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ORIGINAL ARTICLE

ASSOCIATION OF LIPID ACCUMULATION PRODUCT WITH INSULIN RESISTANCE AND METABOLIC SYNDROME IN TYPE 2 DIABETIC PATIENTS IN RELATION WITH DIETARY HABIT IN BANGLADESHI POPULATION

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Abstract

Background: *Lipid accumulation product (LAP) is a novel biomarker of central lipid accumulation related to diabetes and cardiovascular disease risk. In this study, we assessed the association of LAP with glucose homeostasis, lipid profile parameters, and some clinical parameters about fast food-taking habits of diabetic patients. This study evaluated the relationship between lipid accumulating product (LAP) with insulin resistance and metabolic syndromeinfast food-taking patterns in the Bangladeshi type 2 diabetic population.* ***Methods:*** *Three hundred and seventy-five T2DM subjects as cases and three hundred and seventy-five healthyindividuals as control were assessed for anthropometric and biochemical measurements. LAP was calculated as [waist circumference (cm)–65]×[triglycerides (mmol/L)] in men, and [waist circumference (cm)–58]×[triglycerides (mmol/L)] in women. Associations of LAP with fasting glucose, insulin, insulin resistance index, and lipid profile levels, were assessed. Fast food-taking habits per week were also taken from the study subjects. Some clinical parameters (BMI, blood pressure, and waist-hip ratio) were also measured.* ***Results:*** *LAP was significantly correlated with glycemic markers like FBG, ABF,F. Insulin,HBA1C, HOMA-IR, HOMA B%, and Serc-HOMA in type-2 DM subjects. The p-value was less than 0.001. This study was alsosignificantly (p=<0.001) correlated with lipidemic markerslike TAG &LAP in type-2 DM subjects.LAP was significantly associated with BMI, waist-hip ratio (WHR), SBP, and DBP in T2DM subjects. Multiple comparisons of LAP with fast food-taking habits in the study population showed that mean LAP was significantly (p<0.02) higher in the positive fast food-taking habit-containing study group.* ***Conclusion:*** *LAP was significantly correlated with insulin resistance and metabolic syndrome in T2 diabetic subjects.The favorable, fast food-eating habit-containing study group had considerably greater LAP.*

***Key words**: LAP, VAT, VAI, HOMA-IR, HOMA-B%, TAG*

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Introduction:

Excess visceral adipose tissue (VAT) is one of the most dangerous fat depots in the body, linked to heart disease and some types of cancer. [1,2] The LAP index, a newly established biomarker of cerebral fat accumulation, has been recommended to indicate the risk of insulin resistance, metabolic syndrome, type 2 diabetes, and cardiovascular disease. [3–5] In healthy people, higher LAP has been linked to poor glucose homeostasis and insulin resistance, as well as elevated alanine aminotransferase. [6]In a Chinese study, the LAP and the visceral adiposity index (VAI), were efficient markers for stratifying persons into obesity phenotypes. [7]In addition, another study found that LAP was a valuable indicator for metabolic syndrome screening. [8] Diet and lifestyle changes appear to have an impact on the LAP. [9,10]Furthermore, although research on the relationship between macronutrient diet composition and LAP is currently scarce, it has been claimed that non-caloric qualitative features of diet primarily influence LAP. In a low-processed, lower-glycemic dietary setting, consuming energy primarily as carbohydrates or fat for three months did not affect visceral fat and metabolic syndrome, according to a new study. [11]The findings on the relationship between different dietary patterns (DPs), LAP, and VAI are mixed. All studies have not found a significant link between carbohydrate intake, dietary fatty acids, including saturated fatty acids (SFAs), monounsaturated fatty acids (MUFAs), and polyunsaturated fatty acids (PUFAs), and VAT. [12-14] It's crucial to remember that meals and nutrients are ingested together, and complex combinations of nutrients are more likely to interact or have a synergistic effect. [15] The approach of evaluating single nutrients or foods may be limited in terms of potential interactions and high inter-correlations between several food components, making it difficult to estimate the general or independent impacts of different nutrients or foods; perhaps minor and thus untraceable impacts of a single nutrient may be hidden, and the concern of multiple comparisons is also crucial in this area. [16]As a result, the study of DPs has become more critical in resolving these challenges. [15,17] A DP is a multi-nutrient variable with a more significant impact on illness risk than any single nutrient. [16,17]Fast-food consumption has risen dramatically in the United States during the last three decades. The effect of fast food on the risk of obesity and type 2 diabetes, on the other hand, has gotten little attention. Over 15 years in the United States, we wanted to see if there was a link between reported fast-food habits and changes in body weight and insulin resistance. Obesity, which affects 37.7% of people in the United States (US), as well as chronic disorders (such as type 2 diabetes, cancer, and cardiovascular disease), is attributable, at least in part, to the overconsumption of low-nutrition food.[12]There has been a movement toward higher consumption of out-of-home foods and beverages, which often consist of energy-dense, nutrient-poor foods with inferior overall nutritional quality, such as less fiber, more total and saturated fat, and sugar.[13] Indeed, according to time-use data, calorie consumption from household food sources decreased by 24% from 1965 to 2008, with the majority of the decrease occurring until 1996. [14]. According to Powell et al., 36% of American adults ate fast food in 2007–2008, resulting in a daily caloric intake of 877 calories.[15] In a longitudinal study of young adults, Pereira et al. (2005) discovered that eating fast food more frequently (> 2 times per week) was linked to increased body weight and insulin resistance.[18] Evidence suggests that excessive fast-food intake and dining out in full-service restaurants can have negative health consequences.[15-18]

Methods:

The research was conducted on 350 type 2 diabetic patients and 350 normal healthy controls of both genders. These T2DM patients were selected from the outpatient departments of BIRDEM, Hospital, Dhaka. The type 2 diabetic patients were defined based on fasting blood glucose (FBSG) and 75 g oral glucose tolerance test (OGTT). Three hundred and fifty normal healthy participants with a negative history of diabetes or other chronic illness were recruited as control. Controls were selected from workers of BIRDEM and employees of the residential hall campus of Dhaka University. The type 2 diabetic subjects were matched by age and sex with the control subjects. The sociodemographic, clinical, and biochemical data, including gender, age, area of residence, systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), Lipid Accumulation Product (LAP), waist and hip ratio (WHR), fasting blood glucose (FBG), 2 hours after breakfast blood glucose (ABF), HBA1C, and duration of diabetes, exercise history, hypertension, drug history, smoking history and fast food taking history/ week were collected from the people who participated in the study, during the time of whole blood collection. According to the WHO guidelines, anthropometric parameters such as weight, height, and waist and hip circumference were measured for each subject using standard methods.[19]

T2DM subjects, age 30-60 years, and duration of diabetes (2-10) years were considered as case, and non-diabetic healthy volunteers, age 30-60 years, were considered control, respectively. Exclusion criteria of both patient and control: Evidence of any kind of acute infection and any other systemic disorder, Evidence of hepatic dysfunction: ALT (SGPT) or AST (SGOT) >100 units, Evidence of renal dysfunction: S creatinine> 1.7mg/dl, Presence of malabsorption syndrome, presence of autoimmune disease, pregnant women and cancer.

A meter scale measured height and weight using a calibrated weight machine following the standard procedure. Body Mass Indexes (BMI) of the subjects were calculated using the following formula like BMI= (Weight (kg))/(Height /(m)^2

Waist Measurement was done horizontally at the narrowest point between the lower end of the rib cage and the iliac crest in centimeters. Hip Circumference was measured at the greatest horizontal circumference below the iliac crest at the level of the greater trochanter in centimeters using a standard measuring tape. The Waist Hip Ratio was calculated using the standard formula.[20]

Fast food taking habit per week was taken from the study subjects.Blood was drawn by venipuncture under the overnight fasting condition (10 to12 hours) and after 2 hours after breakfast. After 30 minutes, samples were centrifuged at 3000 rpm for 10 minutes to produce serum. The serum was preserved in the freezer ((-20 0Cto – 80 0C) for biochemical analysis. Five-milliliter blood samples were stored. The glucose oxidase method was used to measure the serum glucose level. Serum total cholesterol (TC), triglyceride (TG), and HDL-C were measured using cholesterol oxidase assay, glycerophosphate oxidase assay, and cholesterol oxidase assay, respectively. To calculate serum LDL-C, Friede-wald's equation was used.20Fasting serum insulin levels were determined using the ELISA method (Linco Research Inc., USA). We employed homeostatic model assessment (HOMA) to measure b-cell functional deficiency (HOMA B%), insulin sensitivity (HOMA S%), and insulin resistance (HOMA IR) based on fasting serum glucose and fasting serum insulin level. HOMA IR and HOMA B% were obtained using the following formulas.21 (a) HOMA-IR ¼ Glucose x Insulin/22.5 (b) HOMA-B % ¼ 20 x Insulin/Glucose-3.5, if the glucose in molar units (mmol/L).LAP was calculated as [waist circumference (cm)–65] × [triglycerides (mmol/L)] in men, and [waist circumference (cm)–58] × [triglycerides (mmol/L)] in women.[21,22]

The data were expressed as mean ± SD (Standard deviation). The statistical significance of differences between the values was assessed by univariate and multiple regression analysis, and one-way ANOVA was carried out using Statistical Package for Social Science (SPSS) version 22. At the same time, a t-test was performed to analyze the relationship between lipid profile and type 2 diabetes. Statistical analysis was also performed using Graph Pad Prism version-6 software. The odds ratios (OR) were used to measure relative risk at 95% confidence intervals. Fisher's exact test was performed to analyze the association of respective gene polymorphisms with type 2 diabetes. The p-value of <0.05 was considered statistically significant.

Results:

In Table 1 Biochemical parameters of the glycemic, insulinemic, and lipidemic status were shown.FBG, ABF, and HbA1c% levelsof the T2DM group were significantly(p <0.001) higher than the control groupto determine glycemic status. The fasting serum insulin level of the T2DM group was significantly (p <0.001) higher than the control. On the other hand, the HOMA B% (101.34±26.12vs 309.12±47.23; p<0.001); HOMA-IR(3.39±2.65 vs 9.19±7.62; p<0.001), and secretory HOMA (357.04±101.42 vs 103.01±102.79; p<0.001) were significantly lower in the diabetic group compared to control; whereas insulin was significantly higher (16.03±10.79 vs 23.22±15.73 ; p<0.001) in the T2DM group compared to control. The TG level was significantly (p<0.001) higherin the diabetic group than that of the control, while the totalcholesterol and LDL-C level of the control and T2DM groupswerenot statistically significant. The HDL-C level was significantly (p<0.001) lower in the T2DM group compared to the control as well as LAP wassignificantly (p<0.001) higher in the T2DM groupthan the control group.

Table I

Biochemical (Glycemic and Insulinemic) and (Lipidemic) Characteristics of the Study Population

Variables	Study subjects (n=700)	
	Control (n=350)	T2DM (n=350)
FBG (mmol/L)	4.82±1.21	8.77±3.00**
ABF (mmol/L)	6.93±1.21	12.13±4.05**
Fasting Insulin (ìU/L)	16.03±10.79	23.22±15.73**
HbA_1c (%)	5.23±0.74	7.26±1.76**
HOMA IR	3.39±2.65	9.19±7.62**
HOMA-B%	309.12±47.23	101.34±26.12**
Secr HOMA	357.04±101.42	103.01±102.79**
Triglycerides (mg/dL)	142.57±87.28	189.45±106.31**
Total Cholesterol (mg/dl)	180.00±40.49	184.92±42.86
HDL- Cholesterol (mg/dL)	45.69±17.14	38.20±7.34**
LDL- Cholesterol (mg/dL)	105.38±79.31	113.42±42.03
LAP	3764±160	4813±186**

Values were presented as Mean ±SD; FBG*:* Fasting blood glucose; ABF: 2 hours after breakfast; HOMA B%= Beta Cell Function; HOMA-IR: Homeostasis Model of Assessment Insulin Resistance; Secretory HOMA: Secretory Homeostasis Model of Assessment; HDL= High-Density Lipoproteins and LDL= Low-Density Lipoproteins.

TC= Total Cholesterol; LAP: Lipid accumulation product index; SBP: systolic blood pressure; DBP: Diastolic blood pressure;p-value was obtained from individual sample t-test, **p<0.001; level of significance was set to p<0.05

Table II showed the correlation of LAP with anthropometric and clinical parametersand showed that LAP was significantly correlated with BMI, waist-hip ratio (WHR), SBP, and DBP in T2DM patients but in control, LAP wassignificantly correlated with BMI & WHR.

Table II

Correlation of LAP with anthropometric and clinical parameters in the study population

Parameter	T2DM (n=350)		Control (n=350)	
	r-value	P value	r-value	p-value
BMI	0.399**	0.000	0.152**	0.004
WHR	0.344**	0.000	0.120*	0.03
SBP	0.202**	0.000	0.057	0.288
DBP	0.207***	0.000	-0.038	0.474

Table III showed the Correlation of LAP with glycemic parameters in the study population.LAP had a positive (p<0.001) correlationwith FBS, ABF, HBA_1C, Insulin, HOMA-IR, and Secret-HOMA in diabetic patients.

Table III

Correlation of LAP with glycemic parameters in the study population

Parameter	Control (n=350)		T2DM (n=350)	
	r-value	P value	r-value	p-value
FBS	0.176**	0.001	0.167**	0.002
ABF	0.112	0.036	0.107*	0.04
HBA_1C	0.103	0.05	0.113*	0.03
Insulin	0.091	0.089	0.209**	0.000
HOMA-IR	0.161**	0.003	0.239**	0.000
HOMAB%	0.022	0.688	-0.016	0.763
Secret-HOMA	0.022	0.688	0.993	0.000

LAP had a positive (p<0.001) correlation withTAG and VAI in diabetic patients shown in Table 4.

Table IV

Correlation of LAP with Lipidemic parameter in the study population

Parameter	Control (n=350)		T2DM (n=350)	
	r-value	P value	r-value	p-value
TAG	0.807**	0.000	0.188**	0.000
Cholesterol	0.029	0.593	0.082	0.127
HDL-C	-0.162**	0.002	-0.022	0.688
LDL-C	-0.011	0.835	0.037	0.488
VAI	0.741**	0.000	0.385**	0.000

Table V showed the multiple comparisons of LAP with fast food-taking habits in the study population. A pie chart represented that the Fastfood-takingpopulationhad significantly higher LAP than other groups.

Table V

Multiple comparisons of LAP with fast food taking habits in the study population

Fast food-taking habit	Number of subjects (n=700)	Mean LAP±SD	P-value
Yes	297	4038±168	0.020
No	216	3722±253	0.118
Occasional	187	3288±240	0.589

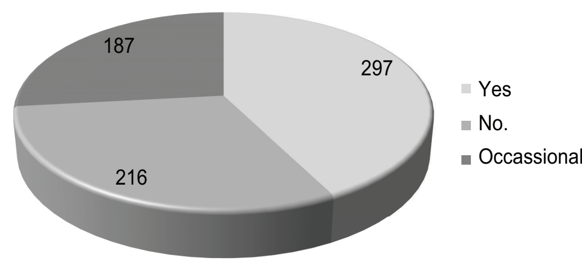

Fig.-1: *Represents the food habit of the study population.*

Figure 1 Represents the food habit of the studypopulation.

Figure 2 showed a comparative box plot diagram between the case and control groups and showed that the mean LAP value was significantly higher in the T2DM patients than in the control group.

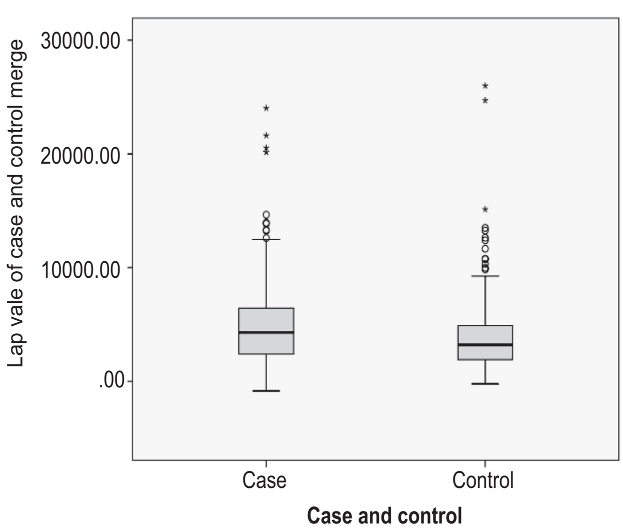

Fig.-2: *Comparative box plot diagram between the case and control group*

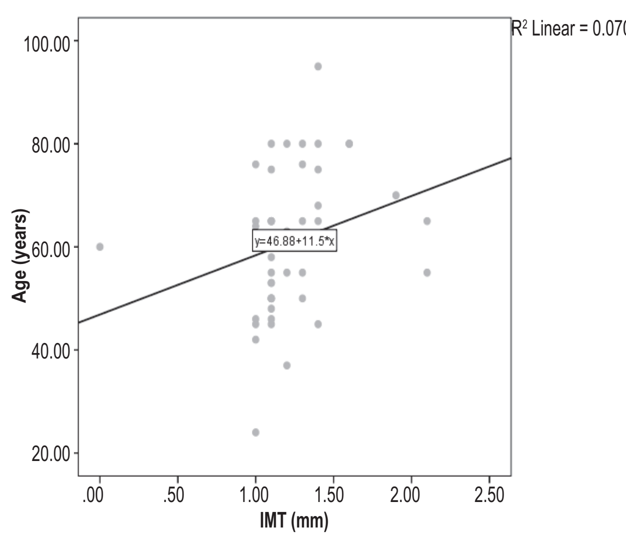

Fig 3: Association of LAP with LDL cholesterol in the study population

Figure 3 showed that LDL-C was significantly associated with LAP value in the study population, where the r square value was 2.82

Discussion:

We discovered that LAP was significantly higher in T2DM participants than in controls. In contrast to our findings, a prospective investigation found no link between LAP and fast food consumption in the study individuals.[23] However, one cross-sectional investigation found a link between fast food consumption and LAP among overweight young individuals aged 17 to 35 [24] . An Iranian study found that boosting MUFA by reducing total protein or PUFA in isoenergetic diets was related with a lower visceral adiposity index and alterations in lipid accumulation products.[25] The concept that MUFAs are good fatty acids stems from studies on the effects of olive oil, however additional research indicates that MUFA intake from animal sources has distinct consequences.[26] In contrast to our findings, other observational studies did not detect a significant association among fast food intake and LAP [27,28]; nonetheless, it has been claimed that replacing carbs with total protein was positively linked with VAI in women only[29]. A recent Iranian study found that larger dietary amounts of protein and animal-derived MUFA were positively linked with VAI; additionally, in an isoenergetic diet, replacing carbs, MUFAs, and PUFAs with protein was positively associated with 3-year improvements in VAI[30,31]. In another prospective trial, total protein intake was not linked with 5-year percent change in VAT in 1114 black and Hispanic overweight people. [30,31]According to one study, LAP and VAI were markers of insulin resistance and metabolic abnormalities in young women with the polycystic ovarian syndrome. A recent meta-analysis looked at how saturated fat, polyunsaturated fat, monounsaturated fat, and carbohydrates affected glucose-insulin homeostasis.[32,33]Only caloric intake substitution with PUFA was linked to decreased fasting glucose, lower HbA1c, enhanced HOMA-IR, and increased insulin secretion capacity Moreover, when PUFA replaced MUFA, insulin secretion capability improved. PUFA was seen in studies to reduce oxidative stress, hepatic lipid synthesis and steatosis, pancreatic lipotoxicity, and insulin resistance.[34] In addition, MUFA ingestion had no effect on fasting glucose when compared to other macronutrients. Nonetheless, it was observed to lower HbA1c and improve HOMA-IR when compared to carbohydrate or SFA.[34,35] This research has significant drawbacks. First, despite being nationally representative, the results of this cross-sectional study cannot indicate a causal association between DPs and VAT. Second, while our study incorporated recognized possible confounding variables that can influence obesity, such as environmental and genetic factors, residual confounding variables may still remain. Furthermore, we lacked data on VAT direct measurement for validation. This study has a number of advantages. Because we used a large sample drawn at random from the general population, the results from nationally representative samples can be extended to the general population. Finally, LAP was found to be substantially linked with insulin resistance and metabolic syndrome in T2 diabetes participants. The study group with a favorable fast food eating pattern had significantly higher LAP.

Conclusion:

LAP was significantly correlated with insulin resistance and metabolic syndrome in T2 diabetic subjects. The favorable, fast food-eating habit-containing study group had considerably greater LAP.

Conflict of Interest:

The author stated that there is no conflict of interest in this study

Funding:

No specific funding was received for this study.

Ethical consideration:

The study was conducted after approval from the ethical review committee. The confidentiality and anonymity of the study participants were maintained

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