A Study of Anthropometric And Lipid Profile Parameters in Non-Alcoholic Fatty Liver Disease Patients Attending A Tertiary Care Hospitalat Puducherry.

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Abstract:
Introduction: *Non-alcoholic fatty liver disease (NAFLD)is a common chronic liver disorder sharing the same factors with metabolic syndrome in pathogenesis and insulin resistance. Stress, altered food habits and sedentary life style has led to the development of fatty liver, a marker of metabolic syndrome, leading to cardiovascular disease and Type2 DM at a younger age. **Aim & objectives :** To estimate anthropometric and lipid parameters in NAFLD cases, and controls with normal ultrasonogram (USG).To correlate these parameters with metabolic syndrome. **Methodology :** A total of 480 patients who were referred for USG from medicine and gynaecology outpatient department were screened. 46 patients with NAFLD and 46 cases with normal USG, of age 18-58 were selected as study and control group respectively. Anthropometric and lipid profile parameters were estimated in both groups. National cholesterol education programme Adult treatment panel III (NCEP-ATPIII) and International Diabetes federation Criteria was used to assess the prevalence of metabolic syndrome. **Results:** The WC was significantly high in the NAFLD group with a X^2 value of 25.77 and 'p' value of 0.0001. The diastolic blood pressure and serum triglycerides had X^2 value of 17.06 and 6.5 and 'p' value of 0.00003 and 0.04 respectively. **Conclusion:** Central obesity and dyslipidemia was significantly higher in the NAFLD group compared to the control group.*
Keywords: *Metabolic syndrome, NAFLD, triglycerides, USG, Waist circumference.*

I. Introduction

Non-alcoholic fatty liver disease (NAFLD) is defined as the abnormal accumulation of lipids, primarily in the form of triglycerides in individuals with either total abstinence or who do not consume significant amounts of alcohol.[1] The maximum allowable level of alcohol intake for definition of NAFLD is 2 standard drinks a day (140 g ethanol/week) for men, and one standard drink a day (70 g ethanol/week) for women.[2] NAFLD is considered as the hepatic representation of metabolic syndrome. Numerous studies have demonstrated that NAFLD is strongly associated with obesity, dyslipidemia, hypertension and insulin resistance, the components of metabolic syndrome. A participant is said to have metabolic syndrome if he/she has two or more of the following criteria as per Modified National Cholesterol Education Programme-Expert Panel-Adult treatment panel III (NCEP-EP-ATP III) criteria.[3]

1. Triglycerides (TG) : >150mg%.
2. High density lipoprotein (HDL) : < 40 mg% in male and < 50 mg% in female.
3. Fasting Blood Sugar : > 100 mg%.
4. Systolic Blood pressure (SBP) : ≥ 130 mmHg and
5. Diastolic blood pressure (DBP) : ≥ 85mm Hg
6. Waist circumference (WC) : > 90 cm in male and > 80 cm in female.

According to the revised BMI cut-off for Asians[4] a BMI of 18.6-22.9 is normal, 23-24.9 is over-weight and above 25 is considered obese. Urbanization and associated changes, such as sedentary life-style, fat rich diet, and a higher inherited tendency for diabetes mellitus makes Indians more prone to metabolic syndrome or insulin resistance and its manifestations such as NAFLD and NASH .[5] The prevalence of non-alcoholic fatty liver disease ranges from 9 to 36.9% of the population in different parts of the world.[6] The prevalence of NAFLD in Asian countries ranges from 9- 40 %.[7] Indians have increased propensity for visceral fat accumulation which may present from birth.[8]

Prevalence of NAFLD in Indian population was found to be 9-32 % with a higher incidence in over weight and diabetic population according to the epidemiological study conducted between periods of 2004 to 2010.[9] Hence this study aims at estimating anthropometric and lipid profile parameters in patients, with and without NAFLD so as to assess the risk of cardiovascular morbidity and mortality in future.

II. Methodology

Over a period of 1 year between December 2013-November 2014 about 480 patients from the Gynaecology and Medicine out-patient departments of Sri Venkateswara Medical College and Hospital (SVMCH) who were referred for ultrasonogram were screened after getting written consent. Among them 280 were female and 200 were male of the age group 18-58yrs. From this 46 patients with fatty liver changes in USG were selected as study group after taking detailed history regarding alcohol consumption and drugs. From the remaining 434 patients 46 age matched individuals with normal liver findings in USG were taken as controls. Chronic alcoholism with clinical and imaging features of cirrhosis of liver, use of drugs such as amiodarone, corticosteroids, high dose of oestrogens, tamoxifen or methotrexate and pregnancy were excluded. This study was carried out in collaboration with the Department of Radiology, Sri Venkateshwara Medical College Hospital and Research Centre, Ariyur, Puducherry after obtaining the approval from Institution Ethics Committee.

All patients underwent USG of the abdomen to detect fatty changes in the liver, performed by a single experienced radiologist, for an average of 20 minutes, using a high-resolution B-mode ultrasonography system (SIEMENS-ACUSON x 300 PE, SI no: 330999) having an electric linear transducer mid frequency of 3–5 MHz. Fatty liver was defined as the presence of an ultrasonographic pattern consistent with "bright liver," with evident ultrasonographic contrast between hepatic and renal parenchyma, vessel blurring, and narrowing of the lumen of the hepatic veins in the absence of findings suggestive of chronic liver disease. Electronic weighing machine was used to record the weight to nearest 0.1 Kg. Prior to each measurement, the machine was calibrated to zero reading. Height was measured using stadiometer. Body mass index was calculated by the formula BMI = Weight/Height^2 (in kg/m^2). Waist circumference was measured at the midpoint between the lower border of 12th rib and the prominent part of anterior superior iliac spine using a stretch resistant tape. Waist circumference $\geq$ 90cm in male and $\geq$ 80 cm in female was considered as central obesity. The systolic and diastolic blood pressure was measured using electronic digital blood pressure monitor, CH-432, CITIZEN Micro Human Tech, Citizen systems Japan Co LTD. Tokyo, Japan after 5 minutes rest.

Fasting blood samples were collected from both groups for estimating lipid profile. The sample was allowed to clot and then centrifuged for 5 minutes at 500 rpm and the plasma used for cholesterol estimation by Trinders method, serum TG by enzymatic colorimetric method and HDL cholesterol by Polyethylene glycol-CHOD-POD method using a well calibrated auto- analyser Chem well. The kits were procured from Erba diagnostics. Serum cholesterol < 200 mg %, TG between 50-150 mg% and HDL-C values between 40-60 mg/dl were considered normal. For the baseline characteristics, continuous variables were summarized by mean (standard deviation) and categorical variables by frequency (percentages %). The mean difference and continuous variables were analysed by independent 't' test. The association in categorical variables was analysed by chi square test. P value of < 0.05 was considered significant. The data was analysed using SPSS 17 software.

III. Results

As shown in Table 1 & 2 in the study group the mean waist circumference was 95.8 ± 5.24, BMI 29.53 ±5.24,SBP 129.6 ± 14.2, DBP 85.2 ± 9.9, TC 190.6 ± 34.1, TG 153.7 ± 78.1, HDL-C 38.9 ± 4.4, and LDL-C 125.9 ±33.7 respectively. In the control group the mean waist circumference was 87.4 ± 5.8, BMI 24.74 ± 2.94, SBP 124.3 ± 12.2, DBP 78.6 ± 7.1, TC 162 ± 31.9, TG 119.5 ± 31.6, HDL 39.7 ± 4.3 and LDL 96.9 ± 32.2 respectively. There was statistically significant 'p' value of 0.001 for waist circumference, BMI and DBP between the study group and control group. There was also statistically significant 'p' value between the two groups for TC, TG and LDL-C as shown in table 2. Table 3 shows statistically significant X^2 value of 25.77 & 'p' value of 0.0001 for waist circumference in NAFLD group as compared to the control group. DBP shows a X^2 value of 17.06 and significant 'p' value of 0.011.

HDL values in male had statistically significant 'p' value. As shown in Table 1about 10.9% (n=5) were in the normal BMI range of 18-22.9Kg/m^2 , 8.7% (n=4) were in the overweight range (BMI:23-24.9 Kg/m^2) 32.6% (n=15) were in the obese range (BMI: >25 Kg/m^2). Moreover the remaining 47.8% (n=22) were in the BMI range above 30Kg/m.^{2} Thus 89.1% of NAFLD patients were in overweight and obese range .On the contrary, in the control group 32.6% (n=15) were in the normal BMI range, 19.6% (n=9) were in the over- weight range, 41.3% (n=19) in the obese range and 6.5% (n=3) had BMI > 30 Kg/m^2. Our study also found a higher waist circumference in 95% of patients with NAFLD and 25% in control group. Among the NAFLD group, 34.6% (n=16) males had waist circumference > 90 cm and 65.2% (n=30) females had waist circumference > 80cm.

IV. Discussion

NAFLD has been shown to be an important hepatic correlate of insulin resistance and metabolic syndrome. The BMI, WC, Diastolic and Systolic BP were significantly higher in the NAFLD group compared

to control group. In the NAFLD group statistically significant increase in TG and decrease in HDL was found. In a study by K. Gokulakrishnan, R.M. Anchana et al at Madras Diabetic Research Foundation and Dr.Mohan's Diabetes Specialities Centre 2009, NAFLD patients had significantly higher BMI, SBP, DBP, TG, and low HDL compared to subjects without NAFLD which is similar to our study.

In our study group about 10.9% (n=5) were in the normal BMI range of 18-22.9Kg/m^2 , 8.7% (n=4) were in the overweight range (BMI:23-24.9 Kg/m^2), 32.6% (n=15) were in the obese range (BMI: >25 Kg/m^2). Moreover the remaining 47.8% (n=22) were in the BMI range above 30Kg/m.^{2} Thus 89.1% of NAFLD patients were in overweight and obese range. This confirms the fact that obesity, an important component of MS, would increase with increase in BMI percentiles from underweight to obesity in NAFLD subjects.[10] This also proves that fatty liver is one of the metabolic surrogate of MS presenting as hepatic insulin resistance .[11] On the contrary, in the control group 32.6% (n=15) were in the normal BMI range, 19.6% (n=9) were in the over - weight range, 41.3% (n=19) in the obese range and 6.5% (n=3) had BMI > 30 Kg/m^2.

In a study conducted by MES Medical College,[12] out of 377 NAFLD patients 137 (36.3%) had a body mass index between 21–25 kg/m². 229 (60.7%) patients were in 26 – 30 kg/m² range and the rest 9 (2.4%) were having a body mass index more than 30 kg/m². Thus 80% of the NAFLD subjects were in over weight and obese range which is almost similar to our study. In a similar study reported by Chalasani N, Younossi Z et al about 74% of patients in NAFLD group were found to be obese.[13] In a study in rural India, 54% of NAFLD patients were neither over-weight nor obese which is in contrast to our study.[14] Probably genetic predisposition, life style, the body build (trunk to leg-length ratio) low muscularity, adaptation to chronic calorie deprivation, and ethnicity[15] could be a contributing factor forthe difference in this indigenous population.

Most studies report obesity especially central obesity, a common finding in NAFLD as an important risk factor for MS.[16] Our study also found a higher waist circumference in 95% of patients with NAFLD and 25% in control group. Among the NAFLD group, 34.6% (n=16) males had waist circumference > 90 cm and 65.2% (n=30) females had waist circumference > 80cm. These datas are similar to that of Fan et al,[17] who found the strongest association of central (WC) and overall obesity (BMI) with metabolic syndrome in Asia Pacific region. Central or abdominal obesity, which is more commonly associated with insulin resistance has been observed in 80–90% of Indian patients with NAFLD.[18] Similarly Asians have been found to have more intra-abdominal adipose tissue than white Caucasians, in spite of having low waist circumference, [19]and hence lower cut-offs (WC ≥ 90 cm in males and ≥ 80 cm in females) are recommended for identifying abdominal obesity in Asian Indians .[19] In a study by Ajay Duseja,[20] central obesity was found in 96.77% of subjects which is similar to the findings in our study. Adipose tissue is a dynamic endocrine organ that secretes a number of pro-inflammatory factors like cytokines and adipokines that are involved in the pathogenesis of atherosclerosis, endothelial dysfunction, insulin resistance and vascular remodelling.[21] The mean systolic blood pressure in the NAFLD group and control group were 129.6 and 123.9 mmHg respectively. The mean diastolic pressure in the NAFLD group and control group were 86.32 and 78.60 mmHg. In the NAFLD group 26.08% of patients (n= 12) had higher systolic blood pressure compared to 13.04% in the control group (n=6). Similarly 56.5% in the NAFLD group n= (26) and (15.2%) in the control group (n= 7) had higher diastolic pressure. Hypertension was observed in 10% to 12% of patients in a study by Ajay Duseja from New Delhi [20] which is low compared to our study. Hypertension was found in 45 (36.29%) of respondents in a study by Ajay Duseja[22] in North India which was high compared to our study. Hypertension, especially systolic hypertension is also an independent NAFLD predictor. [23]Cotrim et al [24] confirmed these data by reporting a very high prevalence of 64% hypertension among NAFLD patients. In a latest study by M.V. Jali, Sanjay Kambar et al [25] hypertension was present in 85% of subjects in NAFLD group, which is very high compared to all studies. In contrast, in a study conducted by Kaushal Madan [26] among Indians and Ajay Dusheja[20] in another study conducted in New Delhi reported hypertension in 10-12 % of patients in NAFLD group.

Dyslipidemia is known to be a risk factor for NAFLD in most Asia Pacific countries (Amarapurkar*et al*, 2007). In our study, in the NAFLD group 26.08% (n=12) and in the control group 13.03% (n=6) had total cholesterol > 200mg% and LDL cholesterol calculated using Friedwalds formula [27] was found to be > 100mg% in 21.7% (n=10) of the NAFLD group. Triglyceride levels were significantly higher among patients with NAFLD. About 26% (n=12) subjects in the NAFLD group had higher TG while it was 6.5% (n=3) in the control group. The HDL cholesterol < 40 mg% was observed in 75% (n=12) and in 50% (n=10) male subjects in the NAFLD group and control group respectively. It was < 50 mg% in 100% (n=30) female subjects in the NAFLD group and 69% (n=18) in the control group. This may be attributed to the increased intake of junk foods rich in trans- fatty acids which may have a role in increasing LDL cholesterol and lowering HDL cholesterol. Contrast to our study, in a study by Ajay Duseja,[23] low HDL cholesterol and high triglyceride level were detected in 38.71% and 66.13% of NAFLD patients respectively. In a latest study by M.V.Jali,[25] dyslipidemia has been reported in high percentage of patients with NAFLD. In a study done at MES Medical

college, Kerala by Sreenag M, Jimnaz PA et.al[21] TG was raised in 72.4% and HDL was low in 77.5% of patients with NAFLD. Unhealthy diet and lack of exercise could be the reason for high incidence of dyslipidemia. The study by Luxmi et al [28] also reported raised serum triglyceride level in patients with fatty liver and the same findings was also observed in our study.

Table no.1 The clinical and anthropometric parameters between the two groups.

Parameters	NAFLD group (mean±SD)	Control group (mean±SD)	't'	'p'
Age	41.26± 8.36	38.5 ± 9.19	1.516	0.133
W C in cm	95.83 ± 7.4	87.4 ± 5.8	6.043	0.001*
BMI - Kg/m^2	29.53± 5.24	24.74± 2.94	5.397	0.001*
Systolic BP in	129.6± 14.2	124.3± 12.2	1.941	0.055
DiastolicBP				
mmHg	85.2 ± 9.9	78.60 ± 7.1	3.697	0.001*

Table no.2 Comparison of Biochemical parameters of NAFLD group and control group.

Parameters in mg/dl	NAFLD group (mean ± SD)		Control group (mean ± SD)		't'	'p'
Total						
Cholesterol	190.6	± 34.1	162.0	± 31.9	4.146	0.001*
TG	153.7	± 78.1	119.5	± 31.6	2.755	0.007*
HDL	38.9	± 4.4	39.7	± 4.3	0.883	0.379
LDL	125.9	± 33.7	96.9 ± 32.2		4.227	0.001*

Table no. 3 Components of metabolic syndrome

Components of Metabolic syndrome		NAFLD Group N (%)	Control Group N (%)	X^2 test	'p' value
BMI-Kg/m^2		31(67%)	31(67%)	NA	NA
	Male	16 (100%)	3(15%)	25.77	0.0001*
WC	>90cm				
	Female	30 (100%)	8(30.1%)	30.61	.0000001*
	>80cm				
S BP		12(26%)	6(13%)	2.486	0.1149
≥135mmHg					
D BP		26(56%)	7 (15%)	17.06	0.00003*
≥ 85 mmHg					
	TG				
		12(26%)	3(6.5%)	6.452	0.011*
>150mg%					
	Male				
		12(75%)	10(50%)	5.3	0.021*
HDL	< 40				
mg%	Female	30(100%)	18 (69%)	3.125	0.077
	<50				

V. Conclusion

A definite association was observed between the anthropometric, clinical and biochemical parameters in NAFLD patients and the components of metabolic syndrome. Prevention is better than cure. Hence, USG evidence of fatty liver should be taken seriously as a predictor of metabolic syndrome as it is atherogenic and predisposes to diabetes, hypertension, dyslipidemia and has a strong potential for development of coronary vascular disease and T2DM at a younger age. The main limitation of our study is the sample size.

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