ORIGINAL ARTICLE

EXPLORING LIPID ACCUMULATION PRODUCT AS A DIAGNOSTIC TOOL FOR INSULIN RESISTANCE AMONG HEALTHY ADULTS IN A TERTIARY HOSPITAL OF BANGLADESH

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ABSTRACT

This study explores the link between lipid accumulation product (LAP) and insulin resistance (IR) in 140 seemingly healthy adults (92 males, 48 females) at a Bangladeshi tertiary hospital. IR, a pivotal factor in cardiovascular and metabolic diseases, primarily associated with obesity and visceral fat, is under scrutiny. LAP, derived from waist circumference and triglycerides, is gaining recognition for its ability to reflect metabolic changes related to lipid accumulation. Despite its efficacy in assessing cardiovascular risk and diabetes in diverse populations, there is limited information on LAP's correlation with IR in Bangladesh context. Anthropometric and physiological measures gauge IR, including LAP, BMI, and WC. Results indicate a robust correlation between LAP and IR, with LAP surpassing BMI and WC, particularly in males. LAP's continuous variable nature is emphasized, rendering it suitable for population-wide comparisons. Multivariate regression analyses underscore LAP's more significant impact on HOMA-IR, highlighting its significance in assessing insulin resistance in both genders. The findings contribute to the growing evidence supporting LAP's superiority in identifying metabolic diseases, cardiovascular risk, and diabetes. LAP emerges as an accessible and straightforward index reflecting anatomical and physiological changes linked to lipid overaccumulation. In conclusion, this study positions LAP as a potent diagnostic tool for recognizing insulin resistance, particularly in large populations, emphasizing its potential utility in the Bangladeshi adult population.

Key words: Lipid Accumulation Product, Insulin resistance, Cardiovascular diseases

Introduction

Insulin resistance (IR) is a condition characterized by a reduced ability of insulin to promote glucose utilization and storage, playing a significant role in cardiovascular and metabolic diseases[1]. The association between IR and obesity, particularly abdominal obesity, where visceral fat strongly correlates with severe insulin resistance, is well-established[2]. Elevated free fatty Acid (FFA) levels and adipocytokine secretion from adipose tissue contribute to insulin dysfunction and lead to IR[3-5].

Various methods are employed for diagnosing IR, with euglycemic hyperinsulinemic clamping being the gold standard despite its limitations of

being complex, time-consuming, and costly[6]. The Homeostasis Model Assessment of IR (HOMA-IR) is a widely applied, simpler, and stable alternative in epidemiological studies[7]. Standard anthropometric measures like BMI and waist circumference (WC) are used but may need more comprehensive insight into an individual's metabolic status[8,9]. While BMI is easy to gauge, it does not differentiate between fat and lean tissues or indicate lipid distribution[2,8]. WC, defined by the IDF consensus as the criterion for abdominal obesity, falls short in distinguishing between subcutaneous and more problematic visceral fat, significantly impacting IR[10,11].

Imaging techniques such as MRI and CT effectively assess lipid accumulation and distribution but are expensive and less feasible for routine clinical practice. In the current era of increasing obesity, it is necessary to define and measure lipid accumulation specifically in contexts where it may pose a physiological danger[12,13]. These contexts might be described as lipid overaccumulation, and caution should be exercised to avoid blaming enlarged adipose or lean tissue components that might enhance physiological processes or reduce disease risk[14].

The Lipid Accumulation Product (LAP) index has garnered recognition for its ability to mirror metabolic changes associated with lipid accumulation status[15,16]. Derived as a product of waist circumference (WC) and triglycerides, LAP aims to capture an individual's anthropometric and physiological status. Initially measured to reflect the risk of cardiovascular disease, LAP attracted increased attention owing to its associations with liver disease, chronic kidney disease, and conditions related to insulin resistance[17-19]. In the Korean population, even in non-diabetic individuals, the LAP index could indicate insulin resistance and beta-cell function[20].

Additionally, a previous study on diabetes, metabolic syndrome, and obesity in other Asian populations reported that the LAP index demonstrated superior predictive value for metabolic syndrome compared to body mass index (BMI) or waist circumference (WC)[21].

The Lipid Accumulation Product (LAP), introduced by Kahn based on NHANES III data[12], combines waist measurements and fasting triglyceride (TG) levels, reflecting anatomical and physiological changes associated with lipid overaccumulation. LAP, designated as the "lipid accumulation product," is based on a combination of two safe and inexpensive measurements - waist circumference (WC), a measure of truncal fat that includes the visceral (intra-abdominal) depot, and the fasting concentration of circulating triglycerides (TG), the esterified, long-chain fatty acids circulating through blood contained stably inside lipoproteins[22,23]. Both waist size and TG concentration tend to rise with age, suggesting that their values are subject to accumulation over time. Waist size and circulating TGs are continuously associated with metabolic insulin resistance[24,25]. LAP exhibits strong correlations with cardiovascular disease, diabetes, and metabolic syndrome, often outperforming BMI in predicting these conditions. In specific cases, such as polycystic ovary syndrome, LAP demonstrates higher sensitivity and specificity than BMI and WC in predicting cardiovascular disease. Although some studies have investigated LAP's association with CVD and diabetes in European populations, few have explored its correlation with IR in Asian cohorts where abdominal obesity is prevalent among obese Chinese individuals[8,26-28].

Not much data are available for the Bangladeshi population. Therefore, this study aims to elucidate the relationship between LAP and IR in the Bangladeshi adult population in a tertiary care hospital and explore whether LAP has superior predictability for IR than WC and BMI.

Materials and Methods

It was a cross-sectional analytical study conducted in the Department of Biochemistry of Sir Salimullah Medical College, Dhaka, Bangladesh from March 2018 to February 2019. A total of 140 subjects were included in this study. Adult people aged 25 to 55 years were included. Among them 92 were male and 48 were female. Participants with acute or chronic inflammatory diseases, chronic liver diseases, major cardiovascular events, chronic alcoholism, and anemia were excluded by history taking and clinical examinations. Patients with history of taking antidiabetic, lipid-lowering agents, or other medication that affect carbohydrate, lipid or insulin metabolism were also excluded. Those with malignancy and pregnancy were excluded. All surveys were conducted after obtaining written informed consent. Anthropometric variables were measured accordingly, and a blood sample was collected to measure biochemical variables.

Study procedure: Subjects were selected from the outpatient Department of Medicine and Endocrinology. Sir Salimullah Medical College and Mitford Hospital. Ethical permission was taken from the Ethical Review Committee of Sir Salimullah Medical College. Before collecting specimens, each eligible person was firmly approached and proper counselling about aims, objectives, and risks. benefit and procedure of the study was given. Only voluntary candidates were recruited as participants. Then they were interviewed, and relevant information were recorded systematically in a pre-designed standard datasheet, including general information and history of chronic diseases, and family history of diabetes. Data were checked and edited. All surveys were conducted after obtaining written informed consent. Anthropometric variables were measured accordingly, and a blood sample was collected to measure biochemical variables. The Lipid Accumulation Product (LAP) was calculated using a previously reported formula: For males, LAP = [waist (cm) × 65] × TG concentration (mmol/L), while for females, LA = [waist (cm)× 58] × TG concentration (mmol/L)[16]. Additionally, Insulin resistance (IR) was estimated by employing the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) formula: FIns (mU/mL) × FPG (mmol/L)/22.5.

Statistical analysis: All statistical analyses were performed with the help of the software SPSS (statistical package for social science).[22] The mean with standard deviation was determined to compare continuous variables. An unpaired Student's t-test was performed to show any significant difference between the mean values. The association between HOMA-IR and other variables was examined by Pearson's correlation analysis. Multiple stepwise regression analyses were performed to identify factors independently associated with HOMA-IR. $p < 0.05$ was considered as significant in all statistical tests. Sample size was determined by applying the formula for a comparison of two means using WC values from Ahn et al[17].

Results

The study included 140 apparently healthy adults (92 males, average age: 41.46±9.40 years; 48 females, average age: 38.08±10.26 years).

Males exhibited higher total cholesterol (TC) and triglycerides (TG) than females ($p < 0.05$). No significant gender-based differences were observed for age, systolic blood pressure (SBP), diastolic blood pressure (DBP), waist circumference (WC), body mass index (BMI), low-density lipoprotein cholesterol (LDL-C), serum insulin, homeostasis model assessment of insulin resistance (HOMA-IR), and lipid accumulation product (LAP) (Table I). Subsequently, participants were divided into LAP quartiles, revealing that higher LAP quartiles correlated with older age and elevated SBP, DBP, BMI, WC, TC, LDL-C, fasting plasma glucose (FPG), serum insulin, and HOMA-IR ($P < 0.05$) in males. However, age, LDL-C, and high-density lipoprotein cholesterol (HDL-C) showed no differences across LAP quartiles. A similar trend was observed in females, with higher LAP quartiles associated with increased age, SBP, DBP, BMI, WC, serum insulin, and HOMA-IR ($P < 0.05$), while TC, HDL-C, LDL-C, and FPG exhibited no significant differences (Table II). Pearson's correlation analysis in males indicated positive correlations between HOMA-IR and age, SBP, DBP, WC, BMI, LAP, TC and serum insulin ($p < 0.001$), excluding HDL-C (Table III). Multivariate regression analyses revealed that LAP had a greater impact on HOMA-IR than BMI in males, while BMI had a greater impact than LAP in females. WC, HDL-C, and non-HDL-C were not included in the respective regression models (Table IV), suggesting that LAP holds significant relevance in assessing insulin resistance in both genders.

Table I: Comparison of general characteristics between males and females

	Male (n=92)	Female (n=48)	p values
Age (in years)	41.46 ± 9.40	38.08 ± 10.26	0.155
SBP (mm Hg)	121.07 ± 10.48	117.50 ± 11.80	0.182
DBP (mm Hg)	80.71 ± 7.94	79.38 ± 10.25	0.529
WC (cm)	91.32 ± 8.40	89.29 ± 12.31	0.394
BMI (kg/m^2)	25.54 ± 2.65	25.40 ± 4.49	0.854
TC (mg/dL)	145.23 ± 40.88	123.21 ± 32.37	0.022
TG (mg/dL)	132.86 ± 53.45	107.63 ± 43.29	0.045
HDL (mg/dL)	29.13 ± 10.61	27.79 ± 7.98	0.583
LDL (mg/dL)	88.17 ± 31.23	82.85 ± 35.69	0.506
FPG (mmol/L)	6.28 ± 2.20	6.37 ± 1.58	0.860
Serum Insulin (ng/L)	8.84 ± 4.07	9.58 ± 4.03	0.457
HOMA-IR	1.23 ± 0.62	1.31 ± 0.55	0.603
LAP	40.03 ± 19.88	41.35 ± 26.65	0.806

Unpaired t test was done.

Table II: Association of hypertension and related factors with cognitive performance of the elderly participants (N = 189)

Characteristics	Cognitive performance			p values
	Normal cognitive function Frequency (%)	Mild cognitive impairment Frequency (%)	Moderate cognitive impairment Frequency (%)	
Diagnosed cases of hypertension by the physician				
Non hypertensive	47 (62.7)	22 (29.3)	6 (8.0)	<0.001
Hypertensive	20 (17.5)	77 (67.5)	17 (14.9)	
History of diabetes mellitus				
No	44 (35.2)	68 (54.4)	13 (10.4)	
Yes	23 (35.9)	31 (48.4)	10 (15.6)	>0.05
Intake of prescribed anti-hypertensive drug by the physician within 2 weeks				
Not taken	47 (62.7)	22 (29.3)	6 (8.0)	<0.001
Taken	20 (17.5)	77 (67.5)	17 (14.9)	
Anti-hypertensive drugs taken by the respondents who were diagnosed as hypertensive				
Beta-blockers				
No	62 (37.6)	82 (49.7)	21 (12.7)	>0.05
Yes	5 (20.8)	17 (70.8)	2 (8.3)	
Calcium-channel blockers				
No	58 (40.8)	69 (48.6)	15 (10.6)	<0.05
Yes	9 (19.1)	30 (63.8)	8 (17.0)	
Diuretics				
No	66 (35.7)	96 (51.9)	23 (12.4)	>0.05
Yes	01 (25.0)	3 (75.0)	0 (0.0)	
ARB				
No	57 (38.5)	72 (48.6)	19 (12.8)	>0.05
Yes	10 (24.4)	27 (65.9)	4 (9.8)	
ACEI				
No	65 (37.1)	89 (50.9)	21 (12.0)	>0.05
Yes	2 (14.3)	10 (71.4)	2 (14.3)	
Others	67 (35.4)	99 (52.4)	23 (12.2)	>0.05
Family history of hypertension				
No	36 (46.8)	30 (39.0)	11 (14.3)	
Yes	31 (27.7)	69 (61.6)	12 (10.7)	<0.05
Family history of diabetes mellitus				
No	37 (41.6)	42 (47.2)	10 (11.2)	>0.05
Yes	30 (30.0)	57 (57.0)	13 (13.0)	
Family history of cerebrovascular stroke				
No	47 (39.5)	57 (47.9)	15 (12.6)	>0.05
Yes	20 (28.6)	42 (60.0)	8 (11.4)	
Family history of ischemic heart diseases				
No	47 (38.8)	58 (47.9)	16 (13.2)	>0.05
Yes	20 (29.4)	41 (60.3)	7 (10.3)	

Table II: Comparison of variables in quartiles of LAP

Male	**Q1 of LAP (<21.25)**	**Q2 of LAP (21.25– 41.24)**	**Q3 of LAP (41.25 - 54.29)**	**Q4 of LAP (>54.29)**	**p values**
Age (in years)	38.63 ± 10.66	41.82 ± 10.56	39.73 ± 7.51	46.29 ± 7.61	0.127
SBP (mm Hg)	115.63 ± 12.63	121.36 ± 9.51	122.00 ± 9.22	126.07 ± 7.38*	0.049
DBP (mm Hg)	76.25 ± 8.47	78.18 ± 7.51	84.00 ± 7.37*	84.29 ± 5.14*	0.006
WC (cm)	84.94 ± 7.89	89.45 ± 5.32	94.27 ± 6.86*	96.93 ± 7.55*	<0.001
BMI (kg/m^2)	23.78 ± 2.48	24.85 ± 1.41	26.27 ± 2.57*	27.32 ± 2.41*	0.001
TC (mg/dL)	114.81 ± 27.90	147.18 ± 32.80	156.93 ±47.23*	165.93 ±34.36*	0.002
HDL-C (mg/dL)	27.19 ± 6.53	33.82 ± 20.38	26.87 ± 6.07	30.07 ± 6.16*$^{\#}$	0.330
LDL-C (mg/dL)	72.59 ± 21.78	96.58 ± 28.48	94.40 ± 41.78	92.67 ± 25.51	0.127
FPG (mmol/L)	5.06 ± 0.72	5.45 ± 0.65	6.41 ± 1.74*	8.19 ± 3.15*$^{\#}$	<0.001
Serum Insulin (ng/L)	5.46 ± 1.91	9.03 ± 2.93*	8.80 ± 2.62*	12.62 ± 4.71*$^{\#}$	<0.001
HOMA-IR	0.71 ± 0.27	1.24 ± 0.43*	1.21 ± 0.39*	1.84 ± 0.73*$^{\#}$	<0.001
Female	**Q1 of LAP (<22.78)**	**Q2 of LAP (22.78– 36.37)**	**Q3 of LAP (36.38 – 53.77)**	**Q4 of LAP (>53.77)**	
Age (in years)	29.67 ± 1.97	37.00 ± 11.50	40.80 ± 9.83	45.50 ± 9.16*	0.042
SBP (mm Hg)	111.67 ± 7.53	110.71 ± 13.67	123.00 ± 4.47	126.67 ± 10.33	0.024
DBP (mmHg)	75.00 ± 5.48	72.86 ± 12.54	85.00 ± 5.00	86.67 ± 8.16	0.024
WC (cm)	75.17 ± 7.91	85.57 ± 7.23	95.20 ± 4.97*	102.83 ± 6.18*$^{\#}$	<0.001
BMI (kg/m^2)	20.88 ± 1.60	24.50 ± 4.33	26.94 ± 1.88*	29.67 ± 3.88*	0.001
TC (mg/dL)	100.00 ± 34.67	127.43 ± 36.46	120.00 ± 15.81	144.17 ± 24.81	0.116
HDL-C (mg/dL)	30.00 ± 8.00	30.00 ± 4.93	20.60 ± 4.04	29.00 ± 10.99	0.155
LDL-C (mg/dL)	57.83 ± 28.72	95.49 ± 50.50	76.00 ± 9.67	98.83 ± 23.88	0.153
FPG (mmol/L)	5.47 ± 0.52	6.07 ± 1.42	6.52 ± 2.73	6.65 ± 0.54	0.166
Serum Insulin (ng/L)	5.40 ± 0.62	8.23 ± 2.59	11.06 ± 2.81*	14.12 ± 3.08*$^{\#}$	<0.001
HOMA-IR	0.72 ± 0.12	1.13 ± 0.37	1.52 ± 0.33*	1.93 ± 0.38*$^{\#}$	<0.001

ANOVA test was done

*$p < 0.05$, Q2, Q3, Q4 vs Q1, respectively. #$p < 0.05$, Q2, Q3 vs Q2. $p < 0.05$, Q4 vs Q3

Table III: Correlation of HOMA-IR with age, SBP, DBP, WC, BMI, TC, HDL-C, LDL-C, FPG, serum insulin and LAP

	Male		Female	
	r	p values	r	p values
Age	0.406	0.002	0.530	0.008
SBP	0.452	<0.001	0.539	0.007
DBP	0.409	0.002	0.552	0.005
WC	0.459	<0.001	0.790	<0.001
BMI	0.472	<0.001	0.857	<0.001
TC	0.464	<0.001	0.628	0.001
HDL-C	0.068	0.621	-0.098	0.650
LDL-C	0.375	0.004	0.455	0.026
FPG	0.716	<0.001	0.331	0.114
Serum Insulin	0.978	<0.001	0.994	<0.001
LAP	0.634	<0.001	0.839	<0.001

Pearson's correlation coefficient test was done.

Table IV: Multivariate stepwise regression analysis showing the impact of variables on HOMA-IR

Dependent variable	Independent variables	Absolute value of standardized coefficients	p values
Male			
HOMA-IR	LAP	0.486	0.001
	BMI	0.218	0.108
Female			
HOMA-IR	LAP	0.372	0.029
	BMI	0.584	0.001
	HDL-C	0.033	0.764

Discussion

Our study developed into the relationship between lipid accumulation product (LAP) and insulin resistance (IR) markers among adults in a Bangladeshi tertiary hospital. Insulin resistance stands as an independent risk factor for type 2 diabetes and cardiovascular disease (CVD), with its early identification crucial for predicting the onset of CVD, fatty liver disease, and metabolic disorders[16]. Moreover, early recognition of IR is important to predict the development of CVD, fatty liver disease and metabolic diseases[17]. Obesity, especially visceral fat, demonstrates a robust correlation with IR, attributed to a hyperlipolytic state and elevated levels of free

fatty acids (FFA), impacting insulin signaling[2,4]. Adipose tissue, functioning as an endocrine organ, releases adipocytokines like TNF-α and leptin, further contributing to IR[4,5]. Our data showed that in heathy subjects, LAP was closely associated with IR and exhibited stronger predictability of IR than WC and BMI. Pearson's correlation analysis showed that LAP positively correlated with HOMA-IR. Multivariate regression analysis suggested that LAP had a greater impact on HOMA-IR than did BMI and specially in male. Compared with LAP, BMI reflects only excess weight. Individuals with various risk levels of CVD and diabetes may have a similar BMI while their WC and metabolic risk profiles may be different[2]. LAP exhibited a more significant impact on HOMA-IR than BMI, especially in males, emphasizing its efficacy in assessing IR and predicting CVD and diabetes[2].

The findings in this study align with Despres' 'hypertriglyceridemic waist phenotype' where LAP's continuous variable nature renders it more suitable for population comparisons[18-20]. Lipid accumulation in the body is accompanied with both increased level of TG and evaluated WC levels[23]. Therefore, increased LAP may indicate ectopic lipid deposition and reflect lipid overaccumulation[12,14]. It suggested that in both the cross-sectional study and the prospective study, LAP was an effective index for assessing the risk of CVD and diabetes. Kahn[12] and Kraegen et al[26] found that LAP outperformed BMI in recognizing cardiovascular risk and diabetes. Another study also affirms LAP's superior performance in recognizing cardiovascular risk and diabetes[13]. Additionally, LAP's effectiveness is highlighted in a 6-year follow-up study for identifying prevalent and predicting incident diabetes[8].

Our research highlights a strong association between lipid accumulation product (LAP) and insulin resistance (IR), underscoring LAP's superior effectiveness compared to BMI and waist circumference (WC) in identifying IR, especially among males. LAP, as a cost-effective and uncomplicated index, proves to be a powerful tool for detecting insulin resistance. It reflects both anatomical and physiological changes associated with lipid overaccumulation. This emphasizes LAP's potential as a valuable instrument for recognizing insulin resistance, particularly in studies involving large populations.

This cross-sectional study focused solely on analyzing correlations between HOMA-IR and various variables without delving into causality or mechanisms. With a limited sample size from a single center, our findings may not be representative of the general population in Bangladesh. Future prospective studies, particularly larger ones across diverse populations, are essential for gaining a more comprehensive understanding of these relationships.

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