

## Serum leptin level as a cardiovascular risk factor in type 2 diabetic patients

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### مستوى اللبتين في مصل الدم كعامل خطر قلبي وعائي عند مرضى السكري من النوع الثاني

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#### الخلاصة:

أن السكري من النوع الثاني مرض أبيض يزيد من خطورة الإصابة بالتهلبي العصيدى . اللبتين هو محرك خلوى (سابتوكين) أو شبيه هرمون يشق فى الدرجة الأساس من النسيج الدهنى فى الجسم وله وظائف أبيضىة متنوعة وكذلك تأثيرات وعائىة وتعصيدىة تم كشفها حديثاً. أن هدف هذه الدراسة هو دراسة مستوى اللبتين فى مصل الدم والعلاقة مع بعض عوامل الخطر القلبي الوعائى عند مرضى السكري من النوع الثانى .

تم مقارنة أربعين مريضاً من الرجال مصابين بالسكري مع داء قلبي أقفارى و أطلق عليهم (مجموعة الداء القلبي الأقفارى ) و أعمارهم ( ≤ ٤٠ سنة ) ، تم مقارنةهم مع أربعين مريضاً من الرجال مصابين بلسكري فقط ومن نفس الفئة العمرية وليس لديهم إصابة سابقة بداء قلبي أقفارى و أطلق عليهم (مجموعة السكري)

أن كل مجموعة دراسة رئيسية قد قسمت الى مجموعتين فرعيتين اعتماداً على وجود أو غياب المتلازمة الأيضىة كما أن مجموعة الداء القلبي الأقفارى كذلك قسمت الى ثلاثة مجاميع فرعية وهى : مجموعة الذبحة الصدرية ومجموعة قصور الشريان التاجى و مجموعة احتشاء العضلة القلبية. تم قياس مرتسم شحوم مصل الدم ومؤشر فوق أكسدة الشحوم (TBARS) كدالة للاجهاد التاكسدى وهرمون اللبتين وأخيراً مكون الليفين فى البلازما كدالة للالتهاب،بالإضافة الى قياسات جسم الإنسان.

اظهرت النتائج وجود ارتفاع معنوي كبير في مستوى اللبتين في مجموعة الداء القلبي الأقفاري عند مقارنتهم بمجموعة مرضى السكري ( $11.56 \pm 10.27$  نانوغرام/مل في الاولى و  $7.39 \pm 3.54$  نانوغرام/مل في الثانية تحت احتمالية  $> 0.01$  ، كما اظهرت مجموعة الداء القلبي الأقفاري ارتفاع معنوي كبير في مستوى مؤشر فوق اكسدة الشحوم عند مقارنتهم مع مجموعة السكري ( $9.00 \pm 3.61$  مايكرومول (MDA)/لتر في الاولى و  $6.65 \pm 2.41$  مايكرومول (MDA) / لتر في الثانية تحت احتمالية  $> 0.001$  وكذلك مكون الليفين كان ارتفاعه معنويا في مجموعة الداء القلبي الأقفاري عند مقارنتهم بمجموعة السكري ( $3.30 \pm 0.65$  غم/ديسيلتر في الاولى و  $2.99 \pm 0.65$  غم/ديسيلتر في الثانية وتحت احتمالية  $> 0.05$  .

كانت الزيادة في مستوى اللبتين ذات فرق معنوي مهم عند مرضى قصور الشريان التاجي وليس عند مرضى الذبحة الصدرية بينما كان مستوى اللبتين اقل عند مرضى احتشاء العضلة القلبية عند المقارنة مع مجموعة السكري .

اظهرت النتائج ايضا ارتفاعا معنويا في مستوى اللبتين عند مرضى الداء القلبي الأقفاري بغياب المتلازمة الايضية عند مقارنتهم مع مرضى السكري بغياب المتلازمة الايضية ( $13.06 \pm 11.01$  في الاولى و  $7.06 \pm 3.08$  نانوغرام/مل في الثانية تحت احتمالية  $> 0.05$  .

في مجموعة الداء القلبي الأقفاري اظهر مستوى اللبتين في مصل الدم علاقة ايجابية مع دليل كتلة الجسم ، محيط خصر الجسم ، فوق اكسدة الشحوم و مكون الليفين أما في مجموعة مرضى السكري فقد أظهر مستوى اللبتين علاقة ايجابية مع دليل كتلة الجسم ، محيط خصر الجسم و مكون الليفين في الدم بينما اظهر علاقة غير معنوية مع مؤشر فوق اكسدة الشحوم (TBARS).

نستنتج مما سبق وجود ارتفاع في مستوى اللبتين في مصل الدم عند مرضى السكري من النوع الثاني المصابين بداء قلبي أقفاري وهذا يكون مرتبطا بأجهاد تاكسدي والتهاب و داء قلبي أقفاري فعال أو متدهور وبالإستقلال عن وجود المتلازمة الايضية لذلك قد يمكن اعتماد اللبتين كعامل اضافي في تقدير الخطر القلبي الوعائي .

## Abstract

Type 2 diabetes mellitus ( T2DM ) is a metabolic disease that is associated with an increased risk for atherosclerosis. Leptin is a hormone – like cytokine that is derived mainly from adipose tissue and has multiple functions. Recently, many vascular and atherogenic effects for leptin have been demonstrated. The aim was to study serum leptin level and its relationship with some cardiovascular risk factors in T2DM patients.

Forty diabetic males with ischemic heart disease (IHD group), aged  $\geq 40$  years old, were compared with 40 diabetic males of similar ages who had no clinical history of IHD (DM group). Each main study group was divided into two subgroups according to the presence or absence of metabolic syndrome. The IHD group was also subdivided according to their clinical endpoints into stable angina pectoris (angina group), significant coronary artery disease on angiography (angiography group) and myocardial infarction (MI group).

In addition to anthropometric measurements; serum lipid profile, thiobarbituric acid -reactive substances (TBARS) and leptin levels as well as plasma fibrinogen level were quantified .

A highly significant increase of mean serum leptin level was observed in IHD group in comparison with that of DM group ( $11.56 \pm 10.27$  vs.  $7.39 \pm 3.54$  ng /

ml,  $p < 0.01$ ). IHD patients showed a highly significant increase in serum level of TBARS in comparison with that of DM group ( $9.00 \pm 3.61$  vs.  $6.65 \pm 2.41$   $\mu\text{mol}$  (MDA)/L,  $P < 0.001$ ). The mean plasma level of fibrinogen is significantly higher in IHD group than in DM group ( $3.30 \pm 0.65$  vs.  $2.99 \pm 0.63$  g/dl,  $p < 0.05$ ).

Serum leptin level was significantly higher in (angiography group) but not in (angina group) while the level was even lower in (MI group) when compared with that of DM group. A significant increase of mean serum leptin level was observed in IHD subgroup with non-metabolic syndrome in comparison with the D.M subgroup with non-metabolic syndrome ( $13.06 \pm 11.01$  vs.  $7.06 \pm 3.08$  ng/ml,  $P < 0.05$ ). In IHD group, serum leptin level showed a positive correlation with BMI, W/h ratio, serum TBARS, and plasma fibrinogen. In DM group, serum leptin level showed a positive correlation with BMI, W/h ratio, and plasma fibrinogen, while insignificantly correlated with TBARS.

In conclusion, T2DM patients with IHD have an elevated serum leptin level that is associated with oxidative stress, inflammation and active or worsening ischemic heart disease independent of metabolic syndrome. Thus, serum leptin level could be an additional factor to assess cardiovascular risk

Key words :Diabetes, Leptin, Cardiovascular Risk, Oxidative stress, inflammation

## Introduction

Type 2 diabetes mellitus (T2DM) is by far the most prevalent endocrine or metabolic disease in the world<sup>(1)</sup>. Adults with diabetes have a two- to fourfold higher risk of cardiovascular disease (CVD) compared with those without diabetes<sup>(2)</sup>. Ischemic heart disease (IHD) is the most common among CVD and is usually due to atherosclerosis of the coronary arteries. Its risk increases with age, smoking, hypercholesterolemia, hypertension, and diabetes, and is more common in men and those who have close relatives with IHD<sup>(3)</sup>.

Inflammation is thought to play an important role in the pathogenesis of atherosclerosis<sup>(4)</sup>.

A chronic low-grade inflammatory state is associated with the presence of obesity and insulin resistance syndrome<sup>(5)</sup>. This is reflected by enhanced production of proinflammatory cytokines by the greater adipose tissue mass associated with obesity and insulin resistance syndrome<sup>(6)</sup>. The so called oxidation hypothesis states that the oxidative modification of low density lipoprotein is important in the pathogenesis of the atherosclerotic lesion<sup>(7)</sup>.

Metabolic syndrome (MetS) is a constellation of interrelated risk factors of metabolic origin that appear to be directly associated with an elevated risk of type 2 diabetes and cardiovascular disease (CVD)<sup>(8)</sup>. A prominent feature of the MetS and then of T2DM is central obesity<sup>(9)</sup>. The risk for major cardiovascular events resulting from the presence of the MetS is approximately twice as high as for those

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without the syndrome<sup>(10)</sup>, and risk for T2DM is approximately five fold greater in those who have it<sup>(11)</sup>. T2DM, although accompanied by increased risk for CVD, has been reported to carry much more risk for CVD when the MetS is concomitantly present<sup>(10)</sup>.

Adipose tissue is a source of a range of adipocyte-secreted factors involved in diverse biological functions and are collectively referred to as adipokines or adipocytokines, some important members of which are leptin and adiponectin<sup>(12)</sup>. Leptin is a non-glycosylated peptide or a hormone – like cytokine and is a member of the interleukin-6 (IL-6) cytokine family<sup>(13)</sup>. Although the main role of leptin is as an adipostat ( promotes weight loss or thinning), many studies have shown that leptin has a broad range of effects in different tissues<sup>(14, 15)</sup>. A potential role for leptin in vascular physiology /pathophysiology is suggested by studies that have demonstrated that leptin leads to sympathoactivation<sup>(16)</sup> and promotes both thrombosis and atherosclerosis in vitro<sup>(17)</sup>. Moreover, leptin receptor has been expressed in atherosclerotic lesions<sup>(18)</sup> and it has been reported that leptin promotes angiogenesis<sup>(19)</sup> which is a feature of atherosclerotic plaque progression and destabilization<sup>(20)</sup>.

Our aim is to study the relationship between serum leptin level and some cardiovascular risk factors in type 2 diabetic patients having ischemic heart disease.

## **Materials and methods**

**Settings:** This study was conducted at department of medical biochemistry, college of medicine and the National diabetes center -University of Al-Mustnasiriya and Ibn-Albeetar hospital for heart diseases-Baghdad-Iraq, from November 2007 to July 2008. Eighty subjects who have type 2 diabetes were enrolled in the study : 40 diabetic males (DM group) and 40 diabetic males with ischemic heart disease ( IHD group).

The age of a patient in the study groups should be  $\geq 40$  years. Subjects with a concurrent acute illness or with a major liver, thyroid or other endocrine diseases were excluded. The following clinical characteristics were reported:

- 1- Weight and height in order to calculate body mass index (BMI)
- 2- Waist: hip ratio
- 3- Blood pressure measurement or a history of hypertension.
- 4- Smoking status.

5-The presence of ischemic heart disease in a first degree relative under the age of 60 years was taken as an evidence of having family history of CHD.

6- Duration of diabetes.

The presence of ischemic heart disease was defined as:

1. Having classical angina pectoris by clinical diagnosis as well as typical electrocardiogram (ECG).Such patients were assigned as (angina group).
2. The presence of a significant coronary artery disease in diagnostic angiography or in case of doing of coronary intervention such as percutaneous transluminal coronary angioplasty (PTCA), or coronary artery bypass graft surgery (CABG) since more than three months. Such patients were assigned as (angiography group). Patients in this group were complaining of worsening angina pectoris or coronary insufficiency.
3. Past history of myocardial infarction. More than three months have elapsed since the onset of the disease. Such patients were assigned as myocardial infarction group(MI group).

Each main study group was divided into two subgroups according to the presence or absence of metabolic syndrome.

#### **Characteristics of metabolic syndrome:**

- 1- Hypertension: Blood pressure measurement higher than 140/90 or the presence of hypertension on treatment was reported as hypertensive <sup>(21)</sup>
- 2- Obesity: BMI > 30 was considered as obese <sup>(21)</sup>
- 3- Serum triglycerides level (TG): TG level >150 mg/dl was considered abnormal <sup>(22)</sup>
- 4- Serum high density lipoprotein-cholesterol (HDL-C): HDL-C level <40 mg/dl in males was considered abnormal <sup>(22)</sup>

#### **Biochemical analyses:**

Serum samples were used for fasting blood glucose and lipid profile. Whole blood specimens that were collected in EDTA tubes were used for fibrinogen measurement . These biochemical analyses were performed on the same day of the visit of a patient. For measurement of leptin and TBARS, serum was divided into aliquots and stored at  $-20\text{ C}^{\circ}$  until analysis.

#### **Methodology:**

**Lipid profile:** Serum total cholesterol (TC) and serum triglycerides (TG) were determined by totally enzymatic methods<sup>(23,24)</sup>. Estimation of serum high-density lipoprotein cholesterol (HDL-C) was done by precipitation with phosphotungstate-MgCl<sub>2</sub> solution followed by enzymatic determination of cholesterol in the supernatant <sup>(25)</sup>.

**Serum leptin:** This was measured using DRG Leptin ELISA Kit (DRG Instruments GmbH, Germany) which is a solid phase enzyme-linked immunosorbent assay (ELISA) based on the sandwich principle. According to this method: Normal mean value for male =  $3.84 \pm 1.79$  ng/ml. Normal value for female =  $7.36 \pm 3.73$  ng/ml.

**Plasma thiobarbituric acid-reactive substances (TBARS):** were measured spectrophotometrically<sup>(26)</sup>.

**Plasma fibrinogen:** was determined by the heat precipitation method<sup>(27, 28)</sup>.

### **Statistical analysis:**

Data were presented in simple statistical measures of number, percentage, mean and standard deviation. Statistical analysis was done by using Student's t-test for the significance of difference of quantitative data between two means. Simple linear correlation was used for determination of correlation between two quantitative parameters for the different groups. A probability value ( $p < 0.05$ ) was considered to be statistically significant.

### **Results**

There were no significant differences between DM group and IHD group in the mean values of age, body mass index, w/h ratio, and duration of DM (table 1). More patients in IHD group had hypertension, were smokers, and had family history of IHD than in DM group. However, the differences were statistically not significant.

The mean serum levels of TC, TG, and HDL-C were compared between DM group and IHD group (table 2), the differences were statistically non significant.

A highly significant increase of mean serum leptin level was observed in IHD group in comparison with DM group ( $11.56 \pm 10.27$  vs.  $7.39 \pm 3.54$  ng/ml,  $p < 0.01$ ), (table 3). IHD patients showed a highly significant increase in mean serum level of TBARS in comparison with that of DM group ( $9.00 \pm 3.61$  vs.  $6.65 \pm 2.41$   $\mu\text{mol (MDA)/L}$ ,  $P < 0.001$ ). Also the mean plasma level of fibrinogen was significantly higher in IHD group than in DM group ( $3.30 \pm 0.65$  vs.  $2.99 \pm 0.63$  g/dl,  $p < 0.05$ ).

When IHD patients were classified according to their clinical endpoints, the mean serum leptin level in (angiography patients) showed a highly significant increase while (angina patients) showed no significant difference from that of DM group (table 4). In myocardial infarction patients, there was a significant decrease of the mean serum leptin level in comparison with DM group ( $5.61 \pm 1.09$  vs.  $7.39 \pm 3.54$ ,  $p < 0.05$ ). The mean serum level of TBARS in (angina patients) as well as in angiography patients showed a highly significant increase compared to that of DM group. On the other hand, there was a highly significant increase of plasma fibrinogen only in myocardial infarction patients compared with DM group (table 4).

Each main study group was then divided into two subgroups according to the presence or absence of metabolic syndrome. On intergroup comparison, a significant increase of mean serum leptin level was observed in IHD group with non-metabolic syndrome in comparison with the mean serum leptin level of DM group with non-metabolic syndrome ( $13.06 \pm 11.01$  vs.  $7.06 \pm 3.08$ ,  $P < 0.05$ ) (table 5). The mean serum leptin level in IHD group with metabolic syndrome showed no significant difference from that of DM group with metabolic syndrome ( $7.59 \pm 2.71$  vs.  $7.95 \pm 4.26$ ,  $P > 0.05$ ) (table 6). A significant increase of mean serum TBARS level is observed in IHD group with non-metabolic syndrome as well as in IHD group with metabolic syndrome in comparison with the mean serum of TBARS level in DM subgroups with and without metabolic syndrome ( $8.96 \pm 3.95$  and  $9.25 \pm 3.24$  vs.  $6.67 \pm 2.43$  and  $6.62 \pm 2.46$  respectively,  $P < 0.05$ ) (table 5 and table 6). No significant difference of mean serum fibrinogen level is observed in IHD group with non-metabolic syndrome in comparison with the mean serum fibrinogen level in DM group with non-metabolic syndrome ( $3.28 \pm 0.89$  vs.  $3.01 \pm 0.64$ ,  $P > 0.05$ ) (table 5), while the mean serum fibrinogen level in the respective metabolic syndrome subgroups showed a significant difference ( $3.55 \pm 0.56$  vs.  $2.94 \pm 0.63$ ,  $P < 0.05$ ) (table 6). In our data the mean serum leptin level showed a highly significant positive correlation with BMI in DM group ( $r = 0.19$ ,  $p < 0.001$ ) and in IHD group ( $r = 0.11$ ,  $p < 0.001$ ) (table 7). It is noticed that the value of correlation coefficient was lower in IHD group. When the correlation between mean serum leptin level and w/h ratio was studied, there was a highly significant positive correlation in both DM group and IHD group ( $r = 0.17$  and  $r = 0.11$ ,  $p < 0.001$ ). Again the value of correlation coefficient was lower in IHD group. While serum leptin level was insignificantly correlated with serum TBARS level in DM group ( $r = 0.37$ ,  $p > 0.05$ ), there was a significant positive correlation of leptin level with TBARS in IHD group ( $r = 0.69$ ,  $p < 0.05$ ) (table 7).

## Discussion

The risk factor hypothesis implies that if a person has a certain risk factor, he is more likely to develop clinical manifestations of atherosclerosis and is likely to do so earlier than in a person with no such risk factor<sup>(29)</sup>. It was believed from the start that the discovery of such risk factors or predictive variables might pave the way to preventive efforts.

The finding of a higher number of hypertensive and smoker patients in our IHD group than in DM group is in line with the known strong relation between hypertension, smoking and IHD<sup>(3,30)</sup>. Also family history of IHD revealed that there were more subjects with such history in IHD group. It has already been reported that family history of CHD is an independent risk factor for CHD in many studies<sup>(3, 31)</sup> and this might be in favor of a genetic predisposition to such

condition. However, the differences in these risk factors between our main study groups were statistically not significant suggesting the presence of differences in other risk factors.

The mean serum levels of TC, TG, and HDL-C were compared between DM group and IHD group. Hypercholesterolemia, if present, is known to have an impact on CVD in diabetic subjects which is substantially greater than in the general population. Also TG and HDL-C have a significantly greater predictive power for CVD in diabetic subjects than does the T.Ch value<sup>(32)</sup>. However, the differences between the two groups were statistically non significant. These findings, in addition to the presence of no differences in other classical risk factors which are age and obesity, necessitates a search for a more predictive risk factors in such patients in particular.

In our study, a highly significant increase of mean serum leptin level was observed in IHD group when it was compared with DM group. Recently, many evidences are in support of a role for hyperleptinemia in vascular disease<sup>(33, 34)</sup>. Many studies have reported an association between serum leptin level and clinical manifestations of CHD whether as first myocardial infarction<sup>(35)</sup> or a first coronary event<sup>(36)</sup> or a further coronary event in patients with angiographically confirmed coronary atherosclerosis<sup>(37)</sup>. However, in one of studies, such an association was not detected<sup>(38)</sup>.

On comparison of serum leptin levels in IHD subgroups with that of DM group, the significant elevation was restricted to angiography group while the higher mean level in angina group was not statistically significant. On the other hand, the mean leptin level was even lower in MI group. These findings may be suggestive of an association between higher serum leptin levels and vulnerable (inflamed) atherosclerotic plaques which histopathologically characterize the worsening clinical states of angiography group<sup>(39,40,41)</sup>.

Our study found a very high significant increase in mean serum level of TBARS in IHD group in comparison with that of DM group. Also the correlation between serum leptin level and serum TBARS level was significantly positive in IHD group but insignificant in DM group. These finding are consistent with the reports that high leptin level is an inducer of oxidative stress<sup>(42,43)</sup>.

On comparison of serum TBARS levels between (DM group) and IHD subgroups, the increase was found statistically significant in angiography group and in angina group but not in MI group. This may be related to the activity of atherosclerotic disease and is consistent with the differences detected on comparison of serum leptin level in study groups and further suggests that hyperleptinemia has an association with oxidative stress.

In regard to the presence of metabolic syndrome in our study patients, a significant increase in the mean serum leptin level was confined to IHD subgroup with non-metabolic syndrome. Such finding favors a role of leptin which seems to be

independent of metabolic syndrome .This was also suggested by many previous studies <sup>(35,44)</sup>.However, this needs more studies because many reports have also proposed hyperleptinemia as a component of metabolic syndrome of cardiovascular risk <sup>(45, 46, 47)</sup> .

Comparison of study groups according to the presence of metabolic syndrome revealed that high TBARS level is a characteristic of IHD in presence or absence of metabolic syndrome. This supports the idea that oxidative stress can be a common pathway for both metabolic syndrome and hyperleptinemia and assists the belief in an association between hyperleptinemia and oxidative stress. Moreover, the finding that the correlation between leptin and TBARS in (DM group) is insignificant but significant in (IHD group) is in line with the belief of a special independent role of leptin in IHD.

Our study revealed that the mean plasma fibrinogen level is significantly higher in (IHD group) than in (DM group). On further analysis in IHD subgroups, the increase in plasma fibrinogen was statistically significant only in myocardial infarction subgroup although it was higher in other subgroups compared to (DM group). These results are consistent with most previous studies that incriminated high plasma fibrinogen as a risk factor for IHD<sup>(48)</sup> and that high level is associated more with thrombo-atherosclerotic conditions like MI than with other manifestations of IHD <sup>(49)</sup>. Since serum fibrinogen is an important positive acute protein and an increased level is a marker of inflammation<sup>(50)</sup> then the results go with the belief that hyperleptinemia may be atherogenic through the induction of an inflammatory response<sup>(34)</sup> .

In conclusion, T2DM patients with IHD have an elevated serum leptin level that is associated with oxidative stress, inflammation and active or worsening ischemic heart disease independent of metabolic syndrome. Thus, serum leptin level could be an additional factor to assess cardiovascular risk.

**Table 1: Clinical characteristics of study groups**

<b>Variables</b>	<b>DM group (n = 40)</b>	<b>IHD group (n = 40)</b>	<b>Comparison (p-value)</b>	<b>Level of significance</b>
<b>Age (Yr) (Mean ± SD)</b>	56.4 ± 9.7	58 ± 7.6	> 0.05	NS
<b>BMI ( kg /m<sup>2</sup>) (Mean ± SD)</b>	29.4 ± 5.3	28.1 ± 4.7	> 0.05	NS
<b>w/h (cm/cm) (Mean ± SD)</b>	0.94 ± 0.03	0.94 ± 0.04	> 0.05	NS
<b>Hypertension:</b>				
Yes	11	13	> 0.05	NS
No	29	27		
<b>Smoking status:</b>				
Smoker	15	19	> 0.05	NS
Non-smoker	25	21		
<b>Family history of IHD:</b>				
Yes	15	22	> 0.05	NS
No	25	18		
<b>Duration of diabetes(Yr)</b>				
<b>1-5</b>	20	25	> 0.05	NS
<b>6-10</b>	14	10		
<b>11-15</b>	4	4		
<b>16-20</b>	2	1		

**Table 2: Lipid profile of DM group and IHD group**

Analyte (mg/dl)	DM group (n = 40)	IHD group (n = 40)	Comparison (p-value)	Level of significance
<b>Lipid profile:</b>				
<b>TC</b>	215.4 ± 38.6	209.4 ± 40.2	> 0.05	NS
<b>TG</b>	160.4 ± 84.47	154.05 ± 86.34	> 0.05	NS
<b>HDL-C</b>	39.87 ± 14.68	41.73 ± 12.05	> 0.05	NS

TC = Total cholesterol

TG = Triglyceride

HDL-C = High Density Lipoprotein-Cholesterol

Values are (Mean ± SD)

**Table 3: Mean serum concentrations of leptin, TBARS and fibrinogen of DM group and IHD group**

Analyte	DM group (n = 40)	IHD group (n = 40)	Comparison (p-value)	Level of significance
<b>Leptin (ng/ml)</b>	7.39 ± 3.54	11.56 ± 10.27	< 0.01 **	HS
<b>TBARS (µmol/L)</b>	6.65 ± 2.41	9.00 ± 3.61	< 0.001***	HS
<b>Fibrinogen (g/L)</b>	2.99 ± 0.63	3.3 ± 0.65	< 0.05 *	S

Values are (Mean ± SD)

\* :Significant ( p < 0.05)

\*\* :Highly Significant ( p < 0.01)

\*\*\* :Highly significant ( p < 0.001)

**Table 4: Mean serum concentrations of leptin, TBARS and fibrinogen of DM group and IHD subgroups**

Analyte	DM group (n = 40)	IHD subgroups (n = 40)		
		Angina (n =12)	angiography (n = 14)	MI (n = 14)
Leptin (ng/ml)	7.39 ± 3.54	9.03 ± 4.39 (NS)	19.67 ± 13.57***	5.61 ± 1.09*
TBARS (µmol/L)	6.65 ± 2.41	9.46 ± 3.00***	10.53 ± 4.53***	7.09 ± 2.06(NS)
Fibrinogen (g/L)	2.99 ± 0.63	3.23 ± 0.86 (NS)	3.15 ± 0.52 (NS)	3.51 ± 0.56**

Values are (Mean ± SD)

- \* :Significant ( p < 0.05)
- \*\* :Highly Significant ( p < 0.01)
- \*\*\* :Highly significant ( p < 0.001)
- N.S :Non-significant ( p > 0.05)

**Table 5: Mean serum concentrations of leptin, TBARS and fibrinogen of DM group with non- metabolic syndrome and IHD group with non- metabolic syndrome**

Analyte	DM group with non- metabolic syndrome (n = 25)	IHD group with non- metabolic syndrome (n = 22)	Comparison (p-value)	Level of significance
Leptin (ng/ml)	7.06 ± 3.08	13.06 ± 11.01	< 0.01	S
Fibrinogen (g/L)	3.01 ± 0.64	3.28 ± 0.89	> 0.05	NS
TBARS (µmol/L)	6.67 ± 2.43	8.96 ± 3.95	< 0.01	S

Values are (Mean ± SD)

**Table 6: Mean serum concentrations of leptin, TBARS and fibrinogen for DM group with metabolic syndrome and IHD group with metabolic syndrome**

Analyte	D.M group with metabolic syndrome (n = 15)	IHD group with metabolic syndrome (n = 18)	Comparison (p-value)	Level of significance
<b>Leptin (ng/ml)</b>	7.95 ± 4.26	7.59 ± 2.71	> 0.05	NS
<b>Fibrinogen (g/L)</b>	2.94 ± 0.63	3.55 ± 0.56	< 0.01	S
<b>TBARS (µmol/L)</b>	6.62 ± 2.46	9.25 ± 3.24	< 0.01	S

Values are (Mean ± SD)

**Table 7: Correlation coefficients between serum leptin and BMI, W/h ratio, TBARS, and fibrinogen values for DM group and IHD group**

Analyte	DM group (N = 40)		IHD group (N = 40)	
	r	p-value	r	p-value
Leptin and BMI	<b>0.19</b>	<b>p &lt; 0.001</b>	<b>0.11</b>	<b>P &lt; 0.001</b>
Leptin and W/h ratio	<b>0.17</b>	<b>p &lt; 0.001</b>	<b>0.11</b>	<b>P &lt; 0.001</b>
Leptin and TBARS	<b>0.37</b>	<b>P &gt; 0.05</b>	<b>0.69</b>	<b>P &lt; 0.05</b>
Leptin and Fibrinogen	<b>0.18</b>	<b>P &lt; 0.001</b>	<b>0.22</b>	<b>P &lt; 0.001</b>

## References

1. Lieberman LS (2003) Dietary, evolutionary and modernizing influence on the prevalence of type 2 diabetes. *Ann Rev Nutr.* 23:245-377.
2. Fox CS, Coady S, Sorlie PD, et al (2004) Trends in cardiovascular complications of diabetes. *JAMA.* 292: 2495–2499.
3. Loria V, Dato I, Graziani F, et al (2008) "Myeloperoxidase: a new biomarker of inflammation in ischemic heart disease and acute coronary syndromes". *Mediators Inflamm.* 135625.
4. Ross R (1999) Atherosclerosis—an inflammatory disease. *New Engl. J. Med.* 340:115–26.
5. Ritchie SA and Connell JM (2007) The link between abdominal obesity, metabolic syndrome and cardiovascular disease. *Nutr Metab Cardiovasc Dis.* 17(4):319-26.
6. Bastard JP, Maachi M, Lagathu C, et al (2006) Recent advances in the relation between obesity, inflammation, and insulin resistance. *Eur Cytok. Netw.* 17(1):4-12.
7. Witztum JL (1994) The oxidation hypothesis of atherosclerosis. *Lancet.* 344 : 793-5.
8. Sattar N, Gaw A, Scherbakova O, et al (2003) Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation.* 108:414-9.
9. Wang JJ, Li HB, Kinnunen L , et al (2007) How well does the metabolic syndrome defined by five definitions predict incident diabetes and incident coronary heart disease in a Chinese population ? *Atherosclerosis.* 192:161-168.
10. JM, Girman C, Rhodes T, et al (2007) Metabolic syndrome and 10-year cardiovascular disease risk in the Hoorn Study. *Circulation.* 112:666-673.
11. Resnick HE, Jones K, Ruotolo G, et al (2003) Insulin resistance, the metabolic syndrome, and risk of incident cardiovascular disease in nondiabetic American Indians. The Strong Heart Study. *Diabetes Care.* 26:861-7.
12. Trayhurn P, Wood IS (2004) Adipokines: inflammation and the pleiotropic role of white adipose tissue. *Br. J. Nutr.* 92:347–55.
13. Maugeri D, Bonanno MR, Speciale S, et al (2002) Leptin a new hormone of adipose tissue: clinical findings and perspectives in geriatrics., *J. Archives of Gerontology and Geriatrics.* 34(1) : 47-54.
14. Wauters M, Considine RV, Van Gaal LF (2002) Human leptin: from an adipocyte hormone to an endocrine mediator. *Eur J Endocrinol.* 143:293–311
15. Meier U, Gressner AM (2004) Endocrine Regulation of Energy Metabolism: Review of Pathobiochemical and Clinical Chemical Aspects of Leptin, Ghrelin, Adiponectin, and Resistin *Clinical Chemistry.* 50:91511–1525.
16. Eikelis N, Schlaich M, Aggarwal A, et al (2003) Interactions between leptin and the human sympathetic nervous system. *Hypertension.* 41 : 1072 –1079.
17. Bodary PF, Westrick RJ, Wickenheiser KJ, et al (2002) Effect of leptin on arterial thrombosis following vascular injury in mice. *JAMA.* 287:1706–1709.

18. Kang SM, Kwon HM, Hong BK, et al (2000) Expression of leptin receptor (Ob-R) in human atherosclerotic lesions: potential role in intimal neovascularization. *Yonsei Med J.* 41:68-75.
19. Bouloumie A, Marumo T, Lafontan M, et al (1999) Leptin induces oxidative stress in human endothelial cells. *FASEB J.* 13: 1231–1238.
20. Libby P, Geng YJ, Sukhova GK, et al (1997) Molecular determinants of atherosclerotic plaque vulnerability. *Ann N Y Acad Sci.* 811: 134–145.
21. Alberti KG, Zimmet PZ (1998) Definition, diagnosis and classification of diabetes mellitus and its complications. Part1. Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. ***Diabet Med.* 15:539- 53.**
22. American diabetes association (2003) Management of Dyslipidemia in Adults With diabetes .*Diabetes Care.* 26(1): S83- S86.
23. Allain CC, Poon LS, Chan CS, et al (1974) Enzymatic determination of total serum cholesterol. *Clin Chem* 1974; 20: 470-475.
24. Fossati P, Prencipe L (1982) Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. *Clin Chem.* 28: 2077.
25. Assmann G, Schriewer H, Schmitz G, et al (1983) Quantification of high density lipoprotein cholesterol by precipitation with phosphotungstic acid/ MgCl<sub>2</sub>. *Clin Chem.* 29: 2026 – 30.
26. Shah SV, Walker PD (1988) Evidence suggesting a role for hydroxyl radical in glycerol induced acute renal failure. *Am J Physiol* 255 ( Renal, fluid, electrolyte Physiol. 24 ) : F438-F443.
27. Millar HR, Simpson JG, Stalker AL (1971) An evaluation of the heat precipitation method for plasma fibrinogen estimation *J Clin Path.* 24 : 827-830.
28. Exner T, Burridge J, Power P et al (1979) An evaluation of currently available methods for plasma fibrinogen. *Am. J. Clin. Pathology.* 71: 521-7.
29. Gotto AM (1977) Diagnosis and management of risk factors for atherosclerosis. In Gotto, AM (ed.): *Atherosclerosis.* Upjohn company. Michigan.
30. Wilson PW, Castelli WP, Kannel WB (1987) Coronary risk prediction in adults ( The Framingham heart study ). *Am J Cardiol.* 59:91G-94G.
31. Fredrickson DS (1977) Atherosclerosis and other forms of arteriosclerosis. In Thorn, et al (eds.): *Harrison's principles of internal medicine.* 8<sup>th</sup> ed. McGraw Hill Kogakusha Ltd. Tokyo.
32. Goldberg RB (2000) Cardiovascular disease in diabetic patients. *Med Clin North Am.* 84: 81-93.
33. Cooke JP, Oka RK (2002) Does leptin cause vascular disease? *Circulation.* 106: 1904–1905.
34. Alexanderaki K, Piperi C, Kalofoutis C, et al (2006) Inflammatory process in type 2 diabetes .The role of cytokines.*Ann N Y Acad Sci.* 1084:89-117.
35. Sodeberg S, Ahern B, Jansson JH, et al (1999) Leptin is associated with increased risk of myocardial infarction. *J Intern Med.* 246:409-418.

36. Wallace AM, McMahon AD, Packard CJ, et al (2001) Plasma leptin and the risk of cardiovascular disease in the West Of Scotland Coronary Prevention Study (WOSCOPS) *Circulation*. 104:3052-3056.
37. Wolk R, Berger P, Lennon RJ, et al (2004) Plasma leptin and prognosis in patients with established coronary atherosclerosis. *J Am coll Cardiol*. 44: 1819-24.
38. Couillard C, Lamarche B, Mauriege P (1998) Leptinemia is not a risk factor for ischemic heart disease in men : prospective result from the Quebec Cardiovascular Study. *Diabetes Care*. 21:782-786.
39. Buja LM, Willerson JT (1994) Role of inflammation in coronary plaque disruption. *Circulation*. 89: 503-505.
40. Braunwald E (1998) Unstable angina: an etiologic approach to management. *Circulation*. 98: 2219 - 2222.
41. Kobayashi S, Inoue N, Ohashi Y, et al (2003) Interaction of oxidative stress and inflammatory response in coronary plaque instability. *Arteriosclerosis, thrombosis, and vascular biology*. 23:1398-1404.
42. Yamagishi SI, Edelstein D, Du XL, et al (2001) Leptin induces mitochondrial superoxide production and monocyte chemoattractant protein-1 expression in aortic endothelial cells by increasing fatty acid oxidation via protein kinase A. *J Biol Chem*. 276:25096–25100.
43. Bouloumie A, Marumo T, Lafontan M, et al (1999) Leptin induces oxidative stress in human endothelial cells. *FASEB J*. 13: 1231–1238.
44. Ciccone M, Vettor R, Pannacciulli N et al (2001) Plasma leptin is independently associated with the intima-media thickness of the common carotid artery. *Int. J. Obes. Relat. Metab. Disord*. 25: 805–810.
45. Leyva F, Godsland IF, Ghatei M, et al (1998) Hyperleptinemia as a component of a metabolic syndrome of cardiovascular risk. *Arterioscler Thromb Vasc Biol*. 18:928–33.
46. Zimmet PZ, Collins VR, de Courten MP et al (1999) Etiology of the metabolic syndrome: potential role of insulin resistance, leptin resistance, and other players. *Ann. N. Y. Acad. Sci*. 892:25–44.
47. Koeva L, Dimitrov D, Rousseva T (2000) Leptin and cardiovascular risk factors among overweight diabetics. *Endocrinologia J. Bulgarian society of Endocrin ( BSE )*. 5: 1(abstract).
48. Thompson SG, Kienast J, Pyke SDM, et al (1995) Hemostatic factors and the risk of myocardial infarction or sudden death in patients with angina pectoris. *N Engl J Med*. 332 : 635-41.
49. Ridker PM, Cushman M, Stamper MJ, et al (1997) Inflammation, aspirin and the risk of cardiovascular disease in apparently healthy men. *N Engl J Med*. 336 : 973-79.
50. Pepys MB (1996) The acute phase response and C-reactive protein. In Weatherall DJ, Ledingham JGG, Warrel DA (ed.) *Oxford textbook of medicine* 3rd ed. Oxford Univer Press.

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