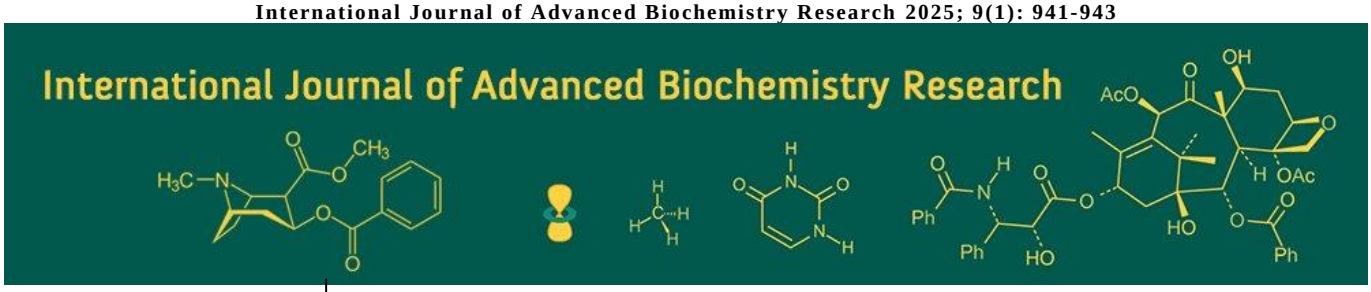

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Estimation of serum L-carnitine levels in relation to insulin and hs-CRP in Type2 Iraqi diabetics

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Abstract
This study aims to focus on serum levels of L-carnitine, insulin, high sensitivity C-reactive protein (hs-CRP), fasting serum glucose FSG, Homeostatic Model Assessment-Insulin Resistance HOMA-IR in type2 Iraqi diabetic patients compared with apparently healthy controls. A case-controlled study included (84) Iraqi subjects were classified into two groups: diabetics (45) and controls(39). L-carnitine and insulin levels were significantly (p<0.05) lowered in diabetics as compared to controls, while high sensitivity C-Reactive Protein (hs-CRP), FSG, HOMA-IR were significantly (p<0.05)elevated in their serums, furthermore, the serum insulin levels have a positive significant correlation with serum L-carnitine levels in both groups, illustrating the influence of L-carnitine in ameliorating diabetes risks by improving glucose level, and ameliorate insulin resistance, beside their anti-inflammatory effect. These findings suggest using of L-carnitine as a therapy in diabetes mellitus and insulin resistance.

Keywords: L-carnitine, insulin, hs-CRP, HOMA-IR, T2DM

Introduction
The prevalence of diabetes in 2021 had been reported to be about 537 million people and is expected to rise to 783 million in 2045 worldwide [1]. A conjugation of demographic and economic changes, with the association of large shifts in physical activity and dietary patterns, properly considered a primary drivers for the rise in diabetes in low- and middle-income countries [2]. Diabetes mellitus (DM) is a chronic disease causing an insulin action resistant that leads to prolonged hyperglycemia besides metabolic disorders of lipids, and protein [3]. Type 2 diabetes (T2DM), the most common type of DM, is characterized by insulin resistance state that leads to a progressive decrease of adequate insulin secretion from β-cells [4]. Many results show the increased levels of Homeostatic Model Assessment-Insulin Resistance HOMA-IR and fasting serum glucose FSG in diabetics when compared to non-diabetics [5]. Although individual susceptibility to T2DM is determined by genetic predisposition, which is related to more than 88 genetic loci involved in susceptibility to T2DM [4], the increase in obesity, a sedentary lifestyle, industrialization and energy-dense diets are responsible for making the T2DM a wide spread state [6]. Carnitine was discovered in 1905 as one of muscle component, while the structure were discovered after about 20 years [7], the synthesis occurs in the liver, kidneys, and brain [8]. The normal level of total carnitine in plasma is 45 µmol/L to 91 µmol/L, free carnitine is 36 µmol/L to 74 µmol/L, and acyl carnitine is 6 µmol/L to 23 µmol/L [9]. L-Carnitine decrease fasting glucose serum level [10]. CRP is a 206-amino acid [11]. C-reactive protein (CRP) estimation is considered as a marker for systemic inflammation [12]. This study is aimed to estimate the serum levels of L-carnitine, in relation to insulin, high sensitivity C-Reactive Protein (hs-CRP), fasting serum glucose, HOMA-IR and their correlations with each others in diabetic patients compared with apparently healthy controls.

Materials and Methods
Design of the study
A case-controlled study was conducted at The National Center for Diabetes/College of Medicine Al- Mustansiriya University. The study was approved by and obtained the Ethical approval of The Committee of The Post Graduate Studies/The College of Pharmacy. The diabetic patients were selected from the out-patient clinic under the supervision of an

endocrinologist from patients attending The National Center for Diabetes/Medicine College Al Mutansryia University.
The selection criteria of patients was listed in a questionnaire included having type 2 DM for at least 1 year, aged 18 years or older, fasting over last night, while the exclusion criteria were malignant, endocrinopathy, renal, chronic liver diseases. Eighty- four subjects included in the present study, were categorized into two groups:

Group-1 diabetic patients: include fourty five diabetic patients (17 males & 28 females) aged between (25-44) years, Group -2 control subjects: include thirty nine subjects (19 males & 20 females) aged between (30-65) years were chosen from general population to be apparently healthy. Venous blood specimen (7 ml) was withdrawn from each subject after an overnight fasting. The samples of blood were placed into a gel tube (no anticoagulant) to permit clotting before centrifugation for 10 minutes. The obtained serum was stored as aliquots and were kept frozen (-20 °C) until their assay for insulin, hs- CRP, L-Carnitin,by specific ELISA kits, besides measuring fasting serum glucose (FSG) in automated Kenza 240 TX Biochemical autoanalyzer device. The results were expressed as (mean ± standard deviation (SD) of mean). To explore the normality of the data the Shapiro-Wilk test was conducted to all parameters. The normally distributed variables were managed by t test to compare the two studied groups. Pearson's correlation coefficient (r) was run to find out the statistical significant correlations between measured parameters. P value less than 0.05 was accepted as a significance difference. The analyses were conducted using the Statistical Package for the Social Science (SPSS), version 25.

Table 1: Analytical kits

Analyte	Suppliers
Glucose	BIOLABO Diagnostic/France
hs C-Reactive Protein	Demeditec Diagnostics/Germany
Insulin	Demeditec Diagnostics/Germany
L- Carnitine	Shanghai Yehua Biological Technology Co., Ltd/China

Results
FSG, HOMA-IR, hs-CRP were significantly higher in diabetics, while fasting insulin, L-carnitine shows significantly lowered levels in diabetics as compared to controls. The diabetics is older (52.111±10.375) than controls (33.333±5.488), the duration of disease in diabetics is (6.42±4.801), Table 2.

Table 2: Descriptive Data of Control &Diabetic Patients

	Control (n=39)	DM (n=45)	P –value
Age (year)	33.333±5.488	52.111±10.375	< 0.0001*
Gender (M/F)	19/20	17/28	------
Disease duration (year)	---------	6.42 ± 4.801	-------
L-carnitin	31.925±7.969209	21.13333±2.608128	< 0.0001*
hs-CRP (µg/ml)	5.492±2.905	17.937±5.979	< 0.0001*
Insulin (µIU/ml)	13.502±6.165	8.411±1.161	< 0.0001*
FSG (mg/ml)	90.0±19.351	176.555±38.927	< 0.0001*
HOMA-IR	2.991±1.532	3.671±0.955	0.0154**
*= t-test (student test) significant at level of p<0.05			
**= t-test (student test) significant at level of p<0.01			

Values are Presented as Mean ± SD, hs-CRP = high sensitive C-Reactive Protein, FSG=fasting serum glucose, HOMA-IR = Homeostatic Model Assessment-Insulin Resistance. A significantly positive correlation between fasting insulin and L-carnitine was found in the two groups, Table 2.

Table 2: Correlation between Serum L-carnitine and Insulin in The Study Groups

	DM	Control
R	0.990	0.490
p	0.000	0.02
N	45	39

r = Pearson Correlation, p = Significance (2-tailed), N= number of subjects in the group.

Discussion
The significantly (p<0.05) higher FSG, hs-CRP and HOMA-IR levels in diabetics with concurrent significantly (p<0.05) lowered L-carnitin and insulin levels compared to the controls (Table-2) may be explained by that the hyperglycemia during type 2 diabetes participates in the inflammation process which agree with Wu *et al*. [13], this inflammation could give a rise to insulin resistance, the same was found in Asimakidou *et al*. [14].

The significantly (p<0.05) lowered level of insulin secretion in diabetics could result from prolonged time exposure to the disease (table-2) which promote hypo-insulinemia and hyperglycemia as β-cells will be exhausted with time, agreeing with Faraj *et al*. [15] besides aging of diabetics as compared to controls (table -2) aging can cause gradual loss of β-cell mass, which agree with Nasteska *et al*. [16].
The significantly (p<0.05) lowered level of L-carnitine may comes from the hyperglycemia which lowers the level of L-carnitine, the same finding in Morgane *et al*. [17].
The significant (p<0.05) positive correlation between L-carnitine and insulin levels could be due to the effect of L-carnitine in ameliorating pancreatic oxidant, which is found by Mesallam *et al*. research [18] as L-carnitine act as antioxidant beside it's action as anti-inflammatory, agreeing with Cao *et al*. [19], promoting pancreatic secretion of insulin.

Conclusion
The significantly (p<0.05) higher levels of serum L-carnitine and insulin with concurrent significantly (p<0.05) lower levels of FSG, hs-CRP and HOMA-IR in controls as compared to diabetics may illustrate the influence of L-carnitine in improving glucose level, and ameliorate insulin resistance, beside their anti-inflammatory effect, thereby

ameliorating diabetes and insulin resistance risks, demonstrating the importance of L-carnitine in the treatment of these two cases, however these findings need further investigations.

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Conflicts of Interest
Authors have no conflict of interest to declare.

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