ASSOCIATION OF ANTHROPOMETRIC AND BIOCHEMICAL PARAMETERS WITH NONALCOHOLIC FATTY LIVER DISEASE

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ABSTRACT

Objective: To study the association of anthropometric and biochemical parameters with nonalcoholic fatty liver disease (NAFLD) diagnosed on ultrasonography (USG).

Study Design: Cross sectional analytical study.

Place and Duration of Study: Department of Pathology, Combined Military Hospital (CMH) Mardan, from Aug 2016 to Jan 2017.

Methodology: Study was conducted on 96 individuals 20-65 years enrolled by non-probability consecutive sampling. They were evaluated by taking anthropometric and biochemical parameters to establish association of nonalcoholic fatty liver disease diagnosed on ultrasonography as compared to healthy individuals.

Results: Mean age was 28.7 ± 10.3 years in control group as compare to 39.9 ± 10.8 years in nonalcoholic fatty liver disease group. Nonalcoholic fatty liver disease was seen in 17 (28%) females as compared to 44 (72%) males showing strong association of males with the disease (p=0.025). There were 31 (50%), 22 (36%) and 8 (14%) cases in mild, moderate and severe nonalcoholic fatty liver disease categories respectively using ultrasonography. Abdominal circumference, systolic blood pressure and body mass index (BMI) were significantly associated with nonalcoholic fatty liver disease. Whereas, among biochemical parameters serum glucose, alanine amino-transferase (ALT), triglyceride and low density lipoprotein cholesterol (LDL-C) were independent parameters strongly associated with nonalcoholic fatty liver disease.

Conclusion: Our study showed that deranged anthropometric along with biochemical parameters was strongly associated with development of nonalcoholic fatty liver disease.

Keywords: Anthropometric, Biochemical parameters, Nonalcoholic fatty liver disease.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) emerged as an appalling public health issue, a leading cause of chronic liver disease[1] due to accumulation of triglyceride exceeding 95th percentile in absence of alcoholic intake, negative viral and autoimmune liver disease[2]. It is a spectrum of disease state from fatty liver to steatohepatitis which ultimately leads to fibrosis followed by cirrhosis[3]. It can be differentiated from nonalcoholic steatohepatitis (NASH) by absence of hepatocellular injury in the form of ballooning. NAFLD prevalence globally is 25.24% [95% Confidence Interval (CI): 22.10-28.65] with lowest in Africa and highest in South America and Middle East[4].

Obesity, type 2 diabetes, insulin resistance, dyslipidemia and metabolic syndrome have been shown to strongly associate with NAFLD along with uptrend of cardiovascular disease which contributes significantly to morbidity and mortality related to liver diseases[5]. A simple and effective technique for diagnosing NAFLD for public health is required. Ultrasound abdomen is a cost effective, noninvasive and fairly accurate test with sensitivity of 73.3% and specificity of 69.6% as compared with standard liver biopsy for diagnosis which is an invasive procedure[6]. However, it is less precise in mild degree of steatosis (<5%). Although some indices based on anthropometric and biochemical parameters have been suggested, much work is required for

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timely identification of NAFLD. Examples of these indices like fatty liver index, hepatic steatosis index and triglyceride glucose index (TyG). But still much work is required to be done for timely identifying NAFLD and its associated diseases before it becomes a public health problem.

Pakistan is one of those countries with high prevalence of metabolic risk factors such as diabetes, dyslipidemia and obesity. These factors along with excessive intake of saturated fats[7] in food especially in north western areas of Pakistan lead to a strong propensity of getting NAFLD. Our study will highlight disease presence in this area in particular along with its association with anthropometric and biochemical parameters.

METHODOLGY

We conducted this cross sectional analytical study at CMH Mardan after approval of the hospital's ethical review committee on 96 individuals (20-65 years) reporting for routine checkup from August 2016 to January 2017 by non-probability convenience sample was calculated by WHO calculator. As per Asia-Pacific Working Party guidelines[8], NAFLD patients were diagnosed by the presence of fatty liver along with ruling out chronic liver disease, hepatotoxic medicines intake and excessive alcohol abuse. Informed consent was taken from the patients. Participants were divided into NAFLD as study group and non NAFLD as control group based on presence and absence of fatty liver respectively.

Demographic, anthropometric and biochemical parameters were used to assess study gps. Demographic data includes age in years and gender (male/female). Anthropometric data include height in cm, weight in kg, abdominal circumference in cm and BMI categories in kg/m^2 as per WHO criteria[9]. BMI of ≤24.9 kg/m^2, 25-29.9 kg/m^2 and ≥30 kg/m^2 were labelled normal, over weight and obese respectively. USG abdomen was used to diagnose patient with NAFLD using 3.5 MHz curvilinear probe on Toshiba Nemio Doppler US Machine (Model: SSA- 580 A) by consultant radiologist. When the echogenicity of liver was just increased, it was grade 1; when the echogenic liver obscured walls of portal vein branches, it was grade 2; and when the echogenic liver obscured the diaphragmatic outline, it was grade 3 fatty infiltration[10]. NAFLD was divided into three categories based on grade 1, 2 and 3 as mild, moderate and severe fatty liver disease respectively based on ultrasonography. Laboratory investigations of all patients were performed at CMH Mardan Laboratory. Blood samples of subjects were drawn aseptically in fasting state in plain serum and ethylene diamine tetra acidic acid (EDTA) tubes for biochemical parameters and blood complete picture (CP) respectively. Selectra Pro M clinical chemistry analyzer was used for analyzing biochemical parameters. Serum Glucose (mmol/L) samples were analyzed utilizing glucose oxidase assay, ALT (U/L) by Kinectic (IFCC) assay, Cholesterol (mmol/L), TG (mmol/L) LDL-C (mmol/L) and HDL-C (mmol/L) by enzymatic assay. Whereas Blood CP was analyzed on Sysmex XP-100 Hematology Analyzer.

Statistical package for social sciences version 20.0 was used for analysis of the data. Descriptive statistics were performed for demographic factors. Categorical variables were expressed as counts and percentages. Odd's ratio with 95% Cl was calculated through regression. OR ≥1 was measured as contributor toward NAFLD. Pearson Chi square test of independence was used to show relationship of gender, age groups and BMI categories with NAFLD respectively. Correlation was measured by pearson's correlation.

RESULTS

Our study showed 61 (64%) suffering from NAFLD as compare to 35 (36%) normal individuals among 96 study participants (table-I).

NAFLD was seen in 17 (28%) females as compare to 44 (72%) males. There is a high prevalence of NAFLD in males as compare to females showing strong association with disease (p=0.025). Mean age was 28.7 ± 10.3 years in non NAFLD individuals as compare to 39.9 ± 10.8 years in NAFLD. Within respective age gps, most

of the individuals 31 (86%) in 36-50 years age gp fall in NAFLD category. There were 31 (50%), 22 (36%) and 8 (14%) cases in mild, moderate and severe NAFLD categories using USG respectively. Some individuals with normal BMI 10 (23%) were also suffering from NAFLD as compare to most of the overweight 32 (94%) and obese 19 (100%) individuals in their respective BMI categories. Abdominal circumference, systolic blood pressure and BMI were significantly associated with NAFLD (table-II).

Table-I: Characteristics of study population with and without non-alcoholic fatty liver disease.

Parameter	Non Nonalcoholic Fatty Liver Disease (n=35)%	Nonalcoholic Fatty Liver Disease (n=61)%	*p*-value
Male	32 (91)	44 (72)	0.025
Female	03 (9)	17 (28)	
20-35	27 (77)	22 (36)	<0.001
36-50	05 (14)	31 (51)	
51-65	03 (09)	08 (13)	
Normal	33 (94.3)	10 (16)	<0.001
Over Weight	02 (5.7)	32 (53)	
Obese	-	19 (31)	

X2, Pearson Chi-square test; BMI, Body mass index, *As per WHO criteria.

Whereas among biochemical parameters glucose, ALT, triglyceride and LDL cholesterol were independent parameters strongly associated with NAFLD (table-II). Serum fasting glucose mean was 5.9 ± 3.4 mmol/L in NAFLD category with 8 patients in diabetic and 4 patients in prediabetes range. However mean value was within reference range in non NAFLD category (5.3 ± 1.7 mmol/L). Serum glucose show strong correlation with serum triglyceride [Pearson Correlation Coefficient (r)=0.260, p=0.043], cholesterol (r=0.303, p=0.018) and BP (r=0.506, p<0.001). Similarly, BMI had also positive correlation with age (r=0.291, p=0.023), BP (r=0.434, p≤0.001) and cholesterol

Table-II: Association of NAFLD with anthropometric and biochemical parameters.

Parameter	Non Nonalcoholic Fatty Liver Disease (n=35) Mean ± SD	Nonalcoholic Fatty Liver Disease (n=61) Mean ± SD	Odds Ratio	95% CI	*p*-value
Age (years)	28.7 ± 10.3	39.9 ± 10.8	1.018	0.858-1.207	0.840
Anthropometric Variables					
Abdominal Circ (cm)	79.0 ± 15.3	92.7 ± 18.7			
Male	76.1 ± 8.8	91.1 ± 17.0	0.791	0.671-0.933	0.005
Female	81.7 ± 2.1	96.7 ± 22.8			
BMI (kg/m^2)	21.4 ± 2.4	27.8 ± 4.4	5.825	1.830-18.544	0.003
BP systolic (mm Hg)	106.5 ± 12.7	125.8 ± 20.0	1.532	1.120-2.096	0.008
BP diastolic (mm Hg)	75.0 ± 10.2	87.6 ± 11.4	1.171	1.2590-3.071	0.071
Hematologic Variables					
WBCs (109/L)	6.9 ± 2.5	8.3 ± 2.6	1.055	0.376-2.958	0.919
MCV (fl)	84.8 ± 5.3	82.8 ± 6.5	0.642	0.426-0.968	0.035
Biochemical Variables					
Glucose (mmol/L)	5.3 ± 1.7	5.9 ± 3.4	0.166	0.041-0.668	0.012
ALT (U/L)	46.2 ± 24.0	50.0 ± 23.1	1.140	1.043-1.247	0.004
Cholesterol (mmol/L)	3.7 ± 0.8	4.4 ± 0.7	70.661	0.673-7414.24	0.073
TG (mmol/L)	2.1 ± 0.9	2.3 ± 1.2	1.182	0.256-5.456	0.830
LDL-C (mmol/L)	1.8 ± 0.9	2.4 ± 0.9	0.069	0.005-1.021	0.052
HDL-C (mmol/L)	1.0 ± 0.3	1.1 ± 0.2	1.275	0.169-	0.186

Circumference, Circ; BP, Blood pressure; BMI, Body mass index; WBCs, White blood cell counts; MCV, Mean corpuscular volume; ALT, Alanine aminotransferase; TG, Triglyceride; LDL-C, Low density lipoprotein cholesterol; HDL-C, High density lipoprotein cholesterol.

(r=0.314, *p*=0.014).

DISCUSSION

The results of our study revealed NAFLD predominance in males as found in Chinese study of Wang *et al*[11] and American study of Lano *et al*[12]. Females were less prone to acquire NAFLD in reproductive age owing to protective role of estrogen as in our case[13]. Similarly middle age group has the highest proportion of NAFLD which declined afterwards. This was called "inverted U-shaped curved" pattern meaning prevalence of disease started declining by 50-60 years[14].

Anthropometric parameters were significantly raised in our NAFLD diagnosed group. BMI[15] and visceral obesity[16] based on abdominal circumference were recognized risk factors for NAFLD. Mean BMI 27.8 ± 4.4 kg/m^2 in study group falling in obese category as compare to normal BMI 21.4 ± 2.4 kg/m^2 in control group. Though most of the NAFLD patients belong to category of BMI >25 kg/m^2 but 10 (23%) of normal BMI individuals were also suffering from the disease. High BMI >25 kg/m^2 association with NAFLD as in our case were also proven from studies of Kaltenbach *et al* and Boyraz *et al*[17-18]. Asians waist cut off limit for metabolic risk stratification for men was 85 cm as compare to 80 cm in women which was less than what was seen in European and American countries due to higher levels of abdominal adipose tissue and body fat[19]. Our study showed markedly increased abdominal circumference in NAFLD group but mean female abdominal circumference was more (96.7 cm ± 22.8) as compared to males (91.1 cm ± 17.0). This was against the finding of Zhu *et al*[20] who found mean abdominal circumference greater in men as compared to women.

Accumulation of triglycerides in hepatocytes were considered main pathogenic trigger of NAFLD[21,22]. In our study, serum triglyceride of 2.3 ± 0.9 mmol/L in high therapeutic decision limit and fasting plasma glucose with a mean of 5.9 ± 3.4 mmol/L in prediabetic range, gave an indication of increased production of glucose and triglyceride in response to hepatic insulin resistance[23]. Insulin resistance possibly played a major role in steatogenis is and further to liver disease[24]. A significant increase was seen in ALT (*p*=0.004).

NAFLD is a multifactorial disease, influence of socioeconomic factors, type of activity, climatic and geographical distribution should also be taken into consideration beside anthropometric and biochemical parameters. There were also certain limitations of our study. Liver USG had limitations in the diagnosis of patients with NAFLD as it could not detect liver infiltration of fat <20% for hepatic steatosis. Secondly, most of the patients came from Mardan district, with male predominance and limited sample size. So results could not be generalized to Pakistani population.

CONCLUSION

Increased BMI, enlarged abdominal circumference, impaired fasting glucose, raised ALT and was strongly associated with NAFLD.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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