Original Article

Prediction of Non-Alcoholic Fatty Liver Disease (NAFLD) in Both Lean and Obese Patients Utilizing the Waist to Height Ratio (WHR) and Fatty Liver Index (FLI)

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is a burgeoning health issue with a global prevalence that mirrors the rise in obesity and metabolic syndrome. Non-invasive diagnostic indices like the Waist to Height Ratio (WHtR) and the Fatty Liver Index (FLI) are crucial for early detection and management, offering an alternative to the invasive liver biopsy. These indices are particularly pertinent for populations with distinctive body compositions, such as those seen in Asian countries, where traditional measures like Body Mass Index (BMI) may not accurately reflect metabolic risk.

Objective: To evaluate the efficacy of WHtR and FLI as non-invasive diagnostic tools for NAFLD in both lean and obese populations, and to identify the most reliable indicator for predicting the presence of fatty liver disease across different body compositions.

Methods: This cross-sectional study was approved by the Ethical Review Board (ERC-771) and conducted at the Sindh Institute of Urology and Transplantation. It included 757 participants aged 18-70 years, with 559 lean and 298 obese individuals based on BMI classifications. Exclusion criteria included other forms of hepatitis, use of steatogenic medication, and significant gastrointestinal disorders. Diagnostic measures included abdominal ultrasonography performed by an expert radiologist and calculation of WHtR and FLI. Statistical analyses were performed using SPSS version 25, and diagnostic accuracy was assessed through sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and Area Under the Receiver Operating Characteristic (AUROC) curves.

Results: Fatty liver was detected in 49% of obese patients and 33% of lean patients. The obese cohort demonstrated a WHtR >0.63 with a diagnostic accuracy of 94.63%, whereas the FLI had a diagnostic accuracy of 83.6% for a cutoff >74. In lean patients, FLI >16.5 was more predictive of NAFLD with a diagnostic accuracy of 96.96%, as opposed to WHtR, which was less effective. The AUROC for WHtR and FLI in obese patients was 0.847 and 0.704, respectively, while in lean patients, the AUROC for FLI was 0.875, suggesting superior diagnostic performance over WHtR.

Conclusion: The study confirms that WHtR and FLI are valuable non-invasive tools for predicting NAFLD, with WHtR being more effective in obese patients and FLI showing greater reliability in lean patients. These findings highlight the need for tailored approaches in diagnosing NAFLD according to body composition. Further large-scale, multicentric research is needed to generalize these diagnostic cut-offs.

Keywords: Non-Alcoholic Fatty Liver Disease, NAFLD, Waist to Height Ratio, WHtR, Fatty Liver Index, FLI, Diagnostic Indices, Hepatic Steatosis, Cross-Sectional Study, Body Mass Index, BMI, Ultrasound Imaging, Sensitivity, Specificity, AUROC.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is characterized by hepatic steatosis confirmed either through radiological imaging or histological assessment, after excluding secondary causes such as significant alcohol consumption, hepatotoxic medication use, or inherited liver diseases (1). With a global prevalence estimated at 25% and varying rates in Asia and specifically Pakistan—ranging from 15-45% and 18% respectively (2-4)—NAFLD represents a significant public health challenge. This condition progresses from non-alcoholic fatty liver (NAFL) to the more severe non-alcoholic steatohepatitis (NASH), the latter associated with a greater risk of advancing to hepatic fibrosis and increased liver-related mortality (5). Notably, despite lower body mass indexes (BMIs) compared to Western populations, Asians, and particularly South Asians, exhibit comparable rates of metabolic disorders and tend to carry more body fat, particularly abdominal fat, at any given BMI level, heightening their risk for metabolic complications (6-10). This higher predisposition to body fat is partly attributed to generally shorter statures among Asians. Interestingly, NAFLD can also manifest in lean individuals, classified as metabolically obese normal weight (MONW) individuals, who display distinct features such as elevated insulin levels and less hepatic necro-inflammatory activity (11).

Given the limitations of BMI as an accurate indicator of adiposity, alternative obesity indices based on anthropometric measurements have been developed to improve NAFLD diagnosis. Among these, the waist to height ratio (WHtR) and the Fatty Liver Index (FLI) stand out for their applicability and effectiveness. WHtR, in particular, has proven to be a straightforward yet effective measure of visceral obesity and associated cardio-metabolic risk, with a WHtR greater than 0.5 showing a significant correlation with NAFLD (12-14). FLI, formulated from variables including serum triglyceride levels, BMI, waist circumference, and Gamma Glutamyl Transpeptidase levels, has also been validated as a predictive index for NAFLD (15). Different optimal cut-off points for these indices have been suggested for different populations; for instance, Chunlong Li and colleagues identified that the optimal cut-offs for WHR and FLI for NAFLD varied across the entire, lean, and overweight/obese populations within a Chinese cohort, being set at 0.50 and 20, 0.47 and 10, and 0.53 and 45, respectively (16).

Despite extensive global research into non-invasive methods for detecting NAFLD, limited studies have been conducted in Pakistan, particularly concerning the non-obese demographic. Earlier studies, such as those by Khan RTY et al., evaluated NAFLD prevalence among non-obese Pakistani individuals (17), underscoring the necessity for further research in this area. By focusing on simple anthropometric parameters like WHtR and FLI, our study aims to determine NAFLD frequency in both obese and lean populations, thereby facilitating early detection without the need for invasive procedures like liver biopsy and helping identify individuals at risk of severe liver complications such as cirrhosis. This approach is crucial in broadening our understanding of NAFLD's impact on diverse body types, thereby enhancing community health strategies and interventions targeted at this escalating condition.

MATERIAL AND METHODS

This cross-sectional study received ethical approval from the Ethical Review Board (ERC-771) at the Sindh Institute of Urology and Transplantation (SIUT), where it was carried out from July 1, 2022, to December 31, 2023. The study involved male and female patients aged 18-70 years presenting with upper abdominal pain. Patients were meticulously screened, and those with any other form of hepatitis (including viral, autoimmune, metabolic, alcoholic, and vascular), those on steatogenic medications, and those with a history of significant gastrointestinal disorders such as tuberculosis, malignancy, inflammatory bowel disease, end-stage renal disease, or familial liver disorders were excluded to eliminate potential biases.

Informed consent was obtained from all participants who met the inclusion criteria at the outpatient department of Hepatogastroenterology at SIUT. Initial assessments included the calculation of body mass index (BMI) and waist circumference (WC) to classify participants into lean or obese categories. Diagnostic imaging involved an ultrasound of the abdomen to assess for hyper-echoic liver tissue indicative of NAFLD, performed by an expert radiologist with over a decade of experience in sonology. Concurrently, blood samples were collected for fasting lipid profiles and fasting blood sugar levels. The waist-to-height ratio (WHtR) and Fatty Liver Index (FLI) were computed for each participant using predefined formulas.

The study utilized a non-probability consecutive sampling technique. Based on prior studies indicating a 25% prevalence of NAFLD in lean or non-obese populations, a sample size of 255 patients was calculated to achieve a 95% confidence level with a 5% margin of error.

Table 1: Operational Definitions

Term	Definition	Reference
NAFLD	Diagnosed based on hyperechoic liver on ultrasound.	(1, 17)
Lean NAFLD	NAFLD in patients with a BMI < 23 kg/m².	(17)

Term	Definition	Reference
Overweight/Obese NAFLD	NAFLD in patients with a BMI ≥ 28 kg/m².	(18)
Waist to Height Ratio (WHtR)	WHtR = Waist Circumference (cm) / Height (cm), with WC measured midway between the lowest rib and the iliac crest.	(13)

Data were collected meticulously and analyzed retrospectively using the Statistical Package for the Social Sciences (SPSS version 25.0). Descriptive statistics such as frequencies and percentages articulated the distribution of categorical variables, while mean ± standard deviation represented quantitative metrics. Comparative analysis of categorical variables was conducted using the Chi-square test, and the Student's t-test was employed for continuous variables. Statistical significance was ascertained at a p-value of ≤ 0.05. Advanced diagnostic performance metrics including the Area Under the Receiver Operating Characteristic (AUROC) curve were generated for WHtR and FLI in diagnosing NAFLD among both lean and obese patients. Optimal cutoffs were determined, from which sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were calculated for each index. This rigorous analysis aimed to validate the effectiveness of WHtR and FLI as non-invasive predictors of NAFLD in diverse patient populations.

RESULTS

In the study comprising a total of 757 participants, distinct variations were observed between the lean population (n=559) and the obese population (n=298) across several health-related variables. The distribution of gender across both cohorts did not show a statistically significant difference with 44% males in the lean group and 48% in the obese group (p=0.124). Age was comparable between the two groups with a mean of 36.2 years in the lean population and 37.6 years in the obese population, with the difference not reaching statistical significance (p=0.543). Notable disparities emerged in hypertension prevalence, with 31% in the lean group and 48% in the obese group, indicating a statistically significant higher incidence in the obese population (p<0.001). The occurrence of diabetes mellitus was similar across groups (p=0.178), as was the case with hypertriglyceridemia (p=0.254). Smoking prevalence was markedly lower in the obese population at 2.4% compared to 5.7% in the lean population, and this difference was statistically significant (p<0.001). Furthermore, the presence of fatty liver was significantly more common in the obese group (49.7%) than in the lean group (33%) (p<0.001). Waist circumference and BMI also differed significantly between the two groups, with means of 87 cm and 21 kg/m² for the lean group, and 108.7 cm and 30.7 kg/m² for the obese group, respectively (p<0.001 for both). Additionally, the Waist to Height Ratio (WHtR) and the Fatty Liver Index (FLI) were notably higher in the obese group, with a WHtR mean of 0.67 compared to 0.54 in the lean group (p=0.002), and an FLI mean of 78 compared to 20 in the lean group (p<0.001), as outlined in Table-2.

Table-2: Baseline Characteristics of the Studied Population (n=757)

Variables	Lean Population (n=559)	Obese Population (n=298)	p-value
Gender (Male/female)	245/314 (44%/56%)	142/156 (48%/52%)	0.124
Age (years) (Mean ± SD)	36.2 ± 8.9	37.6 ± 10.3	0.543
Hypertension (Y/N) (%)	173/386 (31%/69%)	144/154 (48%/52%)	<0.001
Diabetes mellitus (Y/N) (%)	184/375 (33%/67%)	85/213 (29%/71%)	0.178
Hypertriglyceridemia (Y/N) (%)	224/335 (40%/60%)	127/171 (43%/57%)	0.254
Smoking (Y/N) (%)	30/529 (5.7%/94.3%)	7/291 (2.4%/97.6%)	<0.001
Fatty liver (Y/N) (%)	185/374 (33%/67%)	148/150 (49.7%/50.3%)	<0.001
Waist circumference (cm) (Mean ± SD)	87 ± 6.1	108.7 ± 6.8	<0.001
BMI (kg/m²) (Mean ± SD)	21 ± 1.6	30.7 ± 3.3	<0.001
Waist to Height Ratio (WHtR) (Mean ± SD)	0.54 ± 0.46	0.67 ± 0.05	0.002
Fatty Liver Index (FLI) (Mean ± SD)	20 ± 12	78 ± 15	<0.001

Table-3: Comparison of Baseline Characteristics in Predicting Obese NAFLD (n=298)

Variables	Obese NAFLD (n=148)	Obese non-NAFLD (n=150)	p-value
Gender (Male/Female) (%)	67/81 (45%/55%)	75/75 (50%/50%)	0.414
Hypertension (Y/N) (%)	92/56 (62%/38%)	52/98 (35%/65%)	<0.001
Diabetes (Y/N) (%)	40/108 (37%/63%)	45/105 (30%/70%)	0.570
Hypertriglyceridemia (Y/N) (%)	58/90 (39%/61%)	69/81 (46%/54%)	0.348

Variables	Obese NAFLD (n=148)	Obese non-NAFLD (n=150)	p-value
Smoking (Y/N) (%)	4/144 (2.7%/97.3%)	3/147 (2%/98%)	0.662

Table-4: Comparison of Baseline Characteristics in Predicting Lean NAFLD (n=559)

Variables	Lean NAFLD Yes (n=185)	Lean NAFLD No (n=374)	p-value
Gender (Male/Female) (%)	87/98 (48%/52%)	158/216 (42%/58%)	0.284
Hypertension (Y/N) (%)	83/102 (45%/55%)	90/284 (24%/76%)	<0.001
Diabetes (Y/N) (%)	61/124 (33%/67%)	123/251 (33%/67%)	0.980
Hypertriglyceridemia (Y/N) (%)	77/108 (42%/58%)	147/227 (39%/61%)	0.824
Smoking (Y/N) (%)	5/180 (0.2%/99.8%)	25/349 (0.7%/99.3%)	0.170

Table-5: Diagnostic Accuracy of FLI and WHtR in Predicting NAFLD

Parameters	Measure	Obese NAFLD (FLI > 74)	Lean NAFLD (WHtR > 0.63)	Lean NAFLD (FLI > 16.5)
Sensitivity	%	68.9%	97.3%	98.38%
Specificity	%	98%	92%	96.26%
Positive Predictive Value (PPV)	%	97.14%	92.31%	92.86%
Negative Predictive Value (NPV)	%	76.17%	97.18%	99.17%
Diagnostic Accuracy	%	83.6%	94.63%	96.96%

A focused examination of the obese cohort (n=298) with respect to NAFLD revealed that gender distribution between the NAFLD and non-NAFLD subgroups did not significantly differ (p=0.414). However, hypertension was significantly more prevalent in the NAFLD subgroup (62%) versus the non-NAFLD subgroup (35%) (p<0.001). No significant differences were observed in the rates of diabetes and hypertriglyceridemia between the two obese subgroups. The smoking rates were low and comparable in both subgroups (Table-3).
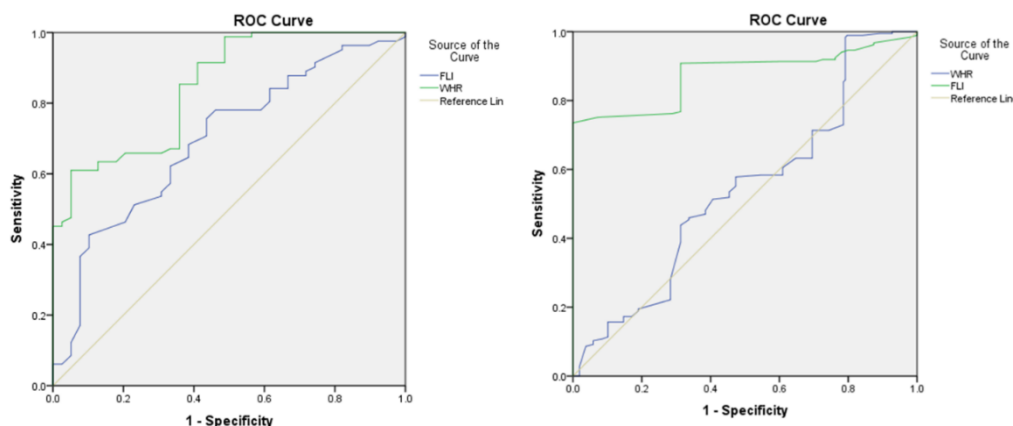

Figure 1 ROC Curves comparing the diagnostic accuracy of WHtR and FLI for NAFLD in obese and lean populations, with corresponding AUROCs and significance levels.

For the lean population (n=559), gender differences were also non-significant between those with and without NAFLD (p=0.284). Hypertension showed a significant association with NAFLD presence (p<0.001), whereas diabetes, hypertriglyceridemia, and smoking did not significantly correlate with NAFLD in lean individuals (Table-4).

The diagnostic accuracy of FLI and WHtR was quantitatively assessed in predicting NAFLD. In the obese group, the FLI demonstrated a sensitivity of 68.9%, specificity of 98%, a PPV of 97.14%, an NPV of 76.17%, and a diagnostic accuracy of 83.6% for an FLI greater than 74. For the lean group, WHtR with a cutoff greater than 0.63 had a sensitivity of 97.3%, a specificity of 92%, a PPV of 92.31%, an NPV of 97.18%, and a diagnostic accuracy of 94.63%. The FLI, with a threshold of greater than 16.5, showed even higher sensitivity (98.38%) and NPV (99.17%) for lean individuals, emphasizing its potential as a strong predictive tool for NAFLD in this population (Table-5).

ROC curves for both groups illustrated these findings graphically, with the WHtR exhibiting a higher AUROC in the obese group (0.847, p<0.001) compared to the lean group (0.541, p=0.119), and the FLI showing robust predictive accuracy in both the obese (0.704, p<0.001) and lean patients (0.875, p<0.001) (Figures 1 & 2). These graphical representations underscore the differential diagnostic performance of the two indices across diverse body compositions.

DISCUSSION

In the conducted study, the application of non-invasive scores, specifically the Waist to Height Ratio (WHtR) and the Fatty Liver Index (FLI), was integral in the diagnosis and monitoring of Non-Alcoholic Fatty Liver Disease (NAFLD) (18). These measures are particularly valuable given their utility in non-invasive assessment, negating the need for more invasive and costly procedures like liver biopsies. The data, gathered from patients undergoing routine physical examinations, provided a foundation for predicting fatty liver presence, a condition found in 49% of obese participants compared to 33% of lean counterparts. Comorbid conditions such as hypertriglyceridemia, diabetes, and hypertension were prevalent within the lean NAFLD group, showcasing a risk factor pattern. In contrast, hypertension followed by hypertriglyceridemia and diabetes was more commonly associated with obese individuals with NAFLD.

The study's findings regarding the predictive efficacy of WHtR and FLI in diagnosing NAFLD among obese patients diverged, revealing WHtR's superior diagnostic accuracy (94.63%) when compared to FLI (83.6%). This contrasted with results in lean NAFLD patients, where the FLI emerged as a more reliable marker for hepatic steatosis with a cutoff value of >16.5, while WHtR performed suboptimally. This discrepancy highlights the complexity of diagnosing NAFLD and the potential need for different diagnostic criteria based on body composition (19, 20). Interestingly, the percentage of fatty liver in the lean population was higher than typically seen in Western populations. This phenomenon might be attributed to the distinct body fat distribution in Asian demographics, wherein visceral obesity is prevalent, potentially leading to normal-range BMI despite significant liver steatosis (19, 20). The association between visceral adiposity, insulin resistance, and increased lipolysis could be contributing factors to the observed hepatic fat deposition (21, 22). This study's observations aligned with previous research, noting that increased serum ALT and GGT levels correlate with intrahepatic oxidative stress and steatosis (23). The majority of lean NAFLD patients in the study also presented with comorbid conditions such as hypertension, diabetes mellitus, and dyslipidemia, aligning with these findings.

Consistent with earlier research, FLI demonstrated its utility as a diagnostic marker for lean NAFLD, with a proposed cutoff value of >16.5, offering a potentially valuable tool for clinicians (24-26). For obese populations, fatty liver's association with metabolic syndrome was evidenced by a 49% prevalence rate among study participants, a finding in line with established literature (27). Notably, WHtR displayed remarkable sensitivity and diagnostic accuracy in obese patients, asserting its relevance in this demographic.

The study illuminated the practicality of calculating non-invasive indices, which could play a significant role in reducing the medical and economic burdens associated with NAFLD diagnosis, potentially impacting related morbidity and mortality rates positively.

The study did, however, encounter limitations. The absence of liver biopsy—considered the definitive diagnostic test for NAFLD—means that ultrasound was the sole modality used to ascertain fatty liver presence. Although a single experienced radiologist conducted all ultrasound examinations to minimize observer bias, the inherent limitations of ultrasound, including operator dependence, must be acknowledged. Additionally, the study did not incorporate measures of insulin resistance and the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) index, both of which have strong correlations with NAFLD. The lean NAFLD sample size was another constraint, indicating a need for more extensive, multicenter studies to validate these findings.

CONCLUSION

In conclusion, the study corroborated the effectiveness of non-invasive markers such as WHtR and FLI in predicting fatty liver disease across lean and obese populations. While the study found that WHtR may not be as accurate for predicting lean NAFLD, the ease of obtaining FLI components makes it a reproducible and cost-effective marker. Nonetheless, to establish these indices as reliable diagnostic tools, further multicentric studies with larger sample sizes are warranted.

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