

University of Baghdad Al-Kindy College of Medicine Scientific Research



PREVEALENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE IN IRAQ POPULATION

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Abstract:

Introduction:

Non-alcoholic fatty liver disease (NAFLD) is defined as the presence of \geq 5% steatosis, usually detected by radiological imaging in absence of any secondary causes of fat accumulation in the liver such as alcohol, drugs, or autoimmunity.

NAFLD has been recognized as the hepatic component of metabolic syndrome. It is prevalent among obese people and those with type 2 diabetes mellitus (T2DM) irrespective of their degree of obesity.

Methodology:

This prospective cross-sectional study investigated medical files of patients diagnosed Non-alcoholic liver diseases who attended to alkindy teaching hospital in Iraq.

A Total of 100 Adult patients aged between (18-84 years), randomly selected, who underwent abdominal US in ultrasound clinic over a period of 5 months, at Al-Kindy teaching hospital **9**

Results:

A sample of a 100 patients diagonsed with fatty liver disease was taken. 55% of them were females and 45% were males. The patients were divided into four categories according to their age. Patients whose age under 25 years were 11% of the sample, patients between 26 and 35 years were 17%, patients between 36 and 45 years were 30% and patients above 45 years were 42%. From these numbers we found that the patients whose age above 45 years presented the majority of cases followed by the age group between 36 and 45 years. Also we found that the prevalence of the first grade of the disease constituted the most prevalent grade of the disease with a prevalence of 54%. We also noticed that there's a strong correlation between obesity and fatty liver disease demonstrated by a large numbers of cases of fatty liver disease who were suffering from obesity represented by a 78% of patients from our sample under study.

Conclusion:

The growing epidemic of obesity and diabetes is likely to lead to even higher prevalence of NAFLD making it the most common cause for advanced liver diseases in the future.

Recommendations:

Lifestyle modification – an appropriate diet, increased physical activity and weight loss are the first line of intervention in patients with NAFLD.

Key words: fatty liver, DM, obesity.

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Chapter one

Introduction

Introduction:

Non-alcoholic fatty liver disease (NAFLD) is defined as the presence of \geq 5% steatosis, usually detected by radiological imaging in absence of any secondary causes of fat accumulation in the liver such as alcohol, drugs, or autoimmunity. (Byrne CD, Targher G. NAFLD)

The term describes a spectrum of progressive liver disease ranging from simple steatosis, non-alcoholic steatohepatitis, and fibrosis to liver cirrhosis. It is the leading cause of liver diseases worldwide and is emerging as the premier cause for end stage liver disease. (Younossi Z global burden of NAFLD)

The presence of NAFLD increases liver-related morbidities and mortalities. It also increases risk of comorbidities like diabetes mellitus and cardiovascular diseases. In patients with NAFLD, half of the deaths are related to cardiac disease and malignancies. Early identification of NAFLD can help improve the patient outcome through prevention and treatment. (Rinella ME NAFLD)

NAFLD has been recognized as the hepatic component of metabolic syndrome (Anstee QM Progression of NAFLD to diabetes mellitus). It is prevalent among obese people and those with type 2 diabetes mellitus (T2DM) irrespective of their degree of obesity. (Gaggini M NAFLD)

The association of NAFLD with obesity and T2DM is due to the compensatory hyperinsulinemia resulting from insulin resistance leading to progressive defective lipid metabolism and triglyceride accumulation in the liver, or to β -cell dysfunction, leading to aggravation of T2DM, which in turn puts further pressure on the liver. (Forlani G NAFLD)

The prevalence of NAFLD is increasing in developed countries with their growing obesity epidemic, Iraq is also following that trend.

The aim of our study is to identify the prevalence and associations between Non-alcoholic fatty liver grade with diabetes mellitus and to assess the risk factors for the same.

Chapter two

Methodology

Methodology:

This prospective cross-sectional study investigated cases of patients diagnosed with Non-alcoholic liver diseases who attended to alkindy teaching hospital in Iraq.

A Total of 100 Adult patients aged between (18-84 years), randomly selected, who underwent abdominal US in ultrasound clinic over a period of 5 months, at Al-Kindy teaching hospital.

Sociodemographic variables of the selected 100 patients such as age, sex, hypertension, Grade of NAFL and DM were collected. The patients' USG reports were gathered with anthropometric measures such as weight, height, and body mass index (BMI). Laboratory data collected related to diabetes included last fasting blood sugar, last glycosylated hemoglobin (HbA1c), last lipids profile, the last liver function profile, and viral hepatitis B and C serology. Liver biopsy results were reviewed.

The data was entered in Microsoft Excel and then transferred to SPSS program version 21 for statistical analysis.

Numerical variables were presented as mean and standard deviation (SD) or median and range. The patients were segregated into three groups based on their BMI (normal, overweight, and obese), and their number and percentage were calculated. Patients were considered to have a metabolic syndrome if, in addition to T2DM, they had at least two of the following: blood pressure $\geq 130/85$ mmHg or were on antihypertensive treatment; triglycerides \geq 1.7 mmol/L or receiving a fibrate; high density lipoprotein (HDL) cholesterol <1.04 mmol/L for men or 1.29 mmol/L for women; waist circumference >102 cm for men or 88 cm for women, according to Adult Treatment Panel III (ATP III) Abdominal ultrasound reports were grouped into four criteria. categories: normal, with hepatomegaly alone, with combined fatty liver and hepatomegaly, and fatty liver alone. In addition, fatty liver was graded using specific characteristics found in ultrasound such as greater echogenicity of the liver parenchyma relative to the renal cortex of the right kidney, along with visibility and sharpness of the diaphragm and hepatic veins' interface, accordingly.

The severity of hepatic steatosis was classified into four grades: Grade 0, no steatosis: liver and renal cortex of the echogenicity; Grade 1, mild steatosis: slightly brighter liver as compared to the renal cortex, clear diaphragm visualization, and interface of hepatic veins with sharp contours; Grade 2, moderate steatosis: brighter liver with attenuated ultrasound beam at deeper parts of the liver, diaphragm and hepatic veins still visible but with blunted contours; Grade 3, severe steatosis: very bright liver, severe ultrasound beam attenuation, diaphragm or hepatic veins not visible among the patients who developed hepatic fibrosis, cirrhosis and malignancy were also reported. The laboratory data like lipids and blood sugar levels were grouped as controlled or uncontrolled according to the diabetes guidelines.

The liver enzyme levels were categorized as normal or abnormal (elevated). analysis was used to study the relationships between different factors or associations including demographic, anthropometric, laboratory factors, use of lipid lowering agents, tobacco smoking, adherence to dietary advice (daily five portions of fruits/vegetables), physical activity recommendations (30 minutes daily, five days per week).

Inclusion criteria obese and DM patient with fatty liver. Exclusion criteria history of alcoholic, drug, autoimmune.

Chapter three

Results

Results:

A sample of 100 patients diagnosed with fatty liver disease was taken. 55% of them were females and 45% were males. The patients were divided into four categories according to their age. Patients whose age under 25 years were 11% of the sample, patients between 26 and 35 years were 17%, patients between 36 and 45 years were 30% and patients above 45 years were 42%. From these numbers we found that the patients whose age above 45 years presented the majority of cases followed by the age group between 36 and 45 years. Also, we found that the prevalence of the first grade of the disease constituted the most prevalent grade of the disease with a prevalence of 54%. We also noticed that there's a strong correlation between obesity and fatty liver disease demonstrated by a large number of cases of fatty liver disease who were suffering from obesity represented by a 78% of patients from our sample under study. The patients who have DM were 60%. The patients who have HT were 15%.

Variables	No.(%)		
AGE categories: Less than 25 yrs. 26-35 yrs. 36-45 yrs. More than 45 yrs.	11(11%) 17(17%) 30(30%) 42(42%)		
Sex Male Female	45(45%) 55(55%)		
Grade of FLD: 1 st stage 2 nd stage 3 rd stage	54(54%) 29(29%) 17(17%)		
Obesity grade: Normal Over weight Obesity	2(2%) 20(20%) 78(78%)		
DM HT	60(60%) 15(15%)		

Table 1: Demographic data of the study population.







We found that the mean of weight of patients from our sample was 96.25, length mean was 161.72, BMI mean was 36.661 and waist mean was 106.79.

Variable	Mean
Weight(kg)	96.25
Length(cm)	161.72
BMI	36.661
Waist	106.79

Table 2: Mean of the weight, length, BMI and waist of the study population

	1 st	2 nd Stage	3 rd Stage	P-Value<0.05
	Stage			
DM:NO	11	13	6	0.03
Yes	34	16	11	
AGE:				
Less Than 25 Yrs	4	2	5	0.02
26-35 yrs	8	7	2	
36-45yrs	24	2	4	
More Than 45	18	18	6	
Yrs				
Gender: Male	28	10	7	0.29
Female	26	19	10	
Obesity Grade:				
Normal	2	0	0	0.003
Over Weight	18	2	0	
Obesity	34	27	17	
HT: NO	46	23	15	0.85
YES	8	5	2	

Table 3: Association between the stage of FLD and the Age gender, DM, HT and obesity grade of the study population.

Previous table shows that there is a statically significant association between the DM and the first stage of FLD. Also, there's astatically significant association between the age (especially those whose age is from 36-45 years) and the first stage of FLD. Also, there is astatically significant association between the obesity and the first stage of FLD.

	1 st stage	2 nd stage	3 rd stage	P-
				value<0.05
Weight(kg)	92	97	108	0.001
Height(cm)	162	162	159	0.001
BMI	35.0	36.3	42.5	0.001
Waist	104	108	112	0.06

Table 4: association between the grade of FLD and the mean of weight, height, BMI and waist of the study population.

Previous table shows that there is a statically significant association between the weight, BMI and the third stage of FLD. Also there is astatically significant association between the height and the second stage of FLD.

Chapter four

Discussion

Discussion:

NAFLD is a common term used to describe a broad range of liver conditions characterized by excessive fat storage in liver cells in individuals who consume little or no alcohol The fact that insulin resistance is the most common risk factor for the development of NAFLD is well-documented in literature. Both T2DM and NAFLD are sharing the same underlying mechanisms of insulin resistance, metabolic stress, and liver inflammation. NAFLD is not a cause of insulin resistance but it has been proven to be a consequence of it.

We noticed that there's a strong correlation between obesity and fatty liver disease demonstrated by a large number of cases of fatty liver disease who were suffering from obesity represented by a 78% of patients from our sample under study. Also, diabetes mellitus and NAFLD commonly exist together so dm considered as independent risk factor, these findings are supported by other studies Williamson RM et al Forlani G The burden of NAFLD et al Alsabaani NAFLD. In addition to that, hypertension is not significant.

The results also show the age is independent risk factor for progression of the disease, the prevalence of the disease is the most among patients who is more than 45 years.

In this study, the presence of fatty liver was evaluated radiologically, mainly by abdominal ultrasonography. USG is known to underestimate the incidence of hepatic steatosis and under-diagnosis NAFLD especially when hepatic steatosis is < 20%.USG is easily available, cheap, and can be performed even at bedside. In the current study, gender was not a significant risk factor for NAFLD, However, from Italy reported more males than females to have the disease. Meanwhile studies by Williamson et al, Mustapic et al, and Alsabaani et al, reported no significant difference based on sex.

In general population, NAFLD is associated with multiple metabolic comorbidities such as obesity, T2DM, hyperlipidemia, hypertension, and metabolic syndrome. In the current study, univariate analysis revealed higher BMI, higher waist circumference, and higher triglyceride levels to

be significant risk factors for fatty liver. BMI was the independent risk factor.

The main treatment goals of NAFLD are to improve steatosis and to prevent disease progression. Unless intervened early, NAFLD can progress to decompensated liver cirrhosis, liver failure, hepatocellular carcinoma, or even mortality. As no single intervention can effectively cure NAFLD.

Early detection of NAFLD is essential to avoid the progression of the disease into decompensated liver cirrhosis and liver transplantation requirement. With the rapid rise of obesity in Iraq in tune with the global trends, NAFLD is expected to become the main indication for liver transplantation in the future. Although liver transplantation is curative and has been shown to enhance survival in patients with advanced liver disease from any cause, patients with NAFLD face specific challenges.

First, there is currently no appropriate pharmacotherapy to prevent the disease from progressing to advanced fibrosis. Second, patients with NAFLD are frequently older, obese, and have multiple comorbidities, raising the risk of mortality during and after liver transplantation. Third, increased prevalence of NAFLD in the donor population may have an adverse effect on potential liver graft availability and efficiency.

Recognized factors increasing the risk of NAFLD and/or associated with the development of the disease include:

- 1. High body mass index (BMI)
- 2. Type 2 diabetes
- 3. Dyslipidemia high level of triglycerides (TG) in blood serum the recognized threshold value is 150 mg/dl, low level of high-density lipoproteins (HDL) (< 40 mg/dl in men and < 50 mg/dl in women);
- 4. Age the prevalence of NAFLD rises with age
- 5. Long-term consumption of even moderate amounts of alcohol in combination with excessive caloric intake and/or obesity.

We should reduce these risk factors to decrease the prevalence of NAFL and we do that by:

- Lifestyle modification: an appropriate diet, increased physical activity and weight loss are the first line of intervention in patients with NAFLD. Body weight reduction by > 5% has been shown to decrease hepatic steatosis, and by > 10% to contribute to histological improvement in patients with NAFL. This management also helps to reduce the risk of cardiovascular diseases. Physical activity must be combined with diet . Basic dietary recommendations include lowering the calorie content of meals (decrease in daily caloric intake by 500-1000 kcal) and avoidance of processed foods, products and drinks that are high in fructose.
- Insulin sensitizers
 - Thiazolidinediones the latest research shows that pioglitazone produces a beneficial effect in patients with NAFL both with and without diabetes. However, increased insulin sensitivity and reduced hepatic fibrosis apply to a greater extent to diabetic patients, so it's recommended to prevent dm from causing NAFLD
 - Metformin despite some studies demonstrating a positive effect of metformin on the activity of liver enzymes and a decrease in insulin resistance, the drug has not been shown to affect the course of NAFL. Consequently, metformin is not recommended for the treatment of NAFL.

even though the study has some limitations, we found that all the cases that we collected have NAFL so we suggest to change the title of our research from the [prevalence of non-alcoholic fatty liver in iraq]to the [The Association between FLD, DM and obesity in iraq population (single center study)].

Further research is needed to determine if NAFLD increases the risk of diabetes or is an indicator for other comorbid diseases, as well as the extent to which the onset of T2DM is linked to different stages of liver disease.

Chapter five Conclusion & Recommendations

Conclusion:

The prevalence of NAFLD among adult patients with T2DM was found to be high. Female, high BMI and high waist circumference were significant risk factors for fatty liver. BMI stood out as an independent risk factor. The growing epidemic of obesity and diabetes is likely to lead to even higher prevalence of NAFLD making it the most common cause for advanced liver diseases in the future. Further studies to assess the prevalence of NAFLD and the related comorbidities in the general population may help estimate the future burden on the health care system and be ready for the same.

Recommendations:

Recognized factors increasing the risk of NAFLD and/or associated with the development of the disease include:

-BMI, type 2 diabetes, dyslipidemia, age

We should reduce these risk factors to decrease the prevalence of NAFL and we do that by:

- Lifestyle modification: an appropriate diet, increased physical activity and weight loss are the first line of intervention in patients with NAFLD.

-Insulin sensitizers like Thiazolidinediones and metformin as treatments for DM.

-Vitamin E: the benefit of vitamin E in the treatment of NAFL is based on its antioxidant activity.

- Further additional time for data collection, and large number of cases improve the result and decrease the underestimation.

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