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The Comparison of Simple Anthropometric and Biochemical Parameters for Predicting Liver Steatosis in Obese Balinese Young Women

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Abstract

BACKGROUND: The prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing globally. Early identification of liver steatosis (LS) status is critical to prevent the development of NAFLD into non-alcoholic steatohepatitis (NASH) fibrosis.

AIM: This study aimed at exploring the validity of simple anthropometric and biochemical parameters to predict LS in young obese women.

MATERIALS AND METHODS: This is a cross-sectional study involving 132 young obese women. We collected the data of measured waist circumference (WC), body mass index (BMI), serum triglyceride (TG), and gamma-glutamyltransferase (GGT). The lipid accumulation product (LAP) was designed from TG and WC variables. Fatty liver index (FLI) was calculated from TG, BMI, WC, and GGT variables. LS status was measured using ultrasonography assay. Statistical significance was set at $p < 0.05$.

RESULTS: A positive correlation was found between BMI, WC, TG, GGT, LAP, FLI, and LS ($p = 0.001$). We found that BMI is a better predictor for LS to WC. Our multiple linear regression analysis revealed that BMI, GGT,and TG could predict 41.4% of LS. The validity (specificity, sensitivity, and odds ratio) of simple body fat parameters in predicting LS were as follows: BMI ≥ 30 kg/m^2 (69.6%, 74.4%, and 6.21), WC ≥ 90 cm (67.4%, 70.0%, and 4.28), TG ≥ 100 mg/dL (70.6%, 70.0%, and 5.62) and GGT ≥ 20 μg/L (69.6%, 77.5%, and 7.87), as well as LAP ≥ 30 (82.6%, 70.0%, and 11.1), and FLI ≥ 2.5 (79.3%, 72.5%, and 10.1), significantly.

CONCLUSION: Simple anthropometric and biochemical parameters (BMI, WC, and TG, GGT), are appropriately predicting LS as well as LAP, and FLI among obese Balinese young women.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is related to metabolic syndrome, while non-alcoholic steatohepatitis (NASH) can develop cirrhosis and liver failure. As the prevalence of NAFLD increases, it arises as a public health problem. It is predicted that within one decade the prevalence of NAFLD will be twice as much. In the western population, its prevalence ranges from 15 to 35%, with 10% of these will progress to NASH.

The prevalence of NAFLD is 58% in overweight people and 98% in non-diabetic, obese population [1]. Within 10 years, NAFLD can progress from liver steatosis (LS) to NASH (47%), and to advanced NASH fibrosis and cirrhosis (20-50%) [2]. The prevalence of NAFLD in Asia is 15-30%, and this figure rises to 50% in those with metabolic syndrome [3] [4].

LS is initiated by the increased of visceral fat mass in an individual with obese. Measuring visceral fat mass is essential for identifying the risk to LS. While computer tomographic (CT) scan is still the gold standard to measure visceral fat, some specific body fat parameters which include waist-to-height ratio (WtHR), conicity index (c-index), visceral adiposity index (VAI), and lipid accumulation product (LAP) can also be used to predict visceral fatness [5]. Bedogni et al., developed the fatty liver index (FLI), that is calculated from the waist circumference (WC), body mass index (BMI), gamma-glutamyltransferase (GGT), and serum triglyceride (TG) [6].

A biopsy of the liver is the gold standard in diagnosing NAFLD, especially in NASH. However, other methods are available as a less invasive option, such as imaging. Ultrasonography (US) is one tool that is generally used for steatosis screening, despite its lack of sensitivity [7]. It is a cost-effective and well-established as an imaging technique in diagnosing LS. Its downside is an operator-dependent diagnosis tool, rather qualitative than quantitative, and lacking accuracy in detecting mild hepatic steatosis [8].

In the early stage, NAFLD presents with asymptomatic LS which can progress further to NASH. However, in many countries, there is no regular screening program for detecting asymptomatic LS. Identification of early and asymptomatic LS is critical because of its progression to NASH, advanced fibrosis, and cirrhosis can be prevented. Simple body fat parameters and biochemical measurements could be used to predict asymptomatic LS, while the progression of asymptomatic LS to the late stage of NAFLD, NASH, advanced fibrosis, and cirrhosis can be achieved through managing lifestyle, body weight, diet, and exercise.

Material and Methods

This was a cross-sectional study involving 132 young, obese (aged 18-25 years, BMI > 25 kg/m^2) women in Bali, Indonesia. Data were collected from April to September 2013. A written informed consent was obtained before commencing the study, and the participants' anonymity was maintained throughout. The study protocol was approved by the Committee of Ethical Research of Udayana University/Sanglah General Hospital.

Anthropometric and biochemical variables were assessed. All anthropometric variables were measured twice, and for the final analyses mean values were used. Body weight (BW) was measured by a digital scale (Omron HBF-362, Japan) and presented in kilogram (kg). Body height (BH) was measured using a stature meter (General Care 26SM) and presented in centimetre (cm). WC was measured using a non-elastic, flexible tape at the middle level of the abdomen. Both TG and GGT were analysed by a colourimetric method (Cobas 6000, Roche Diagnostics, Germany). LAP for women was calculated as [WC (cm) −(5,9,10,11) Finally, FLI was calculated as (e0.953* loge(TG) +0.139*(BMI) +0.718*loge(GGT) +0.053*WC -15.745)/ (1- e0.953* loge(TG) +0.139*(BMI) +0.718*loge(GGT) +0.053*(WC) -15.745) * 100. No adjustment of any kind was made in this study regarding any calculations of the anthropometry [5] [6] [9] [10] [11].

Liver steatosis (LS) was assessed using ultrasonography (US) imaging (Logiq 500, GE, Solingen, Germany), setting at 3-5 MH curve linear frequencies. The imaging was focused on the right subcostal-longitudinal and transversal axis line of the subject. The results were interpreted independently by three radiologists, and the final interpretation was concluded by the majority decision.

LS criteria were described as: (1) normal liver, absence of steatosis and other liver disorder, (2) mild steatosis, marked by the appearance of liver parenchymal or hepatorenal echo contrast, a little bit brighter without disorder of intrahepatic vascular, (3) moderate steatosis, marked by liver parenchymal or hepatorenal appearance brighter in most area without intrahepatic vascular disorder, and (4) severe steatosis, marked by a diffuse and brighter liver appearance with blunting intrahepatic vascular [12] [13].

Statistical analyses were performed using Stata 12.1 (Stata Corp, College Station, TX, USA). The normal distribution of continuous data is presented as a mean ± standard error of the mean (SE). We employed a Pearson correlation test for continues data to assess the relationship between anthropometrical, biochemical, and LS, followed by multiple linear regression. One way ANOVA test was used to compare mean values of risk variables by the stage of LS. For ordinal variables, we employed non-parametric analyses which include calculation of odds ratio (OR), specificity, and sensitivity value to predict liver steatosis. Statistical significance was set at $p < 0.05$ (95% CI).

Results

This study enrolled 132 obese young women. Most of them were Balinese (94.7%), and a university student (90.9%). Table 1 depicts the demographic characteristics and descriptive data of the study participants. Average of BMI and WC were 30.4 ± 0.43 kg/m^2 and 90.4 ± 1.06 cm respectively. Most subjects (87.1%) had abdominal obesity (WC ≥ 80 cm). Mean TG and GGT serum concentrations were 104.6 ± 4.31 mg/dL and 24.4 ± 1.47 µg/L respectively, which were above the normal level. LS was found in 30.3% subjects, varied from mild (13.6%), moderate (6.8%), and severe (9.8%).

Table 1: Characteristics description of subjects (n = 132)

Parameters	Mean ± SE	N (%)
Age (year)	20.7 ± 0.20	
Height (cm)	158.2 ± 0.74	
Weight (kg)	76.7 ± 2.00	
BMI (kg/m^2)	30.4 ± 0.43	
25.0-29.9		70 (53.0)
30.0-39.9		54 (40.9)
≥ 40		8 (6.1)
WC (cm)	90.4 ± 1.06	
< 80		17 (12.9)
≥ 80		115 (87.1)
TG (mg/dL)	104.6 ± 4.31	
GGT (µg/L)	24.4 ± 1.47	
Liver Steatosis		40 (30.3)
Mild		18 (13.6)
Moderate		9 (6.8)
Severe		13 (9.8)

Presented in mean ± SE (standard error of mean) for continous data; N(%) for catagorical data. BMI = body mass index, WC = waist circumference; TG = trygliceride, GGT = gamma-glutamyltransferase.

Table 2 shows the association between all anthropometric variables, biochemical parameters, body fatness, and LS status. We found a strong positive correlation (p-value < 0.001) between anthropometric variables, biochemical parameters (TG, GGT), body fatness, and LS status.

Table 2: Correlation matrix of body mass index (BMI), waist circumference (WC), Waist to Height Ratio (WHtR), Lipid accumulation product (LAP), fatty liver index (FLI), plasma Triglyceride (TG), plasma gamma-GT (GGT) and liver steatosis (LS)

Parameters	BMI	WC	CI	WHtR	TG	GGT	LAP	FLI	LS
BMI	1								
WC	0.867*	1							
CI	0.462*	0.826*	1						
WHtR	0.854*	0.960*	0.823*	1					
TG	0.460*	0.467*	0.361*	0.494*	1				
GGT	0.470*	0.489*	0.319*	0.466*	0.379*	1			
LAP	0.746*	0.797*	0.624*	0.804*	0.861*	0.494*	1		
FLI	0.860*	0.787*	0.446*	0.756*	0.465*	0.529*	0.776*	1	
LS	0.588*	0.588*	0.417*	0.607*	0.449*	0.494*	0.592*	0.567*	1

Presented in Pearson's correlation coefficient. *p < 0.001. LS 1 = none, 2 = mild, 3 = moderate, 4 = severe.

Our multiple linear regression suggested that BMI, GGT, and TG could predict 41.4% of liver steatosis, as shown in Table 3. We found a weak association between WC and LS in comparison to BMI, TG, and GGT. Therefore we removed the WC variable from the final model.

Table 3: Regression of body mass index (BMI), plasma gamma-glutamylTransferase (GGT), and triglyceride (TG) to liver steatosis

Dependent	Independents	B	SE	Beta	*p*	R square
Liver Steatosis	(Constant)	-1.555	0.438		0.001	0.414
	BMI	0.080	0.017	0.395	< 0.001	
	GGT	0.014	0.005	0.242	0.003	
	TG	0.003	0.002	0.171	0.031	
The variation of LS value determined by the model 41.4%.						

Analysed using linear regression, Independent variable enter; BMI, WC, TG and GGT.

Table 4 depicts the relationship between predictor variables and LS status. We found a significant association between all predictor variables and LS status. We found a consistent increase of association based on the stages of LS.

Table 4: Relationship of some determinants parameter to Liver Steatosis

Determinant	Liver Steatosis				
	None (92)	Mild (18)	Moderate (9)	Severe (13)	*p*
Body Mass Index (kg/m^2)	28.7 ± 0.33*†‡	32.0 ± 0.85*§	32.4 ± 1.22$^{\dagger\parallel}$	38.2 ± 2.28$^{\ddagger\S\parallel}$	*0.002 †0.009 ‡< 0.001 §< 0.001 $^{\parallel}$0.001
Waist Circumference (cm)	86.4 ± 0.88*†‡	94.3 ± 2.39*§	95.0 ± 3.71$^{\dagger\parallel}$	110 ± 4.58$^{\ddagger\S\parallel}$	*0.002 †0.014 ‡< 0.001 §< 0.001 $^{\parallel}$< 0.001
Conicity Index	1.18 ± 0.008*†‡	1.22 ± 0.020*§	1.23 ± 0.034†	1.29 ± 0.022‡§	*0.054 †0.057 ‡< 0.001 §0.013
Waist to Height Ratio	0.545 ± 0.005*†‡	0.594 ± 0.012*§	0.606 ± 0.025$^{\dagger\parallel}$	0.686 ± 0.026$^{\ddagger\S\parallel}$	*0.001 †0.003 ‡< 0.001 §< 0.001 $^{\parallel}$< 0.001
Triglyceride (mg/dL)	89.7 ± 3.54*†‡	134 ± 12.3*	122 ± 21.2†	157 ± 20.0‡	*< 0.001 †0.037 ‡< 0.001
Gamma-Glutamyltransferase (µg/L)	19.5 ± 1.26*‡	30.8 ± 3.76*§	25.1 ± 4.80$^{\parallel}$	48.7 ± 6.79$^{\ddagger\S\parallel}$	*0.003 ‡< 0.001 §0.001 $^{\parallel}$< 0.001
Lipid Accumulation Product	29.6 ± 1.81*†‡	55.2 ± 5.81*§	53.1 ± 12.8$^{\dagger\parallel}$	98.3 ± 17.9$^{\ddagger\S\parallel}$	*0.001 †0.017 ‡< 0.001 §< 0.001 $^{\parallel}$< 0.001
Fatty Liver Index	1.88 ± 0.38‡	5.63 ± 1.51§	6.13 ± 3.08$^{\parallel}$	30.5 ± 8.65$^{\ddagger\S\parallel}$	‡< 0.001 §< 0.001 $^{\parallel}$< 0.001

Presented in mean ± standard error of the mean (SE). Analysed using one-way ANOVA. The significance level (*p*-value) of; none vs mild steatosis*, none vs moderate steatosis†, none vs severe staetosis‡, mild vs severe steatosis§, and moderate vs severe steatosis$^{\parallel}$.

Simple anthropometric parameters (BMI, WC, CI, and WHtR), biochemical indexes (TG, GGT), and complex body fatness indicators could predict liver steatosis significantly (Table 5).

Table 5: Specificity, Sensitivity and the OR to predict Liver Steatosis (US) of somebody fatness parameters

Parameters (cut off)	Specificity (None = 92) F (%)	Sensitivity (Steatosis = 40) F (%)	OR (95% CI)	*p*
BMI (≥ 30 kg/m^2)	64 (69.6)	29 (74.4)	6.21 (2.66-14.5)	< 0.001
WC (≥ 90 cm)	62 (67.4)	28 (70.0)	4.82 (2.16-10.8)	< 0.001
CI (≥ 1.2)	59 (64.1)	29 (74.4)	4.53 (1.99-10.3)	< 0.001
WHtR (≥ 0.55)	58 (63.0)	31 (77.5)	6.34 (2.59-15.5)	< 0.001
TG (≥ 100 mg/dL)	65 (70.6)	28 (70.0)	5.62 (2.50-12.6)	< 0.001
GGT (≥ 20 µg/L)	64 (69.6)	31 (77.5)	7.87 (3.31-18.7)	< 0.001
LAP (≥ 30)	76 (82.6)	28 (70.0)	11.1 (4.67-26.3)	< 0.001
FLI (≥ 2.5)	73 (79.3)	29 (74.4)	10.1 (4.29-23.9)	< 0.001

BMI = body mass index, WC = waist circumference, CI = conicity index, WHtR = waist to height ratio, TG = triglyceride, GGT = gamma glutamyltransferase, LAP = lipid accumulation product, FLI = fatty liver index, OR = odd ratio.

The validity indicators (specificity, sensitivity and the odds ratio (95%CI)) of body fat parameters which could predict LS were as follows: BMI ≥ 30 kg/m^2 (69.6%, 74.4% and 6.21(2.66-14.5)), WC ≥ 90 cm (67.4%, 70.0% and 4.28(2.16-10.8)), CI ≥1.2 (64.1%, 74.4%, and 4.53(1.99-10.3)), TG ≥ 100 mg/dL (70.6%, 70.0% and 5.62(2.50-12.6)), GGT ≥ 20 µg/L (69.6%, 77.5% and 7.87(3.31-18.7)), LAP ≥ 30 (82.6%, 70.0% and 11.1(4.67-26.3)), and FLI ≥ 2.5 (79.3%, 72.5% and 10.1(4.29-23.9)).

Discussion

NAFLD has emerged into a serious problem worldwide. LS is an early stage of NAFLD that naturally will progress to NASH (47%), of which as many as 25-50% will eventually progress to cirrhosis or fibrosis. Following the next ten years, as many as 7% will progress to hepatocellular carcinoma, contribute to 20% of liver-related death, and 50% will require a liver transplant [2]. It is important for healthcare providers to understand and identify this entity at an earlier stage and deliver the appropriate treatment.

The objective of treating NAFLD is to prevent fibrosis and improve steatosis. Current treatment relies on treating existing related entities such as obesity and insulin resistance. Weight loss, achieved through the lifestyle and behavioural interventions such as diet and exercise, is still the main strategy to prevent the progression of NAFLD [14]. Our previously randomised clinical trial [15] [16] found that three months restriction energy intake with a supplement of low n6:n3 (2:1) polyunsaturated fatty acid (PUFA) ratio, and weekly moderate exercise, decreased body fat parameters, improved cytokines levels, controlled fasting blood glucose, and reduced LS.

Body fatness, particularly visceral fat, is strongly associated with NAFLD. Oshakbayev et al., [17] reported NAFLD patients were found to have increased visceral fat rating, increased metabolic age by 9.6 years, and a basal metabolic rate of 209 kcal/day.

FLI, LAP, and VAI are body fatness indexes which can be used to predict cardiovascular, metabolic accurately, and liver-related diseases [6] [9] [10]. Both LAP and FLI can be utilised to recognise patients with hepatic steatosis [18]. FLI is a non-invasive diagnostic tool that is known for its strong agreement to SteatoTest and moderate agreement to abdominal ultrasound or hepatorenal imaging [19]. Du et al., [20] reported that VAI and LAP are sensitive in recognising the metabolic obese-normal weight (MONW) phenotype among Chinese adults.

Despite FLI's ability in recognising NAFLD, a simpler visceral fat assessment like waist circumference was found to have a similar performance [21]. Rinella et al., [22] investigated that there was a proven correlation between the overall grade of steatosis and BMI in liver donors. A population-based study by Stranges et al., [23] found that abdominal height was related to GGT and ALT levels, with women showed a stronger correlation.

Our study aims to identify predictors of NAFLD instead of defining the diagnosis of NAFLD. Understanding these predictors can guide the management of NAFLD especially in modifying risk factors associated with the development of NAFLD to NASH. Until recently, there is no definitive and specific pharmacologic regiment available for treating NAFLD. Simple anthropometric and biochemical predictors such as BMI, WC, TG, and GGT are readily available at all level of medical care services, especially at primary care. These predictors can be modified through behavioural interventions to prevent the progression of NAFLD to advanced NASH. Also, managing these predictors is also beneficial to reduce the risk for cardiovascular and metabolic-related diseases effectively.

In conclusion, there is a significant relationship between liver steatosis with all body fat parameters. These phenomena indicate that the simple single anthropometric (BMI, WC) and also the biochemical (TG, GGT) parameters are appropriate as hallmarks for predicting liver steatosis as well as the complex fatness parameters (such as FLI and LAP) among the obese Balinese young women.

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