Original article



Role of Anthropometric Indices in Prediction of Non-Alcoholic Fatty Liver Disease in Type 2 Diabetes Mellitus Patients

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Abstract

Introduction: The growing global incidence of diabetes, obesity and metabolic syndrome presents substantial public health challenges and is now recognized as a contributing factor to various systemic diseases. Also diabetic individuals, in particular, face a heightened risk, emphasizing the gravity of the underlying health issue. Failure to promptly recognize NAFLD can present a formidable healthcare obstacle. Anthropometric indicators are significant in understanding the intricate relationship between obesity, NAFLD, and diabetes in the Indian demography. <u>Aim:</u> Establishing connections between diverse anthropometric indices, such as BMI, WHR, WHR and NAFLD, pinpointing which of the patients diagnosed with type 2 diabetes displayed the most significant predictive efficacy when considering these indicators. <u>Material and Methods:</u> Data from 132 diabetic patients was scrutinized, standard methodologies were employed for collecting anthropometric data, ultrasonography was utilized and routine pathological and biochemical investigations were conducted. <u>Results:</u> The study unveiled correlation between BMI, waist to hip ratio and NAFLD in individuals with type 2 diabetes diagnosis. <u>Conclusion:</u> Anthropometric indices such as BMI, waist to hip ratio and waist to height ratio can serve as efficient methods for identifying NAFLD, followed by an early intervention to tackle obesity, and help in reducing their negative effects on type 2 diabetes mellitus.

Keywords: BMI, NAFLD, Type 2 Diabetes Mellitus, Waist-to-Hip Ratio (WHR), Waist-to-Height Ratio (WHtR), APR (Anthropometric Parameters of Risk).

Introduction

Amidst the escalating prevalence of corpulence and metabolic syndrome, NAFLD and Type 2 Diabetes Mellitus have emerged as conspicuous public health quandaries on a global scale, impacting nations across diverse developmental stages. The intricate inter-play among adiposity, insulin resistance, Type 2 diabetes, dyslipidemia and NAFLD encompasses a myriad of molecular, biochemical, and convoluted immunological mechanisms. This intricate web of connections underscores the global impact of these health issues, influencing populations across a broad spectrum of socio-economic development^[1]. In the realm of hepatic health, NAFLD emerges as a complex condition marked by the excessive accrual of hepatic fat spanning from mere hepatic steatosis to the more severe steatohepatitis and in advanced cases progressing to liver cirrhosis ^[2]. The worldwide prevalence of NAFLD exhibits substantial variance with estimates ranging from 6% to 35% [3]. Also notably there is a rise reported at 25% among the Indian demographic [4] and Type 2 Diabetes Mellitus plays a considerable function as a trigger in the establishment of NAFLD ^[5]. Multiple studies highlight that the occurrence of NAFLD in patients with type 2 diabetes mellitus is more than double that of the general population with a total

prevalence of 55.5% and the worldwide occurrence of non-alcoholic steatohepatitis shortly termed as NASH among persons with type 2 diabetes is estimated at 37.3%. For individuals having liver biopsy among the category of NAFLD, patients with concurrent type 2 diabetes mellitus a worrisome 17% exhibit symptoms of advanced fibrosis ^[6]. The presence of NAFLD with Type 2 DM raises the likelihood of diabetic complications. In the context of Type 2 Diabetes Mellitus, cardiovascular events in NAFLD have risen by 1.87-fold ^[7]. NAFLD also enhances the risk of microvascular complications in diabetes, such as chronic kidney disease and retinopathy^[8]. Also additionally there is a suspicion that advanced forms of NAFLD including NASH, advanced fibrosis, cirrhosis, and hepatocellular carcinoma (HCC), are more frequent in diabetic and prediabetic patients ^[9]. Central obesity, as opposed to total obesity, shows a robust pathogenetic connection to NAFLD ^[10]. The exact measurement of visceral fat appears as a significant technique for identifying patients at high risk of NAFLD [11]. Several investigations have proven relationships between anthropometric measures like BMI and WC ^[12] and metabolic syndrome, insulin resistance, and histological findings particularly steatohepatitis and fibrosis in NAFLD patients ^[13]. These connections are important for analyzing risk and prognosis factors in these individuals. In the arena of surrogate indicators characterizing abdominal adiposity, the pertinence of measurements such as Waist Circumference, Waist to Height Ratio, and Waist to Hip Ratio ascends to critical relevance. Since NAFLD is viewed as the hepatic manifestation of metabolic syndrome ^[14], utilizing these simple anthropometric indices could aid in identifying NAFLD patients at out- patient departments ^[15]. Consequently, early dietary and lifestyle modifications can be implemented to manage obesity and address NAFLD. This investigation aims to delve into the intricate relationship among various factors, particularly exploring the correlation between anthropometric indices such as BMI, Waist to Hip Ratio and Waist to Height Ratio in relation to NAFLD within a group of individuals diagnosed with type 2 diabetes mellitus and the primary focus of this investigation revolves around the population regularly visiting the Medicine Outpatient Department (OPD) within a tertiary care establishment in South Gujarat. The aim is to augment the existing body of evidence delineating the robust correlation between corpulence and the manifestation of NAFLD. In summation, the exhaustive literature review proffers a comprehensive panorama of the labyrinthine interplay connecting T2DM, anthropometric gauges, and NAFLD, underscored by the imperative for meticulously tailored interventions and the implementation of early identification strategies to alleviate the burgeoning burden posed by these intricately interwoven health challenges. The 2008 expert consultation convened by the World Health Organization underscored the pivotal significance of pivotal benchmarks for gauging abdominal obesity ^[16]. These parameters furnish invaluable insights into the distribution of body fat, with abdominal obesity recognized as a noteworthy peril for an array of health repercussions. In their work Cameron et al. explored the consequences of hip circumference in their 2012 study, investigating its impact on the association between abdominal obesity and mortality, unraveling a nuanced interplay among diverse anthropometric gauges and health consequences ^[17]. Ferraioli and Monteiro (2019) delved into ultrasound-based methods for diagnosing liver steatosis, presenting non-invasive alternatives to assess hepatic fat accumulation ^[18]. The significance of these approaches is crucial in promptly detecting and monitoring NAFLD, furnishing healthcare practitioners with potent instruments for holistic patient over- sight. In their study Salamat et al. (2015) delved into prognostic formulas grounded in anthropometric gauges to gauge body composition, underscoring the efficacy of uncomplicated metrics in prognosticating body adiposity and contributing to risk evaluation ^[19]. Snehalatha and colleagues (2003) defined threshold values for standard anthropometric measurements among adults of Asian Indian descent, recognizing the need for population-specific references to understand body fat distribution among diverse ethnic groups ^[20]. In the research conducted by Zeng and colleagues (2014), they explored the optimal threshold values for defining obesity within the context of Chinese adults. Their focus on customizing obesity criteria for specific populations highlights the significance of adopting nuanced approaches ^[21]. Additionally Rungta et al.'s (2021) research explored the efficacy of the Aspartate Aminotransferase to Platelet Ratio Index, also known as APRI and the Fibrosis-4 or FIB-4 indices in evaluating liver fibrosis. Findings shed light on non-invasive methods for assessing liver health, particularly in cases of chronic hepatitis C virus infection ^[22] and in a separate study, Fan et al. (2018) conducted a comprehensive dose-response analysis with the aim of elucidating the correlation between BMI and the likelihood of developing fatty liver. Their research provides nuanced perspectives on the complex interplay between obesity and liver well being ^[23]. Lahsaee and colleagues conducted a study in 2012 examining instances of NAFLD and its connection to BMI and metabolic syndrome. Their research offers valuable insights into the factors contributing to fatty liver among individuals who donate blood and have otherwise healthy profiles ^[24] and in their work Jarvis et al. (2020) conducted a thorough examination and meta-analysis

shedding light on the correlation between metabolic risk elements and the development of advanced liver conditions in NAFLD^[25]. Krakauer and Krakauer (2012) introduced a novel body shape index that predicts mortality hazard independently of BMI. This underscores the importance of considering body shape alongside traditional obesity metrics ^[26]. Motamed et al. (2016) explored the robust associations between the Body Roundness Index and Waistto-Height Ratio with NAFLD, offering further evidence of the utility of anthropometric indices in predicting liver health ^[27]. In summary these studies collectively enhance our understanding of the intricate relationship between anthropometric measures, metabolic health and liver-related outcomes and they provide valuable insights for risk assessment and early intervention strategies in the context of obesity-related liver diseases, thereby improving our ability to tailor interventions for specific populations and promote comprehensive patient care.

Methodology

The observational study took place at the Department of General Medicine in a Tertiary care hospital associated with a Medical College in South Gujarat, spanning from July 2023 to August 2023 after the approval from the Institutional Ethical Committee of Surat Municipal Institute of Medical Education and Research with reference to ethical number IEC 98-03/02/2023. The study focused on diabetic patients attending the Medicine OPD and adhering to the criteria for inclusion, the study encompassed individuals aged 18 and above diagnosed with Type 2 Diabetes Mellitus and willing to furnish written informed consent for participation. Conversely individuals meeting any of the exclusion criteria were not considered for participation. Exclusion criteria encompassed males consuming more than 20g of alcohol or females exceeding 10g per day. The standard measure for one drink has been established as containing 10g of ethanol, which is comparable to a typical can of beer, 120ml of wine, or a 45ml serving (one-shot) of distilled spirits. Other exclusion criteria involved patients with Type 1 Diabetes Mellitus, those using hepatotoxic drugs, a history of Hepatitis B and C (ruled out by considering blood transfusion, sexual history, and Injectable drug abuse history), individuals with chronic liver disease, pregnant females, indoor patients, and those below 18 years old at the time of screening. Anthropometric measurements encompassing weight in kilograms, height in meters, waist circumference in inches and hip circumference in inches were systematically gathered. Standard scales available in the clinic were employed for height and weight measurements, ensuring uniformity across all patients. Waist and hip circumference were measured using an inch tape, applied tightly to the skin surface to maintain tautness without excessive tightness. For waist circumference, a measurement was taken at a point equidistant between the lower edge of the ribs and the border of the superior iliac crest. Similarly, the hip circumference was determined as the maximum measurement around the buttocks. Additionally a proficient radiologist performed abdominal ultrasound examinations for all patients using a high-resolution B-mode ultrasonography system. The assessment of steatosis was categorized as follows:

- 1. Absent (Grade 0): Normal liver echotexture.
- 2. Mild (Grade 1): A slight and diffuse increase in liver echogenicity, with clear visibility of the diaphragm and portal vein wall.
- 3. Moderate (Grade 2): Moderate surge in liver echogenicity, accompanied by a slightly compromised appearance of the portal vein wall and diaphragm.
- 4. Severe (Grade 3): A pronounced escalation in liver echogenicity, resulting in either poor or no discernment of the portal vein wall, diaphragm, and the posterior segment of the right liver lobe.

Anthropometric Tool Formulas are as follows:

- BMI (Body Mass Index): BMI = $\frac{Weight(Kg)}{(Height |m|)^2}$ 1.
- WHR (Waist-to-Hip Ratio): WHR = $\frac{Waist Circumference(cm)}{Wir Circumference(cm)}$ 2.
- WHtR (Waist-to-Height Ratio): WHtR = $\frac{Waist Circumference(cm)}{Waist}$ 3.

Diagnostic Criteria for Obesity is given below as follows based on the BMI classification for adult body weight in Asian populations [20,21]:

- Normal: $18.5 \text{ kg/m}^2 \le BMI < 23.0 \text{ kg/m}^2$ 1.
- 2. Overweight: $23.0 \text{ kg/m}^2 \le \text{BMI} < 25.0 \text{ kg/m}^2$
- 3. Obesity (Peripheral Obesity): BMI $\geq 25.0 \text{ kg/m}^2$

Additional Criteria:

- Central Obesity (+): WHR ≥ 0.88 in men, ≥ 0.81 in women 1.
- 2. Obesity: WHtR ≥ 0.5 for men, ≥ 0.48 for women

Routine Laboratory Investigations for Each Patient including Platelet count, SGOT, and SGPT levels, were conducted. For APRI Calculation ^[22]:

APRI (AST to Platelet Ratio Index) = $\frac{AST\left(\frac{IU}{L}\right)}{Upper normal limit of AST\left(\frac{IU}{L}\right)} / Platelet count (10⁹/L)$

The APRI cutoff for liver cirrhosis was set at > 1.2. Given Below Table 1 showcases Details of Demographic information pertaining to individuals diagnosed with diabetes mellitus.

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	Fatty Liver (n=79)	Normal (n=53)	P-Value
Gender: Male	42	30	0.6973
Gender: Female	37	23	
Hypertension: Yes	34	24	0.9225
Hypertension: No	44	30	
Age	57.7 ± 11.31	55.49 ± 10.73	0.260
Duration of Hypertension	7.95 ± 2.43	6.46 ± 1.37	0.008
Duration of DM	7.35 ± 3.92	4.01 ± 1.62	P < 0.001 ^a

Results

Among the 132 patients examined 54.5% were identified as males and the remaining 55.5% are females and notably 79 patients constituting 60% of the total exhibited signs of fatty liver while the remaining 40% presented with normal liver conditions. Upon analyzing the data, it was observed that there was no apparent association between gender and hypertension in relation to an increased likelihood of fatty liver where P > 0.05. However, the duration of hypertension and diabetes was notably higher among patients with fatty liver, indicating a statistically significant correlation. The investigation also highlighted certain key factors and Body Mass Index, WHtR and WHR emerged as particularly effective indicators and a BMI exceeding 26 kg/m2 was identified as an optimal threshold, demonstrating a sensitivity of 64.6% and

specificity of 50.9%. A waist-to-height ratio surpassing 0.61 exhibited a sensitivity of 43% and specificity of 79.2%. Additionally a waist-to-hip ratio exceeding 0.99 showed a sensitivity of 32.2% and an impressive specificity of 96.2%. Notably BMI demonstrated the highest sensitivity among these parameters while the WHR exhibited the maximum specificity for the detection of fatty liver. These findings underscore the significance of these metrics in assessing and identifying fatty liver conditions in patients. Table 2 offers a juxtaposed scrutiny of anthropometric metrics among individuals with regular liver function and those bearing a diagnosis of fatty liver and within the fatty liver cohort there exists a statistically notable escalation in the average weight, waist circumference, hip circumference, BMI, WHR and WHtR where P < 0.005.



Figure 1: Receiving Operative curve

Table 2: Comparison of Parameters between Normal and Fatty Liver Groups

Parameters	Group	Ν	Mean \pm SD	P-Value
Weight (kg)	Normal	53	63.90 ± 13.11	0.0070^{*}
	Fatty Liver	79	70.14 ± 12.63	
Height (m)	Normal	53	1.56 ± 0.07	0.1069
	Fatty Liver	79	1.58 ± 0.08	
Waist Circumference (cm)	Normal	53	85.64 ± 13.85	0.0113*
	Fatty Liver	79	91.94 ± 13.78	
Hip Circumference (cm)	Normal	53	93.82 ± 10.66	0.0069
	Fatty Liver	79	99.23 ± 11.37	
BMI (Weight[kg]/Height[m ²])	Normal	53	26.24 ± 4.86	0.037^{*}
	Fatty Liver	79	28.06 ± 4.87	
Waist-to-Hip Ratio (WC/HC)	Normal	53	0.89 ± 0.10	0.003*
	Fatty Liver	79	0.94 ± 0.09	
Waist-to-Height Ratio (WC/HT)	Normal	53	0.55 ± 0.09	0.04^{*}
	Fatty Liver	79	0.58 ± 0.09	
SGOT	Normal	53	27.02 ± 8.86	0.133
	Fatty Liver	79	30.30 ± 14.05	
SGPT	Normal	53	23.02 ± 9.61	0.225
	Fatty Liver	79	25.67 ± 13.74	
Platelet Count	Normal	53	259.40 ± 68.45	0.306
	Fatty Liver	79	246.62 ± 71.09	
APRI	Normal	53	0.29 ± 0.17	0.127
	Fatty Liver	79	0.35 ± 0.22	

Conversely, parameters like height, Serum Glutamic Oxaloacetic Transaminase shortly termed as SGOT, Serum Glutamic Pyruvic Transaminase also referred as SGPT, platelet counts, and the APRI index do not manifest discernible variations between the normal and fatty liver strata of patients.

Table 3: Cut offs for predicting anthropometry for presence of fatty liver in DM patients

Variable	AUC	P=Value	Asymptotic	Confidence	Cut-off	Sensitivity	Specificity
			95% (Lower)	Interval (Upper)	Value		
BMI	0.610	0.032	0.512	0.709	26	64.6%	50.9%
Waist-to-Hight Ratio	0.606	0.040	0.507	0.704	0.61	43%	79.2%
Waist-to-Hip Ratio	0.651	0.003	0.003	0.558	0.99	32.2%	96.2%

Table 4 displays the specific cutoff values for anthropometric measurements indicating the presence of fatty liver in individuals with diabetes mellitus. To identify the most accurate cutoff points for predicting fatty liver in DM patients, we employed ROC analysis on all anthropometric parameters as illustrated in Figure 1 and the optimal outcomes were observed with BMI, WHtR and WHR yielding cutoffs of > 26kg/m, > 0.61and > 0.99 respectively and among these parameters BMI exhibited the highest sensitivity while the Waist-to-Hip ratio demonstrated the highest specificity in detecting the presence of fatty liver. In Table 4, the findings of a multifaceted regression examination, probing the correlation between anthropometric variables and hepatic steatosis within the diabetic cohort, are laid out. The unadjusted odds ratio for a waistto-hip ratio surpassing 0.99 notably soared to 13.24 in individuals with fatty liver. Following adjustments for BMI, although the odds ratio experienced a reduction, it remained substantial at 10.53, underscoring an escalated susceptibility to fatty liver.

Methodologically categorical variables were delineated in terms of frequency and percentage, employing statistical procedures and the Chi-square test was enlisted to unearth associations among categorical variables while the normality of continuous variables underwent scrutiny via the Kolmogorov-Smirnov test. A comparative analysis between mean anthropometric and laboratory parameters in fatty liver and normal cohorts was executed through an independent t-test. The Receiver Operating Characteristic analysis, instrumental in determining optimal cut-off values for anthropometric indicators signifying the presence of fatty liver, was deployed. Furthermore, a multivariate logistic regression was enacted to pinpoint anthropometric risk factors associated with fatty liver. All analyses maintained a 95% confidence level. The data interrogation transpired using R Studio and SPSS 20. Figure 2 shows mean comparison of anthropometry parameters. Mean BMI, WHtR and WHR was same in < 40 and > 40 SGOT and < 56 and > 56SGPT

Variable	Unadjusted OR (95% CI)	P-Value	Adjusted OR (95% CI)
BMI (> 26)	2.567 (1.256, 5.246)	0.01	1.56 (0.605, 4.022)
Waist to Hip Ratio (WHR) (> 0.99)	13.24 (2.992, 58.593)	0.001	10.53 (2.33, 47.66)
Waist to Height Ratio (WHtR) (> 0.61)	2.885 (1.297, 6.416)	0.009	1.56 (0.499, 4.254)



Figure 2: Comparison of Anthropometry Parameters

Discussion

The application of basic anthropometric indicators for body composition, including BMI, WC, and WHtR, has conventionally been considered a pragmatic and efficient method for evaluating adiposity. Several studies such as the one conducted by Fan et al. in the Chinese population ^[23] and Lahsaee et al. in a German cohort ^[24], have consistently recognized BMI as a standalone risk factor for NAFLD. In our research we identified a BMI of 26 as the threshold for NAFLD demonstrating a sensitivity of 64.6% and specificity of 50.9%. Additionally, a Waist-to-Hip Ratio of 0.99 was determined as the cutoff yielding a sensitivity of 32.2% and specificity of 96.2%. Several studies across European countries, Thailand, and China have underscored the predictive role of BMI in relation to NAFLD. Furthermore, investigations incorporating BMI and WC, in conjunction with biochemical parameters, have established a robust association between NAFLD and Type 2 Diabetes Mellitus and individuals with T2DM face an elevated risk of developing NAFLD with obesity or BMI amplifying this risk ^[25]. Thus, the significant correlation of BMI and WC with NAFLD spans diverse ethnic groups. Noteworthy are studies that introduce novel anthropometric measures like ABSI and BRI, revealing consequential associations ^[26]. Our investigation revealed a WHtR threshold of 0.61 to anticipate NAFLD, demonstrating a sensitivity of 43% and specificity of 79.2%. This aligns with findings by Motamed et al., who proposed cutoffs of 0.533 for men and 0.580 for women, reinforcing the consistency of our study [27]. These anthropometric indices present uncomplicated, cost-effective, and non-invasive tools for NAFLD screening in Type 2 DM patients. Their applicability extends to outpatient clinics in tertiary care and primary healthcare setups, mitigating the risk of severe complications without resorting to liver biopsy. Our research is limited by the reliance on ultrasound rather than liver biopsy and elastography for identifying NAFLD. While liver biopsy stands as the benchmark, its exclusion in NAFLD cases is primarily due to cost considerations and concerns about potential bleeding risks. Ultrasonography emerged as the pragmatic choice based on feasibility and indications in the patient context. Another limitation is the exclusive focus on the Indian population, recognizing that anthropometric measures are ethnically influenced, potentially introducing inaccuracies and variations when extrapolated to diverse populations.

Conclusions

The correlation between NAFLD and BMI, WHR and WHtR is significant in individuals diagnosed with type 2 diabetes mellitus and also these metrics serve as valuable noninvasive screening tools

in outpatient clinical settings for detecting NAFLD among type 2 diabetic patients. It is essential to establish precise thresholds for each measurement to ensure accurate screening results. Given the preventable nature of NAFLD, implementing effective management strategies involving both pharmaceutical interventions and lifestyle modifications becomes pivotal. By addressing NAFLD through a combination of medication and lifestyle changes, its adverse impact on individuals with type 2 DM can be significantly mitigated, thereby averting potential complications.

List of Abbreviations

NAFLD: Non alcoholic fatty liver disease BMI: Body Mass Index WHR: Waist to Hip Ratio WHtR: Waist to Height Ratio NASH: Non-alcoholic steatohepatitis HCC: Hepatocellular Carcinoma WC: Waist circumference T2DM: Type 2 diabetes mellitus APRI: Aspartate aminotransferase to Platelet ratio index Sgot: Serum glutamic-oxaloacetic transaminase Sgpt: Serum glutamate pyruvic transaminase

Declarations

Ethics approval and consent to participate

The study was conducted following approval from the Institutional Ethical Committee of Surat Institute of Medical Education and Research under ethical reference number IEC 98-03/02/2023. Informed written consent was obtained from all patients for the use of their clinical data in this study. It was ensured that no harm was inflicted upon any of the subjects involved. Detailed explanations of the methods employed, as well as the potential advantages and disadvantages of participating in the study, were provided to both the subjects and their relatives.

Data Availability

The data used in this study are available upon request from the corresponding author, Anvisha Upadhyaya. Please contact anvisha1999@gmail.com for inquiries regarding access to the data.

Conflicts of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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Authors' contributions

Anvisha Upadhyaya and Deepak Shukla collaborated on the conception and design of the study. Anvisha Upadhyaya solely conducted the data collection under the supervision of Deepak Shukla.

Swati Patel conducted the statistical analysis and contributed to the interpretation of results, alongside Anvisha Upadhyaya and Deepak Shukla. Anvisha Upadhyaya led the manuscript preparation, incorporating inputs from all authors.

All authors participated in discussions regarding the results and contributed to the final manuscript.

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