Insulin Resistance and Metabolic Syndrome in Patients with Non-Alcoholic Fatty Liver Disease

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ABSTRACT

Nonalcoholic fatty liver disease (NAFLD) is closely related to obesity and insulin resistance (IR), and it is generally agreed upon that NAFLD is the hepatic manifestation of metabolic syndrome (MetS). MetS is an insulin resistance syndrome comprising glucose intolerance, IR, central obesity, dyslipidemia, and hypertension, all of which are well-established risk factors for cardiovascular disease (CVD).The aim of this study is to assess the prevalence of IR in non-diabetic adult patients with (NAFLD) and its relation with Mets. This study included 40 non-diabetic patients with (NAFLD). We performed full history taking and clinical examination with anthropometric measurements for the patients studied. Investigations included serum analysis for liver functions, fasting and postprandial blood glucose, lipid profile, fasting insulin, and homeostasis model assessment insulin resistance index (HOMA-IR). Patients with HOMA-IR levels ≥ 2 were considered insulin resistant. MetS was assessed according to International Diabetic Federation (IDF) criteria. Abdominal ultrasound was performed for NAFLD diagnosis and exclusion of cirrhosis. Insulin resistance was found in 62.5% of NAFLD patients; their mean age (42.6 ± 8.61 vs. 37.3 ± 6.89 years; p=0.038), triglyceride level (TG) (121.1 ± 79.3 vs. 77.4 ± 23.5 mg/dl; p=0.049) and postprandial blood glucose (PPBG) level (111.1 ± 12.4 vs. 102.7 ± 9.9 mg/dl; p=0.013) respectively were significantly higher compared to those without IR. Fifty percent of NAFLD patients fulfilled criteria of MetS. Obesity and PPBG were statistically higher and HDL-cholesterol level was statistically lower in NAFLD patients with MetS co of obesity and MetS. Patients with NAFLD and MetS are more insulin resistant even in the absence of diabetes. This knowledge may lead to more aggressive management of the MetS risk factors and may lead to improvement in patient's liver disease.

Keywords: *Non-alcoholic Fatty Liver Disease, insulin resistance, metabolic syndrome, HOMA_IR*

INTRODUCTION

Obesity is associated with altered physiological functions in almost all tissues and organ systems of the body. The liver in obese people is characterized by an accumulation of intrahepatic triglyceride (IHTG), i.e., steatosis, which is the hallmark feature of nonalcoholic fatty liver disease (NAFLD). This can progress to nonalcoholic steatohepatitis (NASH) if inflammation is also present, with or without fibrosis, and can ultimately lead to cirrhosis. Inflammatory markers such as circulating interleukin (IL)-6, therefore, can discriminate NAFLD from NASH with high specificity **[Fabbrini *et al.*, 2015].** Due to the increased incidence of obesity worldwide, NAFLD has become an important public health problem because of its high prevalence, potential progression to severe liver disease, and strong link with important cardiometabolic risk factors. NAFLD is associated with increased risk for developing insulin resistance, dyslipidemia (high plasma triglyceride and/or low high density lipoprotein-cholesterol concentrations), and hypertension, and is an independent predictor of the development of pre-diabetes and type 2 diabetes **[Musso *et al.*, 2011].**

Overeating and physical inactivity predispose to both conditions. Excess glucose, fructose and amino acids are converted to triglyceride (TG) in the liver via de novo lipogenesis, which pathway is increased in NAFLD **[Lambert *et al.*, 2014].** Alterations in gut microbiota in obesity increase gut permeability to bacterial components such as lipopolysaccharide (LPS), which may contribute to inflammation in both adipose tissue and the liver **[Cani *et al.*, 2014].** Overeating leads to adipose tissue expansion, hypoxia, increased fibrosis and cell death. Dead adipocytes are surrounded by macrophages, which produce cytokines such as tumor-necrosis alpha and chemokines such as monocyte chemoattractant protein-1. This impairs the

ability of insulin to inhibit lipolysis i.e., inhibit release of free fatty acids (FFA) and leads to deficiency of the insulin sensitizing cytokine adiponectin. The latter two changes promote synthesis of intrahepatocellular TG. The ability of insulin to suppress glucose and very low density lipoprotein (VLDL) production is impaired resulting in mild hyperglycemia and hyperinsulinemia, hypertriglyceridemia (TG↑) and a low HDL cholesterol concentration (HDL chol↓). The fatty liver also overproduces many other factors such as the liver enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gammaglutamyltransferase (GGT), C-reactive protein (CRP) and coagulation factors **[Yaki-Jarvinen, 2014].**

The liver is the site of production of two key components of the insulin resistance and metabolic syndrome (MetS), these are fasting serum glucose and very-low density lipoprotein (VLDL). In subjects with NAFLD attributable to being overweight and inactive ("Metabolic NAFLD"), the ability of insulin to normally suppress production of glucose and VLDL is impaired **[Adiels *et al.*, 2007].** Hyperglycemia stimulates insulin secretion and thereby induces hyperinsulinemia. The high concentration of VLDL leads to lowering of high-density lipoprotein (HDL) cholesterol and to generation of small dense LDL particles, which are known to be highly atherogenic **[Tchernof and Despres, 2013]** .

Due to the simplicity of its determination and calculation, insulin resistance assessment by the homeostatic assay (HOMA-IR) has been the most frequently employed technique both in clinical practice and in epidemiological studies **[Mathews *et al.*, 1985]. Salgado *et al* (2010)** suggested that HOMA-IR values above or equal to 2.0 or 2.5 show enhanced diagnostic value in distinguishing non-alcoholic fatty liver disease carriers. In different Egyptian studies, a HOMA-IR value equal to or greater than 2.0 was used to indicate the presence of insulin resistance **[Ziada *et al.*, 2012].**

Non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome (MetS) are both shown to increase the risk of cardiovascular diseases and type 2diabetes. However, there is a great overlap between these two diseases **[Käräjämäki *et al.,* 2016].** NAFLD is associated with the prevalence of metabolic syndrome, independent of adiposity. **Kim *et al* (2016)** found that in females, NAFLD may be a more important factor than obesity for risk of metabolic syndrome **[Kim *et al.,* 2016].**

The aim of this prospective study is to assess the prevalence of insulin resistance in non-diabetic adult patients with non-alcoholic fatty liver disease and its relation with metabolic syndrome.

SUBJECTS & METHODS

This cross-sectional study was approved by the local ethical committee of the General Organization for Teaching Hospitals and Institutes (GOTHI). Informed consent was obtained from all subjects before the beginning of the study.

Forty (40) patients with NAFLD were selected from patients attending the outpatient clinics of National Nutrition Institute (NNI) from August 2011 to August 2012 according to inclusion criteria. The patients included in the study were defined by the presence of sonographic criteria of fatty liver in abdominal ultrasound.

Exclusion Criteria

Patients excluded from the study were the following:

- patients with Hepatitis B virus infection
- patients with autoimmune hepatitis
- patients with cholestatic or genetic liver disease
- patients with type 2 diabetes or under anti-diabetic treatment
- patients with fasting blood glucose level ≥ 126 mg/dl (7.0 mmol/l) on more than one occasion
- patients under immunosuppressive regimens or previous antiviral treatment
- patients undergoing dialysis
- patients with history of Schistosomiasis

- patients with recent use of lipid lowering agents
- patients with clinical evidence of hepatic decompensation
- history of alcohol intake
- patients with severe cardiac or renal disease
- history of active intravenous drug abuse
- women with ongoing pregnancy or breast feeding
- history of drug intake known to promote steatosis (e.g. salicylates, non-steroidal anti-inflammatory drugs, amiodarone, corticosteroids)
- patients with history of various surgical procedures that can lead to secondary NAFLD (i.e. jejunoileal bypass, extensive small bowel resection, bilopancreatic diversion)
- Patients with ultrasonographically detected cirrhosis.

***CLINICAL &ANTHROPOMETRIC EVALUATIONS*:**

All studied patients were subjected to full history and clinical examination with stress on features of chronic liver disease and alcohol intake.

Blood pressure measurements were obtained and systemic hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg on at least 2 consecutive measures.

Body height was measured to the nearest 0.1 cm. Body weight was measured with an electronic scale to the nearest 0.1 kg with participants wearing light clothes and barefooted. Waist and hip circumferences were measured according to the method of the World Health Organization (WHO) and the International Diabetes Federation (IDF) to the nearest 0.1 cm. Body mass index ($kg/m^{2)}$, overweight as a BMI range of 25-29.9 kg/m^2 and obesity as a BMI ≥30 kg/m^2. The WHO cut-off points for waist circumference are 94 cm. for males and 80 cm. for females. The cut-off points for waist-hip ratio are 0.9cm. for males and 0.85cm for females **[WHO, 2008].**

Metabolic syndrome (MetS) was diagnosed according to the criteria of **International**

Diabetic Federation (2005) which are the following: the patient should have central obesity (defined as waist circumference ≥94 cm. for men and ≥80 cm. for women) plus any two of the following four factors: systemic arterial blood pressure (BP) ≥130/85 mmHg, HDL cholesterol <40mg/dl in males and <50 mg/dl in females, triglyceride ≥150mg/dl, fasting blood glucose ≥100mg/dl.

LABORATORY INVESTIGATIONS:

After an overnight fast of 12 hours, venous blood sample of 5ml. was collected from selected subjects for determination of different biochemical parameters. Two ml. of the blood sample were collected in EDTA tubes for plasma glucose concentration assay and plasma insulin level determination; 3 ml. were collected in plain tubes for separation of serum. Serum was rapidly separated by centrifugation. Separated serum was stored frozen at - 20°C until analysis.

Serum Total Bilirubin was assayed by colorimetric method with sample blank using diazotized sulfanilic acid manufactured by Biomed Diagnostics with reference range up to 1.2 mg/dl **[Walters & Gerarde, 1970].**

Serum Alkaline Phosphatase activity was measured by a kinetic method using 4-nitrophenyl phosphate as substrate using kits from Stanbio laboratory with normal range (adult) 34-114U/L at 37°C **[Bowers & McComb, 1996].**

Serum Aspartate aminotransferase (AST/GOT) was assessed by kinetic method according to the International Federation of Clinical Chemistry (IFCC) using kits from Spectrum Diagnostics with normal range up to 31 U/L For females and up to 37 U/L for males at 37°C **[Bergmeyer et al., 1986].**

Serum Alanine aminotransferase (ALT/GPT) was assessed by kinetic method according to the International Federation of Clinical

Chemistry (IFCC) using kits from Spectrum Diagnostics with normal range up to 31 U/L For females and up to 37 U/L for males at 37°C **[Bergmeyer et al., 1986].**

Serum Gama glutamyl transferase (γGT) was measured by carboxy substrate kinetic determination using kits from Chronolab AG Switzerland with normal range of 4 – 18 UL in females and 6 – 28 U/Lin males **[Burtis *et al.*, 1999].**

Plasma Glucose level was determined in fasting and postprandial blood samples by GOD-PAP method using kits from Noble Diagnostics Company with normal range 75-115 mg/dl for the fasting sample **[Farrance, 1987].**

Serum Cholesterol was assayed by CHOD-PAP enzymatic colorimetric method using kits from Spectrum Diagnostics with desirable range up to 200 mg/dl **[NCEP, 1988].**

Serum Triglyceride was measured by GPO-PAP enzymatic colorimetric method using kits from Spectrum Diagnostics with normal range 35-135 mg/dl for females and 40-160 mg/dl for males **[MGowan *et al.*, 1983].**

Serum HDL-cholesterol was assayed by precipitation method using kits from Spectrum Diagnostics with normal range 48.6-75 mg/dl for females and 41-58.7 mg/dl for males **[NCEP, 1995].**

***Serum LDL-cholester*ol** was calculated using the following equation according to **The National Cholesterol Education Program, 1995.**

LDL cholesterol = Total Cholesterol – Triglyceride/5 – HDL cholesterol

The desirable level of LDL is up to 150mg/dl

Plasma Insulin Level was determined by ELISA technique using kits from Labor Diagnostics Nord Gmbh & Co.KG with reference range 2-25 µIU/ml **[Frier *et al.*, 1981].**

Insulin Resistance was calculated by using the homeostasis model for the assessment of IR(HOMA-IR) method where the Standard Formula is

HOMA-IR = fasting insulin (µIU/ml) x fasting glucose (mmol/L) /22.5 [23].

Patients were defined as insulin resistant when HOMA-IR values were ≥ 2 **[Wasfy *et al.*, 2010].**

Statistical Methods:

Data were analyzed using SPSS win statistical package version 18 (SPSS Inc., Chicago, IL). Numerical data were expressed as mean and standard deviation. Qualitative data were expressed as frequency (number) and percentage. Chi-square test (Fisher's exact test) was used to examine the relation between qualitative variables. For quantitative data comparison between two groups was done using independent samples t-test and Mann-Whitney test). Spearman-rho method was used to test correlation between numerical and different scoring variables. A p-value <0.05 was considered significant.

RESULTS

Demographic, metabolic and biochemical findings of the study population

The demographic, metabolic and biochemical findings of the study population are presented in (Table 1). Females constituted 57.5% of the study population versus males who were 42.5% of the NAFLD patients. Hypertension was seen in 55.5% of the subjects, while MetSe was diagnosed in 50% of the study population. Insulin resistance was recorded in 62.5% of the NAFLD patients.

We compared the demographic, metabolic and biochemical findings of the study population in both females and males (Table 2). We found that prevalence of low HDL-cholesterol (82.6% vs 52.9%, respectively; p=0.043) was significantly higher in females compared to males. BMI was higher in females than in males but this increase was not statistically significant. On the other hand, TC and TG were higher among male subjects but this increase was not statistically significant, probably due to the small sample size.

Subjects with NAFLD were divided into two subgroups: subjects with normal ALT levels (n=32) and subjects with elevated ALT levels (n=8) (ALT >31 U/L in females and ALT >37 U/L in males). (Table3). Female sex was predominant in the high ALT subgroup when compared to the normal ALT subgroup (62.5%vs.56.3% respectively).The prevalence of hypertension (62.5% vs.53.1%, respectively; p=0.634), metabolic syndrome (75% vs. 43.8% respectively; p=0.114), hypertriglyceridemia (25% vs.9.4%; respectively; p=0.232) and insulin resistance (75% vs. 59.4%, respectively; p=0.414) were not significantly different between the high ALT and the normal ALT subgroups. The prevalence of elevated FBG (62.5%vs.9.4%, respectively; p=0.001) and low HDL (100%vs.62.5%, respectively; p=0.038) was significantly higher in the high ALT subgroup (Table 3).

The patients were also divided into two subgroups according to the level of AST into patients with normal AST levels (n=35) and patients with high AST levels (n=5) (AST >31 U/L in females and AST >37 U/L in males). The prevalence of elevated FBG (60% vs.14.3%, respectively; p=0.017) was significantly higher in the high AST subgroup. Serum HDL cholesterol (32.4mg/dl vs.40.8 mg/dl respectively; p=0.021) was significantly lower in the high AST subgroup when compared to the normal AST subgroup (Table 4).

The patients were also classified as insulin-resistant (n=25) and insulin-sensitive (n=15) according to the HOMA-IR value. Statistically significant differences were found between the insulin-resistant and insulin-sensitive groups with regard to age (42.6 years vs.37.3 years, respectively; p=0.038), PPBG (111.1 mg/dl vs. 102.7 mg/dl, respectively; p=0.013), fasting insulin (15.9 µU/ml vs. 7.82 µU/ml, respectively; p=0.000) and HOMA-IR (3.45 vs. 1.6, respectively; p=0.000) (Table 5). Waist circumference, BMI and TG showed positive correlation with HOMA-IR while HDL showed negative correlation as shown in Figures 1, 2, 3 and 4 respectively.

DISCUSSION

Results of this study revealed that insulin resistance was present in 62.5% of NAFLD patients with higher prevalence of MetS in patients with than without insulin resistance. Insulin resistance was positively correlated with waist circumference and BMI (Figure 1,2) These findings are in agreement with data from a prior study conducted by **Sagun *et al.*, 2015.** Although the increase in waist circumference and BMI reported in NAFLD patients with insulin resistance was not statistically significant, yet these results agree with **Marchesini *et al.*, 2001** who stated that insulin resistance was associated with NAFLD, independent of BMI or glucose tolerance.

NAFLD patients with insulin resistance had older mean age compared with NAFLD patients who were insulin sensitive. These findings are similar to the results obtained by **Musso *et al.*, (2008)** which indicated that HOMA-IR was correlated with age in NAFLD patients. This finding could be due to multiple factors including a decrease in insulin mediated glucose uptake by peripheral tissues and a delay in insulin induced suppression of hepatic glucose output **[Couet *et al.*, 1992].**

In our study, NAFLD patients with insulin resistance had significantly higher triglyceride levels compared with those without insulin resistance. This finding is consistent with **Choi & Ginsberg, (2011)** who suggested that IR is associated with increased hepatic assembly and secretion of VLDL and increased plasma TG as well as hepatic steatosis. This result agrees with the multiple logistic regression analysis done by **Erkan *et al.*, 2014** which demonstrated that sex, waist circumference, IR, and triglyceride levels were independently related to NAFLD in non-obese subjects.

In our study NAFLD patients were divided into two subgroups: subjects with normal ALT levels and subjects with elevated ALT levels (ALT >31 U/L in females and ALT >37 U/L in males). (Table2). Our results were in line with the findings reported by **Erkan *et al.*, 2014** as regards the

prevalence of hypertension, metabolic syndrome and hypertriglyceridemia which were not significantly different between the high ALT and the normal ALT subgroups. On the other hand we reported significantly higher levels of blood glucose in the high ALT subgroup compared to the normal ALT subgroup and this finding was in line with the results reported by **Erkan *et al.*, 2014.** We reported in our study that 75% of the NAFLD patients having elevated levels of ALT were insulin resistant. This agrees with the study conducted by **Gómez-Sámano *et al.*, 2012** who observed that in subjects with impaired glucose metabolism, or insulin resistance, ALT levels were an independent marker of hepatic insulin resistance. They focused on ALT because this liver enzyme is more elevated in nonalcoholic steatohepatitis (NASH) than AST. They suggested in their study that hepatic lipotoxicity caused by an oversupply of free fatty acids to the liver results in excess hepatic triglyceride synthesis and an intracellular accumulation of toxic lipid products that impair insulin signaling and activate inflammatory pathways. The adaptation to this metabolic stress involves hepatic IR, dyslipidemia, steatohepatitis with mitochondrial dysfunction, endoplasmic reticulum stress, release of reactive oxygen species, and ultimately, hepatocellular damage [**Gómez-Sámano *et al.*, 2012**].

As regards MetS, it represents constellation of metabolic and cardiovascular risk factors including abdominal obesity, insulin resistance, dyslipidemia, hypertension, and glucose intolerance. It has been generally agreed upon that NAFLD is the hepatic component of Mets, and IR is considered to be the common pathophysiological mechanism [**Erkan *et al.*, 2014**]. Many cross-sectional studies have demonstrated that NAFLD is strongly associated with MetS **[Fung *et al.*, 2014]; [Koehler *et al.*, 2012].** Few prospective studies have indicated that NAFLD can predict a higher incidence of MetS **[Zhang *et al.*, 2014].** These studies are in line with our results which revealed that MetS was found in 50% of the NAFLD patients.

NAFLD is not a currently recognized component of MetS; however, NAFLD has been recommended as an additional criterion. It is generally accepted that insulin resistance is the mechanism underlying MetS. One study with non-obese and non-diabetic Korean middle-aged adults demonstrated that individuals with NAFLD exhibited significantly higher insulin resistance than those without NAFLD, regardless of the number of abnormal metabolic factors **[Sinn *et al.*, 2012].**This finding is in line with our study which showed that 70% of the NAFLD patients with MetS are insulin resistant. This also agrees with **Kanwar *et al.*, (2016)** who declared that the patients, with NAFLD and MetS, enrolled in their study had significantly greater IR. They observed also that, approximately, 80% of their patients with NAFLD and MetS were obese compared with only 50% with NAFLD participants without MetS. This finding is in line with ours as we reported, in our study, that WC and BMI were significantly higher in NAFLD patients with MetS compared with those with no MetS.

There were some limitations to our study. Ultrasonography was utilized to detect fatty liver disease rather than a liver biopsy. Ultrasonography is currently the most widely utilized method for screening asymptomatic patients with elevated liver enzymes and suspected NAFLD. Nevertheless, ultrasonography cannot provide precise quantitative information about the degree of fat accumulation, or detect inflammation and fibrosis, and thus it cannot be utilized to diagnose NASH and hepatic fibrosis. However, we consider it unethical to perform liver biopsy for obese or overweight patients with evident fatty liver in ultrasound. In the future studies a precise and non-invasive method to detect the presence of NAFLD could replace or augment abdominal ultrasound like MRI.

Another limitation of our study was the relatively small sample size, however in this small number; IR was detected in most of the studied patients. Regarding NAFLD, being a corner disease, the

small number examined cannot represent the general population and a greater sample size is recommended to be included in future studies.

CONCLUSION

In conclusion, this study found that in a non-diabetic cohort, NAFLD is associated with a high prevalence of obesity and MetS. We concluded that patients with NAFLD and MetS are more insulin resistant even in the absence of diabetes and a recommendation of a liver biopsy to evaluate for NASH may be reasonable in these patients. This knowledge may lead to more aggressive management of the MetS risk factors and may lead to improvement in patient's liver disease. Treatment may include weight loss through diet and exercise, which could improve several components of the MetS.

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Table 1: Demographic, metabolic and biochemical findings of the study group

Variables	NAFLD Patients (n=40)
	N (%)
Females	23 (57.5)
Males	17 (42.5)
Hypertension	22 (55.5)
MetS	20 (50)
Elevated FBG	8 (20)
Low HDL	28 (70)
Elevated TG	5 (12.5)
IR presence	25 (62.5)
	Mean ±SD
Age (years)	40.7 ± 8.3
WC (cm)	108 ± 10.7
BMI (kg/m^2)	34.3 ± 5.5
FBG (mg/dl)	88.3 ± 13.9
PPBG (mg/dl)	107.9 ± 12.1
TC (mg/dl)	178.8 ± 48.3
LDL(mg/dl)	120.9 ± 42.3
HDL (mg/dl)	39.7 ± 8.6
TG (mg/dl)	104.7 ± 67.3
AST (IU/ml)	21.1 ± 12.2
ALT (IU/ml)	22.6 ± 14.7
GGT (IU/ml)	14.4 ± 5.9
ALP (IU/ml)	30.5 ± 16.4
T.Bilirubin (mg/dl)	0.69 ± 0.13
Fasting Insulin (µU/ml)	12.9 ± 6.1
HOMA-IR	2.8 ± 1.2

***Met S**:metabolic syndrome, **FBG**:fasting blood glucose, **HDL**:high density lipoprotein **TG**:triglyceride, **IR**: insulin resistence, **WC**:waist circumference, **BMI**:body mass index, **PPBG**:postprandial blood glucose, **TC**:total cholesterol, **LDL**:low density lipoprotein, **AST**:aspartate aminotransferase, **ALT**:alanine aminotransferase, **GGT**:gama glutamyl transpeptidase,**ALP**:alkaline phosphatase*

Table 2: Demographic, metabolic and biochemical findings of the study group according to Gender

Variables	Female patients (n=23)	Male Patients (n=17)	P value
	N (%)	N (%)	
Hypertension	11(47.8%)	11(64.7%)	0.289
MetS	11(47.8%)	9(52.9%)	0.749
Elevated FBG	3(13.0%)	5(29.4%)	0.201
Low HDL	19(82.6%)	9(52.9%)	0.043
Elevated TG	2(8.7%)	3(17.6%)	0.397
IR presence	14(60.9%)	11(64.6%)	0.804
	Mean ±SD	Mean ±SD	P value
Age (years)	41(±9.1)	40.2(±7.4)	0.779
WC (cm)	110.5(±11.4)	106.2(±9.9)	0.206
BMI (kg/m2)	35.7(±5.8)	32.4(±4.6)	0.062
FBG (mg/dl)	88.9(±14.3)	87.5(±13.9)	0.768
PPBG(mg/dl)	108.3(±12.5)	107.4(±11.9)	0.814
TC (mg/dl)	166.3(±41.4)	195.6(±52.9)	0.057
LDL(mg/dl)	112.7(±37.1)	132.1(±47.3)	0.154
HDL (mg/dl)	39.5(±8.4)	40.1(±9.2)	0.836
TG (mg/dl)	88.3(±52.4)	127(±79.6)	0.071
Fasting Insulin (µU/ml)	12.6(±5.9)	13.3(±6.4)	0.696
HOMA-IR	2.7(±1.2)	2.8(±1.3)	0.709

***Met S**: metabolic syndrome, **FBG**:fasting blood glucose, **HDL**:high density lipoprotein **TG**:triglyceride, **IR**: insulin resistence, **WC**:waist circumference, **BMI**:body mass index, **PPBG**:postprandial blood glucose, **TC**:total cholesterol, **LDL**:low density lipoprotein,*

Table 3: Demographic, metabolic and biochemical findings of the study group according to ALT

Variables	NAFLD patient with Normal ALT (n=32)	NAFLD patients with Elevated ALT (n=8)	P value
	N (%)	N (%)	
Females	18 (56.3%)	5 (62.5%)	0.749
Males	14 (43.8%)	3 (37.5%)	
Hypertension	17 (53.1%)	5 (62.5%)	0.634
MetS	14 (43.8%)	6 (75.0%)	0.114
Elevated FBG	3 (9.4%)	5 (62.5%)	0.001
Low HDL	20 (62.5%)	8 (100%)	0.038
Elevated TG	3 (9.4%)	2 (25%)	0.232
IR presence	19 (59.4%)	6 (75%)	0.414
	Mean ±SD	Mean ±SD	P value
Age (years)	40.2 (±8.4)	42.8 (8.4)	0.388
WC (cm)	107.4(±10.6)	110.4(±11.4)	0.516
BMI (kg/m2)	34.1 (±5.8)	35.4 (±4.7)	0.510
FBG (mg/dl)	85.8 (±12.4)	98.4 (±16.1)	0.037
PPBG(mg/dl)	105.9(±11.9)	116.3(±10.2)	0.019
TC (mg/dl)	175.1 (±40.9)	193.5 (±72.7)	0.735
LDL(mg/dl)	118.2 (±39.7)	131.9 (±53.1)	0.521
HDL (mg/dl)	40.9 (±8.9)	35.0 (±5.3)	0.072
TG (mg/dl)	98.9 (±48.2)	128.1 (±119)	0.866
Fasting Insulin (µU/ml)	12.7 (±5.8)	13.5 (±7.5)	0.879
HOMA-IR	2.7 (±1.2)	3.1 (±1.3)	0.318

***Met S**:metabolic syndrome, **FBG**:fasting blood glucose, **HDL**:high density lipoprotein **TG**:triglyceride, **IR**: insulin resistence, **WC**:waist circumference, **BMI**:body mass index, **PPBG**:postprandial blood glucose, **TC**:total cholesterol, **LDL**:low density lipoprotein, **ALT**:alanine aminotransferase*

Table 4: Demographic, metabolic and biochemical findings of the study group according to AST

Variables	NAFLD patients with Normal AST (n=35)	NAFLD patient with Elevated AST (n=5)	P value
	N (%)	N (%)	
Females	20(57.1%)	3(60%)	0.904
Males	15(42.9%)	2(40%)	
Hypertension	20(57.1%)	2(40%)	0.471
MetS	17(48.6%)	3(60.0%)	0.633
Elevated FBG	5(14.3%)	3(60.0%)	0.017
Low HDL	23(65.7%)	5(100%)	0.118
Elevated TG	4(11.4%)	1(20%)	0.588
IR presence	21(60.0%)	4(80.0%)	0.388
	Mean ±SI	Mean ±SD	P value
Age (years)	41.2(±7.9)	36.8(±10.7)	0.316
WC (cm)	108.1(±10.8)	107.6(±10.2)	0.923
BMI (kg/m2)	33.9(±5.2)	36.7(±7.5)	0.540
FBG (mg/dl)	87.2(±13.1)	95.8(±18.9)	0.306
PPBG(mg/dl)	106.5(±11.4)	118.4(±13.9)	0.047
TC (mg/dl)	176.2(±45.9)	196.8(±66.1)	0.437
LDL(mg/dl)	119.04(±42.8)	134.2(±41.03)	0.449
HDL (mg/dl)	40.8(±8.5)	32.4(±5.2)	0.021
TG (mg/dl)	98.1(±48.9)	151.2(±143.7)	0.638
Fasting Insulin (µU/ml)	12.9(±6.4)	13.04(±3.7)	0.540
HOMA-IR	2.7(±1.2)	3.03(±0.86)	0.336

***Met S**:metabolic syndrome, **FBG**:fasting blood glucose, **HDL**:high density lipoprotein **TG**:triglyceride, **IR**: insulin resistence, **WC**:waist circumference, **BMI**:body mass index, **PPBG**:postprandial blood glucose, **TC**:total cholesterol, **LDL**:low density lipoprotein, **AST**:aspartate aminotransferase*

Table 5: Demographic, metabolic and biochemical findings of the study group according to HOMA-IR index

Variables	Insulin Sensitive (HOMA-IR < 2) (n=15)	Insulin Resistar (HOMA-IR ≥ 2 (n=25)	P value
	N (%)	N (%)	
Females	9 (60.0%)	14 (56.0%)	0.804
Males	6(40.0%)	11(44.0%)	
Hypertension	6(40.0%)	16(64.0%)	0.140
MetS	6(40.0%)	14(56.0%)	0.327
Elevated FBG	2(13.3%)	6(24.0%)	0.414
Low HDL	11(73.3%)	17(68.0%)	0.722
Elevated TG	0(0%)	5(25%)	0.064
	Mean ±SI	Mean ±S	P value
Age (years)	37.3(±6.89)	42.6(±8.61)	0.038
BMI (kg/m2)	32.4(±4.89)	35.4(±5.67)	0.102
FBG (mg/dl)	84.9(±11.6))	90.3(±15)	0.342
PPBG(mg/dl)	102.7(±9.9)	111.1(±12.4)	0.013
TC (mg/dl)	172.6(±42.9)	182.5(±51.7)	0.696
LDL(mg/dl)	125(38.5)	118.5(±45.1)	0.567
HDL (mg/dl)	39.47(±9.93)	39.9(±7.9)	0.654
TG (mg/dl)	77.4(±23.5)	121.1(±79.3)	0.049
Fasting Insulin (µU/ml)	7.82(±1.50)	15.9(±5.72)	0.000
HOMA-IR	1.61(±0.220)	3.45(±1.03)	0.000

***Met S**:metabolic syndrome, **FBG**:fasting blood glucose, **HDL**:high density lipoprotein **TG**:triglyceride, **IR**: insulin resistence, **WC**:waist circumference, **BMI**:body mass index, **PPBG**:postprandial blood glucose, **TC**:total cholesterol, **LDL**:low density lipoprotein, **AST**:aspartate aminotransferase*

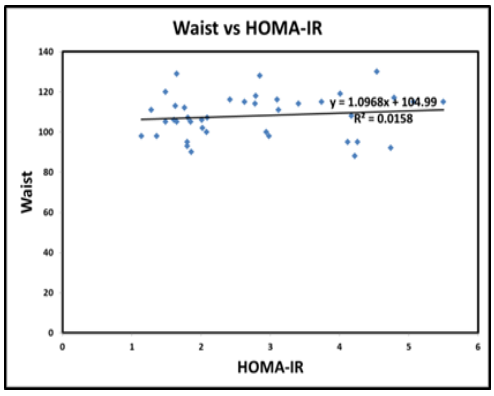

Figure 1: Correlation between WC & HOMA-IR

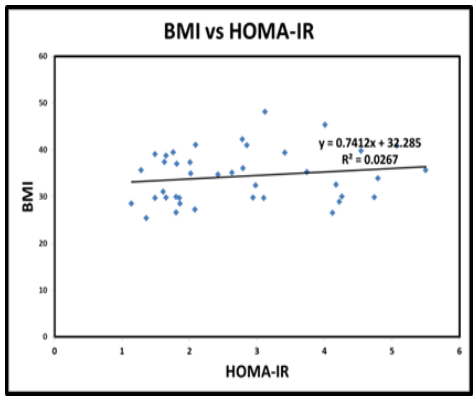

Figure 2: Correlation between BMI & HOMA-IR

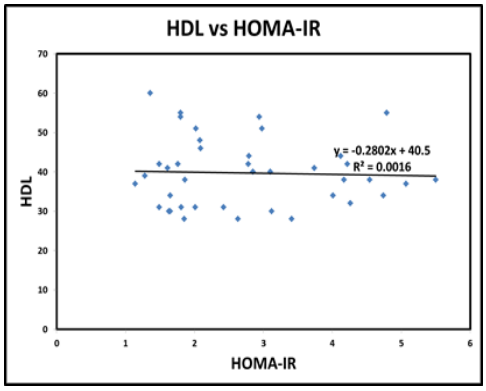

Figure 3: Correlation between HDL & HOMA-IR

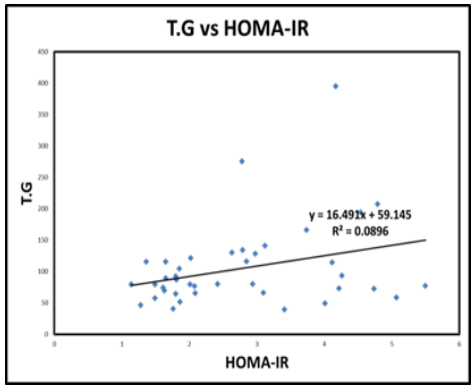

Figure 4: Correlation between TG & HOMA-IR

دراسة مقاومة الأنسولين و متلازمة الأيض في مرض التدهن الكبدي اللاكحولي

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الملخص العربي

التدهن الكبدي اللاكحولي مرتبط إرتباطا وثيقا بالسمنة و مقاومة الإنسولين، ومن المتفق عليه أيضا أن التدهن الكبدي اللاكحولي يعتبر العرض الكبدي في متلازمة الأيض ، هذا المرض الذي يعتبر مرض مقاومة الأنسولين و يضم الأعراض الآتية: خلل في مستوي سكر الدم، و مقاومة الأنسولين، و السمنة المركزية، و خلل في دهون الدم، مع ارتفاع ضغط الدم و جميع هذه الأعراض هي عوامل خطورة لأمراض القلب و الدورة الدموية. تهدف الدراسة إلى تقييم مدى انتشار مقاومة الأنسولين في المرضى البالغين غير المصابين بمرض السكري و يعانون من مرض التدهن الكبدي اللاكحولي إلى جانب دراسة علاقة مقاومة الأنسولين مع متلازمة الأيض. شملت هذه الدراسة ٤٠ مريضا من البالغين غير مصابين بمرض السكري و يعانون من مرض التدهن الكبدي اللاكحولي و اشتملت طرق البحث على الآتي: التاريخ الطبي و الفحص الإكلينيكي و تسجيل القياسات الجسمية و فحص عام لاستبعاد وجود أمراض بالقلب و الرئة و الكلى أو أمراض أخرى بالكبد. و تم عمل فحص الكبد و الطحال و استبعاد وجود استقساء بالبطن. الفحوص المعملية شملت وظائف الكبد، و دهون الدم، و سكر صائم و بعد ساعتين، و قياس مستوى الأنسولين بالبلازما بواسطة اختبار اليزا و حساب معامل مقاومة الأنسولين عن طريق (معادلة هوما) و جرى تقييم متلازمة الايض باستخدام معايير الاتحاد الدولي للسكر. تم إجراء الموجات فوق الصوتية في البطن لتشخيص مرض التدهن الكبدي و استبعاد تشمع الكبد. كشفت الدراسة أن نسبة مقاومة الأنسولين في مرضى التدهن الكبدي هي (62.5%) وأظهر البحث زيادة معنوية في مستوى الدهون الثلاثية بالدم و مستوى السكر بعد الأكل في المرضى الذين يعانون من مقاومة الأنسولين مقارنة مع تلك المجموعة التي لا تعاني من مقاومة الأنسولين. كشفت الدراسة وجود زيادة معنوية في متوسط العمر في مجموعة مرضى التدهن الكبدي اللاكحولي التي تعاني من مقاومة الأنسولين مقارنة مع تلك المجموعة التي لا تعاني من مقاومة الأنسولين. لوحظ أن ٥٠% من المرضى لديهم أعراض متلازمة الأيض. ثبت من الدراسة وجود زيادة معنوية في السمنة و مستوى سكر الدم بعد الأكل في مجموعة المرضى المصابين بمتلازمة الأيض مقارنة بالمجموعة التي لا تعاني من متلازمة الأيض كما وجد انخفاض معنوي في مستوى الدهون عالية الكثافة في مجموعة المرضى بمتلازمة الأيض. نستخلص من هذه الدراسة ارتفاع معدل انتشار السمنة و متلازمة الأيض في مرضى التدهن الكبدي اللاكحولي كما ظهر أن مرضى التدهن الكبدي اللاكحولي و متلازمة الأيض يعانون من مقاومة الأنسولين بالرغم من عدم وجود مرض السكري . هذه المعلومات قد تؤدي إلى معالجة قوية لعوامل خطورة متلازمة الأيض مما يؤدي إلى تحسن حالة مرض الكبد.

الكلمات المفتاحية: *مرض التدهن الكبدي اللاكحولي، مقاومة الأنسولين ، متلازمة الأيض ، معادلة هوم*