes mellitus patients (38 without hypertension and 42 with hypertension) having age group (36-59) year and (40) number of healthy subjects having age group (30-50) year, has been done at National Diabetes Center / Mustansiriyah University in Baghdad, Iraq. The results showed a significant increase ( $P < 0.05$ ) of FBG and HbA1c values in male and female patients with type 2 diabetes mellitus for both groups (with hypertension and without hypertension) compared to control group. While, HOMA-B% and HOMA-S% which significantly decreased ( $P < 0.05$ ) in male and female patients with type 2 DM for both groups (with hypertension and without hypertension) compared to control group. The values of lipid profile (total cholesterol, triglyceride, low density lipoprotein and very low density lipoprotein) which significantly increased ( $P < 0.05$ ) in male and female patients with type 2 diabetes mellitus for both groups (with hypertension and without hypertension) compared to control group. While high density lipoprotein value was significantly decreased in male and female patients. Also significantly increased ( $P < 0.05$ ) in CRP level in male and female patients with type 2 diabetes mellitus for both groups (with hypertension and without hypertension) compared to control group. While IFN level was significantly decreased in male and female patients with type 2 diabetes mellitus for both groups (with hypertension and without hypertension) compared to control group. In conclusion, this study demonstrated that type 2 diabetes mellitus patients have disorder levels of Interferon  $\gamma$  and C-reactive Protein may lead to several diseases also, increased level of glycosylated hemoglobin levels point toward poor control of blood glucose levels, dyslipidemia is obvious in patients with type 2 diabetes which may lead to several diseases.

**Key words:** Interferon  $\gamma$ , Lipid profile, Diabetic patients, Hypertension

## Introduction

Diabetes (DM) is a large-scale global public health service that includes a heterogeneous pathogenesis of diseases characterized by hyperglycemia [1]. Type 2 diabetes is a complex disease characterized by an imbalance between insulin resistance and insulin secretion, which releases glucose into the liver by preventing glycogenolysis and stimulating glycogenolysis and gluconeogenesis [2]. Type 2 DM have increased prevalence of dyslipidemia [3]. DM changes in lipid levels and consequent disorders of lipid metabolism [4], such as increases in circulating level of free fatty acids (FFA) and triglycerides [5]. The lipid disorders occur in DM because insulin deficiency or resistance effects on enzymes and lipid metabolism [6]. Macrovascular and microvascular complications, including neuropathy, retinopathy, nephropathy, and cardiovascular disease (CVD) occur uncontrolled to the glucose level in diabetics [7,8].

Interleukin (IL) 17 and T helper 17 (Th 17) cells have play in the many pathogenesis diseases like multiple sclerosis, rheumatoid arthritis and systemic psoriasis [9], as well as in type 1 diabetes pathogenesis [10]. In T1DM, pancreatic beta cells destruction occur lead to the immune cells and their cytokines inflammatory mediators [11]. Therefore, this type of DM is characterized by change in levels of IL<sub>1</sub>β (IL<sub>1</sub>β), IL<sub>6</sub>, TNF<sub>α</sub> and C<sub>reactive</sub> protein (CRP) [12,13]. IL<sub>1</sub>β and IL<sub>6</sub> is also increased in type 2 DM due to the development of insulin resistance [14].

Patients with type 2 DM and hypertension have an elevated of TNF<sub>α</sub> secretion, IL<sub>6</sub> and IL<sub>7</sub> but low secretion of IL<sub>10</sub> in comparison with controls [15]. In the current study, we aimed to research association between serum lipid profile and cytokines in type 2 DM patients with hypertension and without hypertension in comparison to control.

## Materials and method

### ●Subjects

The study has been done at National Diabetes Center (Mustansiriyah University) in Baghdad province during the period from May 2018 to May 2019. The study samples include of (80) type 2 DM patients' (38 without hypertension and 42 with hypertension) having age group (36-59) year and (40) number of healthy subject as control group having age group (30-50) year.

### ●Measurement of Insulin Resistance Parameters

The homeostatic model assessment (HOMA2) calculator software/ oxford have been used to measured (HOMA2- IR), beta cell activity (HOMA%B) and insulin sensitivity (HOMA%S)). The serum glucose was determined by enzymatic colorimetric method according to [16]. The

determination of the HbA1c according to instrument Bio Rad, which dependent by ion-exchange high performance liquid chromatographic[17]. The employed methods to measure of serum total cholesterol(TC),triglycerides (TG),and high density lipoprotein(HDL)were based upon an enzymatic colorimetric methods according to [18],[19] and [20].The concentration of low density lipoprotein (LDL) and very low density lipoprotein (VLDL) was determined according to methods by [21].Serum C-peptide was estimated according to [22]. Serum CRP and INF- $\alpha$  concentration was estimated according to[23] by sandwich ELISA.

#### ●Statistical analysis

The data obtained during the current study were statistically analyzed using SPSS to determine the significance of various parameters by one-way ANOVA. Data represents the mean  $\pm$  SE, P & It. 0.05 was considered significant.

### RESULTS AND DISCUSSION

The results in table (1) showed significantly increased ( $P < 0.05$ ) of FBG , HbA1c and HOMA values in male with T2DM for two groups ( with HP and without HP) compared with control group. While, HOMA B% and HOMA S% which significant decreased(  $P < 0.05$ ) in male T2DM for both groups ( with HP and without HP) relative to control group.

The values of lipid profile ( TC,TG,LDL and VLDL) which significant increased(  $P < 0.05$ ) in male patients for both groups ( with HP and without HP) when compared with control group. While HDL value was decreased significantly in male patients for both groups ( with HP and without HP) relative to control( Table,2).

The current study show significantly increased (  $P < 0.05$ ) in CP level in male patients with type 2 DM for two groups ( with HP and without HP) relative to control group. While IFN level was significant decreased in male patient for both groups ( with HP and without HP) relative to control, Table (2).

A significant increased in table (3) of FBG and HbA1c values in female patients with type 2 DM for two groups ( with HP and without HP) when compared to control. The value of HOMA as seen in the table (1) are no significant difference among all groups. While, HOMA B% which significant decreased in female patients for both groups ( with HP and without HP) relative to healthy group. But significant decreased to HOMA S% in female patients with and without hypertension , table (3).

The values of lipid profile ( TC, TG, LDL and VLDL) which significant increased ( P<0.05) in female patients with T2DM for both groups ( with HP and without HP) relative to control group. While a significantly decreased to HDL value in female patients with type 2 DM for both groups ( with HP and without HP) relative to control group( Table,4). Increased significantly of CP level in female patients with type 2 DM for both groups ( with HP and without HP) relative to control group. While IFN level was significant decreased in female patients with type 2 DM for both groups ( with HP and without HP) relative to control group , Table(4).

Results in table (5) showed increased significantly of FBG and HbA1c values in patients ( male and female) with type 2 DM for two groups ( with HP and without HP) relative to control group. The value of HOMA as seen in the table (5) are no significant change (P≥0.05) between all groups. While, HOMA B% and HOMA S% which significant decreased ( P<0.05) in patients with DM for two groups ( with HP and without HP) when compared with control.

The values of lipid profile ( TC, TG, LDL and VLDL) which significant increased ( P<0.05) in patients ( male and female) with type 2 DM for both groups ( with HP and without HP) relative to control group. While HDL value was significant decreased in patients with T2DM for both groups ( with HP and without HP) but patients with hypertension did not differ significantly in compared to healthy group( Table,6).

The present study show non-significant differences in CP level among all groups . While IFN level was significant decreased ( P<0.05) in patients with T2DM for both groups ( with HP and without HP) but patients with hypertension did not differ compared to healthy group ( Table,6).

**Table (1): The FBG, HbA1c and insulin resistance parameters in male groups.**

Parameters	Groups			P value
	Control (n=18)	Type 2DM with HP(n=20)	Type 2DM without HP( n=23)	
FBG(mg/dl)	96.88 ± 1.04 <sup>b</sup>	169.40±7.54 <sup>a</sup>	152.00 ±7.10 <sup>a</sup>	0.000
HbA1c%	4.90 ± 0.07 <sup>c</sup>	8.02±0.24 <sup>b</sup>	8.74±0.32 <sup>a</sup>	0.000

CRP (ng/ml)	1.95±0.13 <sup>b</sup>	4.90±0.88 <sup>a</sup>	4.66±0.93 <sup>a</sup>	0.000
HOMA-IR	1.35±0.03 <sup>b</sup>	3.30±0.22 <sup>a</sup>	3.62±0.23 <sup>a</sup>	0.000
HOMA B%	87.99±4.76 <sup>a</sup>	70.38±4.96 <sup>b</sup>	56.27±4.52 <sup>c</sup>	0.000
HOMA S%	82.18±3.43 <sup>a</sup>	33.14±2.16 <sup>b</sup>	30.17±2.00 <sup>b</sup>	0.000

Different letters indicate significant differences between groups at the level of (P <0.05). The same letters indicate slight differences between groups.

**Table (2): The lipid profile , C protein and INF levels in male groups.**

Parameters	Groups			P value
	Control (n=18)	Type 2DM with HP(n=20)	Type 2DM without HP( n=23)	
TC (mg/dl)	155.17±7.35 <sup>b</sup>	251.95± 7.50 <sup>a</sup>	233.52±12. 09 <sup>a</sup>	0.000
TG (mg/dl)	96.00±3.25 <sup>b</sup>	198.60±16.58 <sup>a</sup>	187.83±14.18 <sup>a</sup>	0.000
HDL (mg/dl)	50.72±1.09 <sup>a</sup>	39.35±1.18 <sup>b</sup>	38. 52±0.89 <sup>b</sup>	0.000
LDL (mg/dl)	76.61±7.90 <sup>b</sup>	149.40±10.07 <sup>a</sup>	156.74±11.37 <sup>a</sup>	0.000
VLDL (mg/dl)	19.16±0.63 <sup>b</sup>	39.20±3.34 <sup>a</sup>	39.56±3.80 <sup>a</sup>	0.000
CRP (g/dl)	1.72±0.05 <sup>b</sup>	3.56±0.21 <sup>a</sup>	3.93±0.22 <sup>a</sup>	0.000
IFN-γ (pg/ml)	25.46±1.03 <sup>a</sup>	12.42±1.34 <sup>b</sup>	9.77±1.03 <sup>b</sup>	0.000

Different letters indicate significant differences between groups at the level of (P <0.05). The same letters indicate slight differences between groups.

**Table (3): The FBG,HbA1c and insulin resistance parameters in female groups.**

Parameters	Groups			P value
	Control (n=22)	Type 2DM with HP(n=22)	Type 2DM without HP(n=15)	
FBG (mg/dl)	95.86 ± 1.15 <sup>c</sup>	210.23±12.67 <sup>a</sup>	177.27 ±6.21 <sup>b</sup>	0.000
HbA1c%	4.70 ± 0.06 <sup>b</sup>	8.70±0.35 <sup>a</sup>	8.53±0.32 <sup>a</sup>	0.000

CRP (ng/ml)	1.09±0.71 <sup>b</sup>	4.00±0.83 <sup>a</sup>	4.20±0.11 <sup>a</sup>	0.000
HOMA-IR	3.25±1.28 <sup>a</sup>	3.76±0.28 <sup>a</sup>	3.55±0.39 <sup>a</sup>	0.906
HOMA B%	88.73±5.19 <sup>a</sup>	51.43±4.59 <sup>b</sup>	47.15±4.15 <sup>b</sup>	0.000
HOMA S%	73.16±3.04 <sup>a</sup>	68.51±19.48 <sup>a</sup>	31.56±3.29 <sup>b</sup>	0.000

Different letters indicate significant differences between groups at the level of (P <0.05). The same letters indicate slight differences between groups.

**Table (4): The lipid profile ,C protein and INF levels in female groups.**

Parameters	Groups			P value
	Control (n=22)	Type 2DM with HP(n=22)	Type 2DM without HP( n=15)	
TC (mg/dl)	160.86±6.05 <sup>c</sup>	250.05± 9.19 <sup>a</sup>	212.73±8.05 <sup>b</sup>	0.000
TG(mg/dl)	91.22±0.67 <sup>b</sup>	209.05±16.38 <sup>a</sup>	199.60±22.28 <sup>a</sup>	0.000
HDL (mg/dl)	54.00±1.19 <sup>a</sup>	38.72±0.97 <sup>b</sup>	40.66±1.37 <sup>b</sup>	0.000
LDL (mg/dl)	88.72±6.14 <sup>b</sup>	151.36±9.19 <sup>a</sup>	139.07±8.90 <sup>a</sup>	0.000
VLDL (mg/dl)	18.72±0.14 <sup>b</sup>	41.13±3.26 <sup>a</sup>	38.86±4.58 <sup>a</sup>	0.000
CRP (g/dl)	1.88±0.07 <sup>b</sup>	3.70±0.26 <sup>a</sup>	3.60±0.36 <sup>a</sup>	0.000
IFN -γ (pg/dl)	25.25±1.11 <sup>a</sup>	10.56±0.67 <sup>b</sup>	10.75±0.77 <sup>b</sup>	0.000

Different letters indicate significant differences between groups at the level of (P <0.05). The same letters indicate slight differences between groups.

**Table (5): The FBG,HbA1c and insulin resistance parameters in both male and female groups.**

Parameters	Groups			P value
	Control (n=40)	Type 2DM with HP(n=42)	Type 2DM without HP( n=38)	
FBG(mg/dl)	96.32± 0.78 <sup>c</sup>	185.52±9.16 <sup>a</sup>	161.97±5.29 <sup>b</sup>	0.000

HbA1c%	4.79±0.05 <sup>b</sup>	8.37±0.22 <sup>a</sup>	8.66±0.22 <sup>a</sup>	0.000
CRP (ng/ml)	1.83±0.73 <sup>b</sup>	4.06±0.89 <sup>a</sup>	3.33±1.07 <sup>a</sup>	0.000
HOMA-IR	2.39±0.71 <sup>a</sup>	3.54±0.45 <sup>a</sup>	3.59±0.20 <sup>a</sup>	0.292
HOMA B%	88.40±3.53 <sup>a</sup>	63.80±5.53 <sup>b</sup>	52.67±3.23 <sup>b</sup>	0.000
HOMA S%	77.22±2.36 <sup>a</sup>	55.41±10.97 <sup>b</sup>	30.72±1.75 <sup>c</sup>	0.000

Different letters indicate significant differences between groups at the level of (P <0.05). The same letters indicate slight differences between groups.

**Table (6): The lipid profile ,C protein and INF levels in both male and female groups.**

Parameters	Groups			P value
	Control (n=40)	Type 2DM with HP(n=42)	Type 2DM without HP( n=38)	
TC(mg/dl)	158.30±4.65 <sup>c</sup>	248.34± 6.34 <sup>a</sup>	224.02±7.96 <sup>b</sup>	0.000
TG(mg/dl)	93.37±1.53 <sup>b</sup>	205.02±11.32 <sup>a</sup>	192.02±11.83 <sup>a</sup>	0.000
HDL(mg/dl)	52.52±0.85 <sup>a</sup>	43.81±4.84 <sup>ab</sup>	40.89±1.70 <sup>b</sup>	0.030
LDL(mg/dl)	83.27±4.93 <sup>b</sup>	152.62±6.91 <sup>a</sup>	148.46±7.68 <sup>a</sup>	0.000
VLDL(mg/dl)	18.67±0.30 <sup>b</sup>	44.97±5.27 <sup>a</sup>	40.82±3.20 <sup>a</sup>	0.000
CRP (g/dl)	1.81±0.05 <sup>a</sup>	3.63±0.49 <sup>a</sup>	3.80±0.19 <sup>a</sup>	0.244
IFN-γ (pg/dl)	25.34±0.76 <sup>a</sup>	17.02±5.35 <sup>a</sup>	10.16±0.69 <sup>b</sup>	0.010

Different letters indicate significant differences between groups at the level of (P <0.05). The same letters indicate slight differences between groups.

The DM is a group of metabolic disorders characterized by hyperglycemia, the elevation in FBG level may be resulting from deflection in insulin secretion, insulin action or both. Two ways can controlled blood glucose : first insulin secretion by β cells found in the pancreas in response to a nutrient materials and second by insulin action on target tissues such as liver [24]. Diabetes is associated with result from decreased insulin production and insulin resistance [25].The HbA1C value should be kept less than 7% in all diabetes

according to the American Diabetes Association (ADA) [26]. Bad controlled of the patients in this study because HbA1C of the patients groups > 9.9 % and this result is reported in another reports and related with other complication of diabetes in patients with increased levels of HbA1C in DM [27]. In comparison with a study done by [28] they found HbA1C in diabetes groups was  $6.7 \pm 0.1\%$ .

In current study, results showed that lipid profile TC, TG, LDL, VLDL which increased significantly but HDL decrease significantly in diabetic patient (with HP and without HP) as compared with control. These finding were in agreement with the study done by [29]; [30].

Dyslipidemia is found to be correlated with both, insulin resistance and coronary heart disease [31,32]. The high triglycerides and low levels of HDL are the most common form of dyslipidemia profile in patients with T2DM. In studies done by [33,34], indicated that LDL absorption of fibroblasts may be weak in patients with T2 DM. This may be lead to an decreased in HDL and increased in LDL levels. Similar results have been reported by [35], which noted a decreased in HDL in the patients with Type2 DM this may be an effective increase of hepatic lipase, which plays a significant role in HDL metabolism, excess FFA and hyperglycemia leads to hyper triglycerides, which in turn decreases HDL-C level in patients with T2DM.

The HDL level is strongly and independently associated with cardiovascular disease, but the relationship is inverse lower HDL being an important signal of Cardiovascular disease and increased levels of HDL is protecting against Coronary heart disease. These findings explanation lead to played HDL in reverse cholesterol transport as an acceptor of cellular free cholesterol [36]. The patients of diabetes dyslipidemia is characterized by hypertriglyceridemia and decreased levels of HDL [37]. Hypertriglyceridemia predisposes the patients to life exacerbating complications such as diabetic ketoacidosis, coronary artery disease [38]. Which is more common in diabetics as compared with non-diabetics lead to increase in VLDL triglycerides [39].

T2DM is a chronic metabolic disorder, the CRP is a first inflammatory marker that is elevated in the sera of patients with severe inflammation and diseases including CVD and T2DM. A Chinese study people noted that of CRP value was increased in patients than in controls [40]. The study done by [41], found the plasma CRP levels were significantly decreased ( $p < 0.05$ ) in the controls subject than in the hypertension and T2DM groups.

The mechanism of the relationship between CRP and T2DM is not known, some factors such as oxidative stress and genetic factors may play a role in this mechanism [42]. Mechanism of DM due to induce inflammation by increased advanced glycation end products that may activate macrophages and elevated oxidative stress and IL-6 synthesis, resulting in the production of CRP [43].

The study done by [44], to assess the combination of CRP with incident Type 2 DM and to determine the joint action of obesity and hypertension on them in the large-scale population-based Korean cohort, The associations between CRP and incident T2DM were more prominent between patients in older group ( $\geq 50$  years), the CRP and its combination with metabolic syndromes such as hypertension and obesity are associated with high risk of T2DM.

The IFN- $\gamma$  has an important role in the pathogenesis of T2DM [45]. This study done by [46]. They found of IFN- $\gamma$  was increased significantly in rheumatoid arthritis patients with or without T2DM relative to control group. Also [47]. found in their results a significant high serum levels of IL-1 $\beta$ , IL-17 and TNF- $\alpha$  among male and female suffer from T2DM. In present results the serum level of IFN- $\gamma$  was significantly decreased in patients T2DM (with hypertension or without hypertension) compared to control group.

#### **CONCLUSIONS:**

This study demonstrated that type 2 diabetes mellitus patients have disorder levels of Interferon  $\gamma$  and C-reactive Protein may lead to several diseases also, increased level of glycosylated hemoglobin levels point toward poor control of blood glucose levels, dyslipidemia is obvious in patients with type 2 diabetes which may lead to several diseases.

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