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Insulin Growth Factor-1 and Insulin Level in Obese Simple Steatosis and MASH Patients

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Abstract

Background: Obesity is a worldwide epidemic health issue that has increased in recent years. MASLD is considered the hepatic manifestation of metabolic syndrome. The prevalence and severity of MASLD are increasing in parallel with the increasing prevalence of obesity.

Aim of Study: Study the role of IGF-1 and insulin level in patients with MASH and patients with simple steatosis.

Patients and Methods: IGF-1 and insulin levels were measured by ELISA in sixty obese patients thirty patients with MASH compared to thirty patients with simple steatosis as a control group.

Results: The serum levels of insulin and HOMA-IR were significantly increased in the MASH patients as compared to the simple steatosis patients. The serum level of IGF-1 was significantly lower in the MASH patients: As compared to the simple steatosis patients. Serum IGF-1 at a cutoff value of 75µg/mL predicted obese MASH patients with a sensitivity of 73.33% and a specificity of 56.67%, while the best cutoff value for insulin was 3.8µg/mL with a sensitivity of 70% and a specificity of 90%.

Conclusions: IGF-1 and insulin are promising and cost-efficient biomarkers for discriminating MASH patients from simple steatosis patients and differentiating the stage of fibrosis in obese patients with MASH.

Key Words: *Insulin growth factor 1 – Insulin resistance – MASH – Obesity – Simple steatosis.*

Introduction

METABOLIC dysfunction-associated steatotic liver disease (MASLD) is the recent term for steatotic liver disease associated with metabolic syndrome. MASLD is considered now the most common cause of chronic liver disease and is the leading cause of liver-related morbidity and mortality **[1].** MASLD has been estimated to affect about 30% of the adult population worldwide, with increasing prevalence from 22% to 37% from 1991 to 2019 **[2,3]**. The increasing prevalence of MASLD parallels the increasing prevalence of obesity and obesity-related disorders.

The modification of "NAFLD" to "MASLD" is expected to highlight the role of metabolic factors in the disease aetiology, which will improve patient understanding of the disease and highlight the significant role of public health interventions in prevention and management **[4]**. MASLD includes a wide range of pathology ranging from accumulation of fat only (isolated steatosis), to accumulation of fat with associated inflammation and liver cell damage (hepatocyte ballooning), collectively termed as metabolic dysfunction associated steatohepatitis (MASH); previously known as non-alcoholic steatohepatitis (NASH), and increasing degrees of fibrosis up to cirrhosis (F0-4) **[5,6].**

Pathogenesis of MASH is poorly understood but seems to be linked to insulin resistance such as in obesity or metabolic syndrome. Most patients are asymptomatic. Non-invasive diagnostic tests are usually sufficient for diagnosis of MASH **[7].**

Although liver biopsy is considered the gold standard for assessing disease activity and severity in MASLD, its invasiveness, expense, unpredictability in sampling and interpretation, and all of these drawbacks mostly interfere with widespread use in clinical practice in screening of advanced fibrosis, track the course of the illness, and assessment of therapeutic response in patients with MASLD **[8].** The diagnosis of MASLD is made by the presence of hepatic steatosis (detected by serum biomarker

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scores, imaging techniques or histology) and at least one of the following; overweight/obesity; T2DM; or metabolic dysregulation [8].

Moreover, biomarker scoring systems (such as the ELF test, NFS and FIB-4 test) and different imaging techniques (such as transient elastography [TE] and magnetic resonance imaging techniques) are proven to be reasonably accurate, and comparable with histology, in the diagnosis of MASLD and evaluation of disease severity and [4].

There are many established scoring systems for the assessment of fibrosis such as FIB-4, NFS score (NAFLD fibrosis score), BARD score, enhanced liver fibrosis score, and European liver fibrosis to predict the advanced fibrosis [9]. NFS score was constructed from the routine clinical and laboratory variables which accurately predict the presence or absence of advanced fibrosis in MASLD, rendering liver biopsy unnecessary in the vast majority of patients [10].

Generally in obesity, the insulin-like growth factor1 (IGF-1) is present in lower levels than normal which may affect insulin resistance significantly [11]. Moreover, Cristin et al., assumed that insulin-like growth factor1 (IGF-1) may have an important role in the regulation of immune and metabolic functions. Yet the association between the changes in the levels of IGF-1 and MASH or MASLD is still not established [12].

Simple steatosis is a benign condition, while MASH could deteriorate to cirrhosis. Therefore, it's crucial to differentiate MASH from simple steatosis [13]. The aim of this study is to investigate the clinical utility of serum insulin growth factor-1 (IGF-1), insulin, and homeostatic model assessment for insulin resistance (HOMA-IR) among obese MASH patients in comparison to obese simple steatosis patients.

Patients and Methods

This study was conducted on thirty obese patients with simple steatosis and thirty obese MASH patients who were attending the outpatient clinic of Ain Shams University Hospitals (period from 6-2023 till 12-2023). Their median ages were 40 and 38.5 years, respectively. All recruited patients were obese with a BMI ≥30 kg/m^2. The exclusion criteria were any patient with a history of alcohol consumption of more than 20g per day for women or more than 30g per day for men, or using medications known to precipitate steatohepatitis, including valproate, amiodarone, or prednisone. Any patient with viral hepatitis B, viral hepatitis C, hemochromatosis, Wilson disease, or any autoimmune liver disease.

MASH was diagnosed by abdominal ultrasonography and elevated liver enzymes, with the exclusion of other causes of elevated liver enzymes. Patients with simple steatosis were diagnosed by abdominal ultrasonography. The NFS (NAFLD fibrosis score) was calculated for all patients with MASH. Patients were classified as having low fibrosis or intermediate/high fibrosis according to the NFS score. The probability of fibrosis was classified using the NFS score as follows: >–1.455 to <0.676 for intermediate probability, <–1.455 for low probability, and >0.676 for high probability [14,15].

All patients were subjected to full medical history, thorough clinical examination, and laboratory investigations, including a complete blood count (CBC), serum total cholesterol, triglycerides, fasting blood sugar, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, direct bilirubin, alkaline phosphatase, albumin, and ferritin, prothrombin time (PT), INR, serum IGF-1, and insulin level.

Sample collection was performed after receipt of the patient's informed consent and the Institutional Review Board's approval, in accordance with the Declaration of Helsinki. Six milliliters (6mL) of venous blood were withdrawn from all subjects under complete aseptic conditions after 10–12 hours fasting. They were divided into three vacationers:

- Two milliliters (2mL) of blood were collected in a plain sterile vacutainer and left to clot for thirty minutes. Centrifugation was used to separate the serum for ten minutes at 4000. Separated serum was divided into two aliquots. The first aliquot was used for the immediate assay of total cholesterol, triglycerides, fasting blood sugar, creatinine, AST, ALT, albumin, total bilirubin, direct bilirubin, alkaline phosphatase, albumin, and ferritin. Hemolysed samples were discarded. The second aliquot was stored at –20°C for measurement of IGF-1 and insulin. Repeated freezing and thawing were avoided.
- Two milliliters (2mL) of blood were collected in a sterile citrated vacutainer for the assay of PT and INR.
- Two milliliters (2mL) of blood were collected in sterile K3 EDTA vacutainers for the CBC assay.

HOMA-IR is a method for assessing beta-cell function and insulin sensitivity through a computer model: [Fasting insulin (mIU/L) × FPG (mg/dL)]/405 [16]. The serum levels of IGF-1 and insulin were analyzed by enzyme-linked immunosorbant assay using the Sandwich ELISA technique (Bioassay Technology Laboratory, USA).

Statistical analysis:

MedCalc version 20 (MedCalc, Ostend, Belgium) was used to analyze the data. Median and interquartile range (IQR) were used to depict

the non-parametric data. To compare qualitative data across groups, a chi-square test was used. Mann-Whitney U test was used to compare the median of two groups.

Multiple, logistic regression analysis was performed to study the outcomes of MASH; and its relative independent predictors. The list of predictor variables included the following; age, sex, basic clinical data, radiological data, and laboratory investigations.

The best cutoff point was identified by determining the sensitivity, specificity, and area under a receiver operating characteristic (ROC) curve (AUC). Results are considered significant when the *p* is less than 0.05.

Results

The study was conducted on thirty simple steatosis obese patients and thirty obese MASH patients. Comparative statistics between the two studied groups are shown in Table (1).

Table (1): Descriptive and comparative statistics between the two studied groups as regards the various studied parameters.

Variable	Simple steatosis group (n=30)	MASH group (n=30)	*p*-value
Clinical data:			
Age (years)	40 (34 – 48)	38.5 (34 – 45)	= 0.8357
Sex:			
Female	13 (43.3%)	9 (30%)	= 0.2879
Male	17 (56.7%)	21 (70%)	
BMI	31.7 (30.5 – 33.7)	32.9 (31.6 – 34)	= 0.0720
Lab investigations:			
Hemoglobin (g/dL)	14 (12 – 14.5)	14.3 (13 – 15)	= 0.1129
PLT ($10^3/_{\mu}L$)	215 (199 – 281)	243 (217 – 277)	= 0.5200
TLC ($10^3/_{\mu}L$)	7.4 (6.5 – 9.5)	7.5 (5.7 – 9)	= 0.3178
Total Cholesterol (mg/dL)	170 (162 – 239)	211 (188 – 230)	= 0.2309
Triglycerides (mg/dL)	156 (92 – 200)	165 (142 – 182)	= 0.5152
Fasting blood sugar (mg/dL)	126 (100 – 150)	116 (101 – 120)	= 0.055
HbA1c	7 (6.4-8.1)	6.4 (6.3-6.7)	0.0630
Serum creatinine (mg/dL)	0.8 (0.8 – 1)	0.9 (0.8 – 0.9)	= 0.3071
AST (U/L)	19.5 (17 – 22)	46.5 (40 – 58)	< 0.001
ALT (U/L)	24 (19 – 30)	81.5 (66 – 95)	< 0.001
Total bilirubin (mg/dL)	1 (0.8 – 1)	1.1 (1 – 1.1)	< 0.001
Direct bilirubin (mg/dL)	0.3 (0.3 – 0.4)	0.4 (0.4 – 0.5)	< 0.001
Alkaline phosphatase (mg/dL)	78 (65 – 90)	79.5 (70 – 97)	= 0.1927
Albumin (g/dL)	4.2 (4 – 4.3)	4.2 (4 – 4.3)	= 0.3724
INR	1 (0.9 – 1)	1 (1 – 1)	= 0.0513
PT (sec)	12.4 (12 – 13)	12.6 (12 – 13)	= 0.1176
Ferritin (ng/dL)	50.5 (30 – 95)	101.5 (92 – 115)	= 0.0064
IGF-1 (ng/mL)	135 (55 – 325)	70 (50 – 193)	= 0.048
Insulin level (mIU/L)	2.2 (1 – 3.2)	4.7 (3 – 7.5)	< 0.001
HOMA-IR	0.6 (0.3 – 1)	1.5 (1 – 3)	< 0.001
Interpretation:			
Normal	8 (26.7%)	11 (36.7%)	< 0.001
Insulin sensitive	22 (73.3%)	6 (20%)	
Insulin resistance	0 (0%)	13 (43.3%)	
Fibrosis:			
Fibrosis score	-0.97 (-2 – -0.54)	–	–
Fibrosis score interpretation:			
High fibrosis	–	2 (6.7%)	–
Intermediate score	–	15 (50%)	
Low fibrosis	–	13 (43.3%)	

The serum levels of AST, ALT, total bilirubin, direct bilirubin, ferritin, insulin, and HOMA-IR were highly significantly increased in the MASH patients ascompared to the simple steatosis control group (p<0.001, respectively). While the serum level of IGF-1 was significantly lower in the MASH patients as compared to the simple steatosis control group (p<0.05).

The platelets andthe serum levels of total bilirubin and IGF-1were significantly increased among the patients with low fibrosis as compared to the patients with intermediate/high fibrosis (p<0.05, respectively). While HOMA-IR was significantly decreased among the patients with low fibrosis as compared to the patients with intermediate/high fibrosis (p<0.05) (Table 2).

The univariate and multivariate logistic regression models for the factors affecting MASHoccurrence are shown in Table (3); the increase in serum levels of direct bilirubin and insulin and the decrease in serum levels of FBS; had an independent effect on increasing the probability of MASH (p<0.05, respectively).

Table (2): Descriptive and comparative statistics between the different studied fibrosis patients among the MASH group as regards the various studied parameters.

Parameter	Intermediate/High fibrosis (n=17)	Low fibrosis (n=13)	*p*-value
Clinical data:			
Age (years)	36 (33.7 – 48.2)	41 (33.7 – 44.2)	= 0.8173
Sex:			
Female	7 (41.2%)	2 (15.4%)	= 0.1331
Male	10 (58.8%)	11 (84.6%)	
BMI	31.7 (30.5 – 33.7)	32.9 (31.6 – 34)	= 0.0720
Lab investigations:			
Hemoglobin (g/dL)	14.7 (12.9 – 15.2)	14.2 (13.2 – 14.9)	= 0.3899
PLT (10^3/µL)	225 (214 – 255)	280 (256 – 284)	= 0.0019
TLC (10^3/µL)	8 (6.3 – 8.9)	7 (5.2 – 9.2)	= 0.3563
Total Cholesterol (mg/dL)	219 (202 – 233)	195 (185 – 214)	= 0.0860
Triglycerides (mg/dL)	162 (134 – 183)	165 (154 – 180)	= 0.9332
Fasting blood sugar (mg/dL)	106 (103 – 117)	104 (93 – 124)	= 0.3789
Serum creatinine (mg/dL)	0.9 (0.8 – 0.9)	0.9 (0.8 – 0.98)	= 0.8968
AST (U/L)	46 (39 – 52)	52 (42 – 58)	= 0.3680
ALT (U/L)	76 (64 – 83)	86 (69 – 113)	= 0.1867
Total bilirubin (mg/dL)	1.1 (1 – 1.1)	1.2 (1 – 1.4)	= 0.047
Direct bilirubin (mg/dL)	0.4 (0.3 – 0.4)	0.5 (0.4 – 0.6)	= 0.0650
Alkaline phosphatase (mg/dL)	75 (69 – 95)	81 (73 – 106)	= 0.4505
Albumin (g/dL)	4.3 (4.1 – 4.4)	4.1 (4 – 4.3)	= 0.0817
INR	1 (1 – 1)	1 (0.9 – 1)	= 0.5057
PT (sec)	12.7 (12.2 – 13)	12.5 (12 – 13)	= 0.9481
Ferritin (ng/dL)	95 (44 – 112)	105 (100 – 117)	= 0.1162
HbA1c	6.3 (6.3-6.7)	6.7(6.3-7.2	=0.1452
IGF-1 (ng/mL)	53 (48 – 126)	88 (54 – 214)	= 0.009
Insulin level (mIU/L)	5.5 (2.5 – 9.1)	3.9 (2.5 – 6.3)	= 0.4251
HOMA-IR	2.8 (0.8 – 4)	1.4 (1 – 2.9)	= 0.012

Table (3): Univariate and multivariate logistic regression model for the factors affecting MASH occurrence.

	Univariate logistic regression			Multivariate logistic regression		
Predictor Factor	Coefficient	OR	*p*-value	Coefficient	OR	*p*-value
Age	0.017973	1.0181	1.0000	–	–	–
BMI	0.11953	1.1270	1.0000	–	–	–
Fasting blood sugar (mg/dL)	–0.040675	0.9601	0.045	-0.040675	0.9601	0.045
Serum creatinine (mg/dL)	44.81596	2.9062	0.9998	–	–	–
AST (U/L)	–0.12082	0.8862	0.9999	–	–	–
ALT (U/L)	1.07504	2.9301	0.9994	–	–	–
Total bilirubin (mg/dL)	–16.03984	0.8293	0.9999	–	–	–
Direct bilirubin (mg/dL)	14.77289	2.6006	0.0083	14.77289	2.6006	0.0083
Ferritin (ng/dL)	0.006957	1.0070	1.0000	–	–	–
IGF-1 (ng/mL)	0.016204	1.0163	0.9999	–	–	–
Insulin level (mIU/L)	0.54272	1.7207	0.013	0.54272	1.7207	0.013
HOMA-IR	–6.28919	0.0019	0.9998	–	–	–

The ROC performance of the various studied serum biomarkers to predict the occurrence of MASH and the poor outcome of the occurrence of fibrosis are illustrated in Tables (4,5) respectively.

Table (4): ROC-performance of the various studied serum biomarkers to predict the occurrence of MASH.

Variable	AUC	SE	Best Cut off point (Criterion)	NPV (%)	PPV (%)	Sensitivity (%)	Specificity (%)	*p*-value
IGF-1(ng/mL)	0.648	0.0722	>75	68	62.9	73.33	56.67	0.039
Insulin level (mIU/L)	0.778	0.0628	>3.8	87.5	75	70	90	<0.001
HOMA-IR	0.818	0.0597	>1.1	95.5	76.3	70	96.6	<0.001

Table (5): ROC performance of various studied biomarkers to predict the occurrence of fibrosis.

Variable	AUC	SE	Best Cut off point	NPV (%)	PPV (%)	Sensitivity (%)	Specificity (%)	*p*-value
IGF-1 (ng/mL)	0.946	0.0550	≤50	100	28.6	100	82	<0.001
Insulin level (mIU/L)	0.580	0.165	>1.1	100	10	100	35.7	0.6261
HOMA-IR	0.554	0.141	>0.4	100	10	100	35.7	0.7041

Discussion

MASH is a multisystem disorder. Whether MASLD and MASH are distinct entities that diverge in the early stages of the disease or if they are a continuum of disease stages and temporal transition, is still up for debate **[17]**. Therefore, the identification of confounding factors is very crucial. IGF-1 might be used as a potential biomarker and therapeutic target for MASH patients.

In this work, we conducted a comparative cross-sectional study on thirtyobese patients with simple steatosis, and thirty patients with MASH, with a special emphasis onassessing the levels of serumIGF-1, insulin, and HOMA-IR and their clinical utility.

Interestingly, our results showed that patients with MASH had lower serum levels of IGF-1 than those with simple steatosis, with a median and IQR of 70ng/mL (50–193) versus 135ng/mL (55–325), respectively. These results were compared to the results of a retrospective study performed by Dichtel et al., **[18]**. Who recruited 141 subjects from Boston, USA and reported that patients with MASH had a

lower mean of serum IGF-1 levels than those without MASH; 109±45 vs. 136±57ng/ml, respectively.

A previous study reported that insulin resistance in adipose tissue results in increased lipolysis with a subsequent increase in circulating free fatty acids, which further exacerbates steatosis and insulin resistance [19]. Our study revealed a highly significant increase in insulin levels and HOMA-IR in MASH patients as compared to simple steatosis patients. Our findings were similar to those of Kim et al., who noted that insulin resistance is mostly present in MASH patients. It is thought to be a major factor in the pathophysiology of MASH, as insulin resistance is both a causative factor and a consequence of MASH [20].

In our work, we noticed that the levels of serum ferritin were significantly higher in MASH patients as compared to simple steatosis patients. These findings were consistent with Barros et al., who suggested that hyperferritinemia in MASH patients was more often related to hepatocellular injury than hemochromatosis [21]. Furthermore, it was reported in several studies that ferritin may be an important independent predictor of inflammation and liver fibrosis. Also, it may be useful in the decision to obtain a biopsy from individuals clinically diagnosed with MASLD [22,23].

Our univariate and multivariate logistic regression models for the factors affecting the occurrence of MASH showed that the increase in serum levels of direct bilirubin and insulin had an independent effect on increasing the probability of MASH. While IGF-1 did not show any significant effect on the probability of MASH. Our findings were compared to the results of Polyzos et al., [24] who performed a binary logistic regression, and they reported that IGF-1 did not remain robustly associated with MASH or liver fibrosis.

Our findings were in disagreement with García-Galiano et al., who enrolled 36 patients with morbid obesity: Thirteen patients with probable MASH, nine patients with MASH, and twelve healthy individuals. A significant correlation was observed between the presence of NAS >4 (MASH) and lower IGF-1 levels in their univariate binary logistic regression. They found that IGF-1 <130ng/mL was an independent predictor of the degree of steatosis (OR = 0.015, $p \leq 0.01$) and IGF-1 <110ng/mL was an independent predictor of MASH (OR = 0.096, $p \leq 0.02$) in their multivariate logistic regression analysis. They further suggested IGF-1 as a non-invasive diagnostic tool [25].

In this study, we found that IGF-1 at a cutoff value of 75ng/mL predicted the MASH, with sensitivity of 73.33%, specificity of 56.67%, and an AUC of 0.648. Regarding the serum insulin level, at a cutoff value of 3.8mIU/L, showed a sensitivity of 70%, a specificity of 90%, and an AUC of 0.778. While the HOMA-IR at a cutoff 1.1 showed a sensitivity of 70%, a specificity of 96.6%, and an AUC of 0.818. García-Galiano et al., suggested the cutoff 110 ng/mL for IGF-1 with an 81% sensitivity, 67% specificity, and an AUC of 0.80 for predicting the occurrence of MASH. According to these data, IGF-1 may be used as a non-invasive biomarker for MASH [25].

The relationship between elevated severity of fibrosis and decreased serum IGF-1 levels has been the subject of a few clinical studies [25,26]. Clinical studies are consensual when reporting the association of the low serum IGF-1 with the severity of fibrosis [18,26,27].

Notably, our study is considered the first to be performed among Egyptian MASH/simple steatosis patients, evaluating the role of serum IGF-1, insulin, and insulin resistance. Our study showed that the serum levels of IGF-1 were significantly higher among patients with low fibrosis as compared to patients with intermediate/high fibrosis, with a median and IQR of 88 ng/mL (54–214) versus 53ng/mL (48–126), respectively. These results are consistent with those of Dichtel et al., who reported that levels of IGF-1 were higher in patients with lower fibrosis stages (0–1) as compared to patients with higher fibrosis stages (2–4): 125±51 versus 96±40ng/mL, respectively [18]. Also, in a previous study performed byColak et al., who recruited 92 MASH patients, they reported that patients with moderate-to-severe fibrosis (stages 2-3) had significantly lower serum IGF-1 levels than patients with no or mild fibrosis (stages 0–1) [28].

In addition, another study performed by Marques et al., reportedthat patients with MASH and advanced fibrosis had significantly lower serum IGF-1, and that this biomarker alone could distinguish patients with low/mild fibrosis from those with advanced fibrosis with an accuracy of 63% [29]. Furthermore, Polyzos et al., reported that IGF-1 was lower in fibrotic MASH patients than in controls who had no or milder liver histologic lesions [24].

Our study revealed a highly significant decrease in the levels of total bilirubin among the patients with intermediate/high fibrosis as compared to the patients with low fibrosis. Most previous studies did not assessthe utility serum bilirubin in patients with MASH who developed fibrosis; only a previous study confirmed the inverse relationship between serum bilirubin level and the occurrence of MASH, but they did not study its relation to liver fibrosis [30], and another previous study suggested that serum bilirubin levels are unlikely to be associated with MASH in non-obese subjects. Both studies also did not evaluate its relationship to liver fibrosis [31].

Also, we found a highly significant decrease in platelets among the patients with intermediate/

high fibrosis as compared to the patients with low fibrosis.These findings were consistent with earlier studies that propose platelets play a significant role in the development of liver fibrosis by up-regulating the expression of matrix metalloproteinases and down-regulating the primary fibrogenic cytokine TGF-β ***[32,33]***. Platelet count is included in many prognostic scores for liver fibrosis and cirrhosis. However, only a few of these studies assessed platelets in MASH patients ***[34]***. The platelet indices are not widely investigated among patientswith liver steatosis or fibrosis. It might be useful in the future to include platelets as a part of diagnostic scores for the detection of liver steatosis and fibrosis.

Regarding the performance of IGF-1 in differentiating patients with intermediate/high fibrosis from patients with low fibrosis, the serum level of IGF-1 at a cutoff value of 50ng/mL predicted the fibrosis with excellent performance of 100% sensitivity and 82% specificity. The performance of IGF-1, regarding distinguishing fibrosis grades of F0-2 from advanced fibrosis (F3–4), was previously studied by Marques et al., who reported that IGF-1 was significantly lower in MASH patients with F3-4 grades than patients with F0-2 grade. The IGF-1 at a cutoff of 98.83ng/ml had 70% sensitivity, 61% specificity, and an AUC of 0.67 ***[29]***.

Regarding the performance of HOMA-IR in differentiating patients with intermediate/high fibrosis from patients with low fibrosis, our results showed that HOMA-IR, at a cutoff value 0.4, predicted the grades of fibrosis with 100% sensitivity and 35.7% specificity. Our reported cutoff has a very low specificity compared to that reported in Cetin et al., ***[29]***. They evaluated 64 MASH patients, 21 patients with non-MASH, and 40 healthy control subjects. Their optimal cutoff value for HOMA-IR for the differentiation of cases with advanced fibrosis and mild fibrosis was 3.32, with a sensitivity of 69%, a specificity of 64%, and 0.68 AUC ***[35]***.

In another study, involving 15,728 adult participants and evaluating the non-invasive fibrosis index, the authors revealed a correlation between alterations in HOMA-IR and changes in fibrosis status in MASLD patients. They further reported that the greater the HOMA-IR, the higher the OR for progression. Specifically, individuals with HOMA-IR values higher than 1 were more than twice as likely to develop fibrosis in comparison to those with lower HOMA-IR values (OR, 2.34). The likelihood of fibrosis regression declined as HOMA-IR change increased in degree ***[36]***.

Conclusion:

There is an important relationship between serum IGF-1 and insulin in obese patients with MASH as compared to simple steatosis patients, which reflects the value of serum IGF-1 as a potential therapeutic target in MASH patients. Moreover, serum IGF-1, insulin, and HOMA-IR showed a promising performance regarding the differentiation of patients with intermediate/high fibrosis from those with low fibrosis. More studies are required to prove our results.

Declarations:

Ethics approval and consent to participate:

The study was conducted according to the World Medical Association Declaration of Helsinki, after the approval of the local Research Ethics This study was approved by the Ethics Committee of the Faculty of Medicine, Ain Shams University, Egypt (FMASU R135/2023).

Consent for publication:

Written informed consent for publication regarding the data of the studied patients was obtained.

Availability of data and materials:

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests as defined by Nature Research, or other interests that might be perceived to influence the results and/or discussion reported in this paper.

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Authors' contributions:

Dina Morsy and Marwa Ali wrote the manuscript, Marwa Ali conducted laboratory and data interpretation. Dina Morsy and Dina Mostafa contributed to the patients' recruitment, sample, and data collection. All authors read and approved the final manuscript.

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دراسة علاقة عامل تحول النمو الشبيه بالانسولين وحساسيه الانسولين فى مرضى زياده الوزن ومرضى السمنه اللذين يعانون من تشحم الكبد

الخلفية العلمية والهدف من إجراء البحث: تعتبر السمنه من اكثر الامراض انتشارا ويعتبر مشكله عامه. ويحدث نتيجه ترسب الدهون فى الانسجه الدهنيه ويجب محاوله منع حدوثه لما يصاحبه من أمراض مزمنه مثل امراض القلب والشرايين وارتفاع الكوليسترول وارتفاع ضغط الدم ومقاومه الانسولين وداء البول السكرى وبعض الأورام.

ويعتبر عامل تحول النمو الشبيه بالانسولينمن البروتينات التى تؤدى إلى زياده السمنه اذا نقصت فى الدم والتى تتواجد بتركيز عالى فى الدم.حيث يعتقد انه له دور هام في عمل هرمون الانسولين فى الانسجه الحساسه لهرمون الانسولين كالكبد والعضلات فى الانسان والحيوان خاصه فى الكبد.

ينتج مرض تشحم الكبد من ترسب الدهون فى انسجه الكبد ويتم تشخيصه باستبعاد الاسباب الاخرى التى تؤدى إلى ترسب الدون بالكبد مثل مرض تشحم الكبد الكحولى. وغالباً يصاحب مرض تشحم الكبد مقاومه الانسولين ويكون معظم المرضى مما يعانون من السمنه يعانون من ارتفاع الكوليسترول فى الدم او ارتفاع ضغط الدم.

إن الهدف من هذه الدراسة هو تقييم عامل تحول النمو الشبيه بالانسولينوعلاقته بحساسيه الانسولين فى المرضى اللذين يعانون من السمنه او زياده الوزن والمصابين بتشحم الكبد

عدد المشاركين فى البحث وطريقه البحث: تم عمل الدراسه علي ستون مريضاً من مرضى زياده الوزن ومرضى السمنه المفرطه ممن يعانون من مرض تشحم الكبد بعيادات قسم الباطنه العامه بمستشفى عين شمس الجامعى حيث تم قياس عامل تحول النمو الشبيه بالانسولين ونسبه مقاومه الانسولين حيث تم التشخيص عن طريق السونار مع حساب كتله الجسم مع قياس درجه تليف بالكبد.

نتائج البحث: يوجد علاقه مهمه بين عامل تحول النمو الشبيه بالانسولينوحساسيه الانسولين فى مرضى تشحم الكبد مع وجود التهاب فى خلايا الكبد بالمقارنه بمرضى تشحم الكبد فقط مما يثبت اهميه وامكانيه استخدام عامل تحول النمو الشبيه بالانسولين فى تشخيص وعلاج مرض تشحم الكبد بالاضافه لاهميته فى تشخيص درجات تليف الكبد اذا تم استخدامه مع حساب نسبه الانسولين ومقاومه الانسولين.