Original Research Article

Weight to Height Ratio is a Better Predictor of Non-Alcoholic Fatty Liver Disease in the South Asian Population

Abstract:

INTRODUCTION:

Numerous obesity indices have been developed that predict non-alcoholic fatty liver disease (NAFLD). We in our study aimed at evaluating a few of these tools including waist to height ratio (WHtR), waist circumferences (WC), body mass index (BMI) and fatty liver index (FLI) and used them to determine their ability in diagnosing NAFLD.

METHODS:

This cross sectional study was conducted at the outpatients' department of our hospital.NAFLD was diagnosed on the basis of ultrasound abdomen. Anthropometric parameters like Height (in), weight(cm), WC (cm), BMI, WHtR were calculated and later the FLI (comprising of BMI,WC, triglyceride and gamma glutamyl transferase) was calculated. The Receiver operating characteristic analysis (ROC) was then conducted to determine the discriminatory ability and related cut-off points and a P value of ≤0.05 was taken as statiscally significant.

RESULTS:

A total of 300 participants were included and the prevalence of NAFLD was 44.8% in men and 54.8% in women. Univariate analysis reported statistical significant association of NAFLD with all of the applied indices (P = 0.00). The WHtR (AUC = 0.87, 95% CI:0.77-0.97) showed slight superior ability as compared to FLI (AUC = 0.86, 95% CI:0.76-0.97) in diagnosing NAFLD. Regression analysis revealed a stronger association of WHtR (OR = 9.3, P = 0.00) with NAFLD compared to FLI (OR = 6.0, P = 0.02) .

The performance of WHtR was similar regardless of gender (AUC = 0.89) while different in FLI with a AUC of 0.88 in men and AUC of 0.85 in female

CONCLUSION:

Hence our study showed a strong association of WHtR in prediction of NAFLD and a similar discrimatory ability regardless of gender. WHtR is simple and easily performable modality for NAFLD prediction.

Keywords: Non alcoholic fatty liver disease, BMI, Fatty liver index; Waist circumference

INTRODUCTION:

Non-alcoholic fatty liver disease (NAFLD) is developing as a substantial health burden raising serious clinical and public health concerns [1]. It is defined as hepatic fat accumulation in the absence of other causes including significant alcohol consumption (more than 14 standard drinks per week for men and more than 7 standard drinks for females[2]) and use of steatogenic medications.

NAFLD encircles a wide spectrum of diseases, ranging from simple steatosis; steatohepatitis without and with fibrosis (NASH); and cirrhosis or even hepatocellular carcinoma).[1] Globally the prevalence of NAFLD is reported to be around 25%, while in the Asian countries it ranges between 15–45%.[3,4] It's estimated prevalence in Pakistan has been documented to be 18%.[5] NAFLD is a multifactorial disorder and most frequently associated to obesity, diabetes mellitus, dyslipidaemia and metabolic syndrome. Studies have documented that the Asian population have a high percentage of body fat that too at a low BMI.[6,7] Liver biopsy is considered the gold standard for quantification of liver steatosis in NAFLD.[8] However, being an invasive procedure, it is seldom performed and has its own complications .[9] Therefore, noninvasive methods including imaging techniques, anthropometric indices i.e: waist to height ratio (WHtR), fatty liver index (FLI), waist circumference (WC); and blood test based formulas have been developed to asses liver steatosis.10-12

Fatty liver index (FLI) is a simple score that is based upon 4 parameters: namely the body mass index (BMI), waist circumference (WC), triglyceride (TG), and gamma glutamyl transferase (GGT) levels. It gives a quantitative estimate of steatosis, ranging from 0 to 100. A FLI score of <30 rules out steatosis while a FLI score ≥60 is suggestive for fatty liver.[13] One study from Italy reported on how the FLI could accurately identify NAFLD with AUC of 0.827.[14] While Jae-Hyung Roh et al.[15] stated in their study that increased FLI was independently associated with a greater risk for hypertension.

Hence we in our study aimed to assess the discriminatory ability of these anthropometric indices for the early prediction NAFLD. This would in turn help us avoid health related complications in our population.

As we are using ultrasound for fatty liver we should use some justification .. some study related to compare it with liver biopsy

Material and Methods:

This cross-sectional study was performed at the outpatients' setting at the Hepatogastroenterology department of Sindh Institute of Urology and Transplantation, SIUT, Karachi, Pakistan. All patients aged between 18 years to 65 years were included in this study.A total of 300 participants were inducted during a 6 months period. Those having significant alcohol consumption, testing positive for the presence of hepatitis B surface antigen or anti-hepatitis C virus antibodies, previously diagnosis with Fatty liver disease or diagnosed with fatty liver disease secondary to drugs were excluded.

Data collection:

All those inducted were subjected to blood tests (including Liver function test, fasting Lipid profile, Fasting blood sugar) after an over night fasting of 8 hours.Later on anthropometric parameters were checked, namely waist circumference, weight and height to calculate the BMI. The height was measured (centimetres) in an upright position in all patients with the heels and buttocks in contact with the wall. Waist circumference was measured at the midpoint of the distance between the lowest costal ridge and the upper border of the iliac crest. Blood pressure was measured, after a minimum 5-min rest period in a quiet room, while participants were in the sitting position.

Following which the subjects underwent an ultrasound abdomen. All ultrasound examinations were carried out by a single sonographer, having a 5 years of experience in the field.A 3-5 MHz transducer was used to examine the liver parenchyma and thereby provide sagittal, longitudinal, lateral, and intercostal views. Fatty liver disease was confirmed if a marked increase of hepatic echogenicity was diagnosed or if the hepatic vessels and diaphragm appeared abnormal.Later on, weight, height, waist circumference, and blood pressure were measured by trained healthcare staff.

NAFLD (full form) was determined *via* evidence of hepatic steatosis in the sonogram and a lack of evidence of other causes of acute or chronic hepatitis.

FLI was calculated based on laboratory and anthropometric measures, including TG, GGT, BMI, and WC, by using the following formula:

$$FLI = [e0.953 \times \ln(TG) + 0.139 \times BMI + 0.718 \times \ln(GGT) + 0.053 \times WC - 15.745/(1 + e0.953 \times \ln(TG) + 0.139 \times BMI + 0.718 \times \ln(GGT) + 0.053 \times WC - 15.745)] \times 100$$

WHtR (full form) was calculated by dividing waist circumference (unit) with height. (unit)

BMI was calculated by weight in kg / height in m^2

Statistical analysis

The capability of FLI to discriminate NAFLD was evaluated by using receiver operating characteristic (ROC) curve, while related area under curve (AUC) was plotted to calculate cut off values for FLI. The lower boundary line for AUC was considered to be 0.5, with a significantly greater area than 0.7 showing the ability of FLI to discriminate NAFLD. The optimal cutoff point of FLI was also determined using maximal values of Youden's J statistics [max (J = sensitivity + specificity- 1)]. The value of FLI corresponding to a maximum value of the Youden's index was considered the optimal cutoff point for FLI.

Multivariate logistic regression analysis was conducted on NAFLD as an outcome variable alongside additional relevant predictor variables. Three potential predictor variables, including age, gender and waist to height ratio (WHtR) were entered into the model in addition to FLI. The odds ratio and related confidence intervals were reported along with *P* values. The significance level for all analyses was considered to be 0.05. All statistical analyses were conducted using version 21 of SPSS.

Results:

A total of 300 patients with mean age of 41.6 ± 11.8 years (range: 18-65 years) were enrolled in this study. Table 1 shows the mean age, anthropometric characteristics, and laboratory values of the study participants.

Table 1. Anthropometric characteristics and laboratory values of study population. (units)	
Characteristic	Mean ± SD
Age (years)	41.6 ± 11.8
Gender	
-Male	136 (45.33%)
-female	164 (54.66%)
BMI (kg/m^2)	26.75 ± 6.1
WC (cm)	96.1 ± 15.1
Height (cm)	156.45 ± 8.35
WHtR	0.59 ± 0.09
FLI	49.6 ± 30.8
ALT	35.5 ± 28.7
GGT	39.3 ± 34.3
Triglycerides	165.8 ± 84.4
HDL	42.2 ± 10.8

In the total population, the AUC of FLI in predicting NAFLD was 0.887 (95%CI: 0.77-0.97), in which significant difference was seen between men (AUC = 0.8648, 95%CI: 0.8504-0.8791) and women (AUC = 0.857, 95%CI: 0.76-0.97). WHtR (AUC = 0.877, CI: 0.77-0.97) showed slight better performance compared to FLI. The performance of WHtR was similar between men and women (AUC = 0.897). optimal cut off point of WHtR in men was 0.55 (sensitivity = 81% and specifity = 76%) and in women was 0.6 (sensitivity = 85% and specifity = 86%).

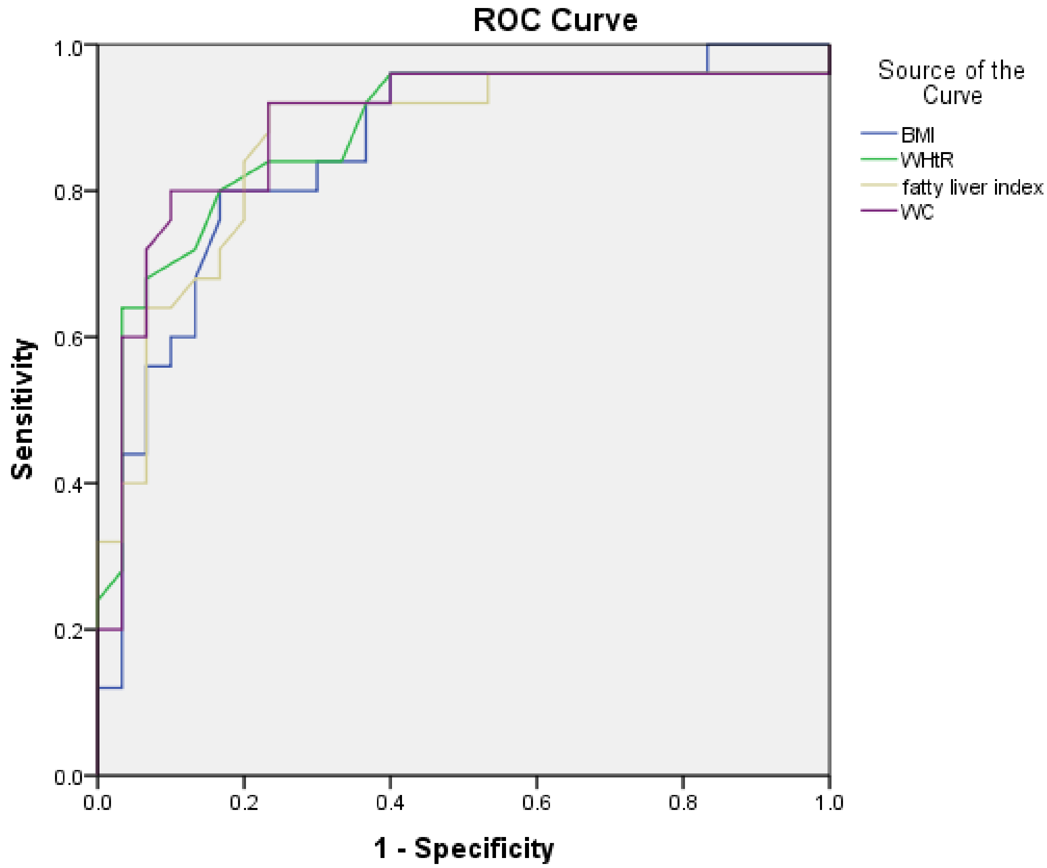

Fig 1: Sensitivity and ROC curve distribution

As shown in Table 2 univariate analysis revealed statistically significant association of NAFLD with all the applied indices (p= 0.001), while regression analysis reported stronger association of WHtR (OR = 9.3, p= 0.001) compared to FLI (OR = 6.0, p= 0.002) with NAFLD.

Discussion

With the growing epidemic of obesity, the prevalence of fatty liver is also increased.The Asian population have a high percentage of body fat at a low BMI.[6-7] This can also be attributed that Asians have lower height than western population. Asian people have a significantly higher incidence of metabolic syndrome than other ethnic groups with similar BMI. In sight of the public health issue of the ever growing prevalence of NAFLD and its hepatic and extrahepatic consequences, the development of simple cost-effective screening methods has become extremely important. In the present study, we aimed at evaluating various obesity indices based upon anthropometric measures including waist to height ratio (WHtR), waist circumference (WC), body mass index (BMI) and fatty liver index (FLI) and to determine the discriminatory ability of these indices in diagnosing NAFLD.

NAFLD is more common in obese patients and it has been noted that prevalence of NAFLD in obese is up to 44.87%.[16] In our study population 69% were obese had BMI >25kg/m^2 and most of subjects were females with average BMI of 26.75 ± 6.1 had a statistically significant association with NAFLD (p=0.001). However BMI representative of body adiposity differs in different ethinic groups and is not true representative of visceral obesity. Wang J *et al.*[6] and Deurenberg *et al.*[7] have documented that Asian population have a high percentage of body fat at a low BMI. Therefore, BMI may not be an accurate measure of body adiposity in the Asian population. Furthermore, Grasgruber *et al*.[17] demonstrated that population of tropical Asia have short stature due to low protein consumption in diet. Although we reported statistical significant association with NAFLD; BMI may not be an accurate predictor of NAFLD in this population.

Waist-to-height ratio (WHtR), a simple and effective anthropometric index, has recently received attention as a marker of "early health risk".[18] Several studies have shown that WHtR has strong relationship with NAFLD and it varies in different population. In the present study, WHtR was used as an indicator of central obesity and the effect of WHtR on the NAFLD was investigated.

Motamed *et al.*[19] showed that average WHtR in Iranian NAFLD patients is 0.61 ± 0.07 majority of which were males (53.76%). Similarly Zheng *et al.*[20] proposed 0.59 ± 0.06 is the average WHtR in Chinese NAFLD patients and majority of their study population were males (75.6%). Hyun-Jae Lim *et al.*[21] observed 0.52 ± 0.05 is the lower cut off value of WHtR in Korean women with NAFLD. We documented optimal cut off point of WHtR in men was 0.55 (sensitivity = 81% and specificity = 76%) and in women was 0.6 (sensitivity = 85% and specificity = 86%)

with average WHtR of 0.66 ± 0.08 and the majority of patients were females (54.66%). This can be accredited to the sociocultural norms of our country where women have limited physical activities. Our results also showed WHtR has statistically significant association with NAFLD (p=0.0001). WHtR (AUC = 0.877, CI: 0.77-0.97) showed slight better performance compared to FLI.

FLI is a feasible marker that involves four clinical available parameters, and it is easily calculated in an office setting. It has been proven to correlate well with fatty liver diagnosed by ultrasonography.[13] Calori et al. further showed that FLI was associated with all-cause, hepatic-related, cardiovascular disease-related, and cancer mortality.[22] This suggests that FLI could be applied not only for screening fatty liver disease, but also for identifying high-risk groups of subjects for metabolic and cardiovascular disorders, which are critical public health issues that are worthy of concern. However, due to variations in ethnicity, dietary, and environmental factors, the cut-off for waist and BMI is different for Asian people.[23] Our study confirmed the significance of FLI as an indicator of ultrasonogrphic fatty liver and its close link to metabolic syndrome. We found that FLI could accurately detect NAFLD with a good AUC of 0.887 (95%CI: 0.77-0.97) and the optimal cut-off point of the FLI for diagnosing NAFLD was 30. We documented slight difference in the performance of FLI for both sexes. This could be explained by the fact that female population in our society had higher BMI and showed more metabolic derangement, which are both important determinants of fatty liver disease. Two studies on Caucasian population by Carvalhana et al[24] (2013) and Meffert et al[25] (2014) has also reported satisfactory performance of FLI for diagnosing NAFLD with AUC of 0.930 and 0.890 respectively. Recently a population based study from Pakistan has provided strong evidence on discriminatory power of FLI to diagnose NAFLD (AUC: 0.84 (95% CI: 0.81–0.87).[26] These results are in concordance with findings of our study. Our study confirmed FLI had better discriminative ability for identifying ultrasonogrphic fatty liver than other serum markers and could therefore be recommended for Asian subjects.

There were few limitations in our study since liver biopsy, which is the gold standard to diagnosing NAFLD was not performed in our study population, however; ultrasound abdomen has sensitivity ranging from 89-91% with specificity between 82-93% in diagnosis of NAFLD.[27-29] Furthermore; since our study was a non-randomized observational study and was limited by patient selection bias along with being a single centre based study having a small sample size, therefore the results might not be generalized to larger populations. Thus, further validation of results through large clinical studies are required to assess the true association of NAFLD and FLI.

Conclusion

In conclusion, FLI has a promising predictive value in the diagnosis of NAFLD. However, according to our findings, FLI was not more effective than WC and WHtR in the discrimination of NAFLD.

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