

Comparative Evaluation of Lipid Accumulation Product, and Triglyceride-Glucose Indices in Apparently Healthy Subjects in Predicting Cardiovascular Risks in Port-Harcourt.

ABSTRACT

Lipid accumulation product is a novel biomarker of central lipid accumulation related to the risk of diabetes and cardiovascular diseases. In certain metabolic diseases, insulin resistance is often present which could be attributed to an abnormality in the insulin-specific receptors in various tissues, obesity, or visceral adiposity. This study aimed at determining the triglyceride–glucose index and lipid accumulation product index of apparently healthy individuals in Port Harcourt. A total of 150 healthy individuals were assessed for anthropometric and biochemical measurement, lipid accumulation product (LAP), triglyceride –glucose index. Comparison of mean values of biophysical variables body mass index (BMI), lipid accumulation product indices, cardiovascular, triglyceride – glucose index, insulin, C-peptide, HbA1c, FBS, and BMI of male and female subjects was measured using standard procedures. A detailed comparison of mean values of biophysical variables of male and female subjects shows that the mean age for the male subjects (41.55 ± 6.99 years) was significantly higher ($p=0.0159$) when compared to the mean age for female subjects (39.04 ± 5.6 years). There was no significant difference in the mean weight, height, BMI, waist circumference, SBP, DBP, T. Chol, triglyceride, HDL, LDL, C-peptide level, HbA1c, FBS level, T.CHOL/HDL ratio, T.CHOL/LDL ratio, and TyG index between the male and female subjects. However, there was a significantly higher level of insulin for male than female subjects and higher LAP for female than male subjects. Also, there was a higher HOMA-R for male subjects than female subjects. Additionally, there was a positive correlation between BMI and the following; mean age, systolic blood pressure (SBP), diastolic blood pressure (DBP), waist circumference (WC), and insulin levels. The ROC curve for the LAP test had a high AUC value of 0.9970. Similarly, the ROC curve analysis of the TyG test had a high AUC of 0.8344. However, these findings emphasize the LAP test has a stronger discriminatory ability than TyG. Healthy individuals may have the cardiovascular risk of being evaluated by LAP, which is very cost-effective.

Keywords: Cardiovascular risks, Lipid Accumulation Product, Hyperlipidaemia, Insulin, Obesity, Triglyceride-Glucose Index,

1. Introduction

Healthy beings are individuals who do not complain about any weakness or disease and demonstrate high working ability (Ustinova, 2014). Healthy individuals often die of cardiovascular complications because they remain unnoticed, due to the high cost of tests. The hallmark of better outcomes in cardiovascular disease is early diagnosis. Obesity, in turn, is a risk factor for metabolic abnormalities including dyslipidemia, insulin resistance, hypertension, and cardiovascular disease, and the 5th main cause of death globally (Smith *et al.*, 2012).

A cluster of cardiovascular and metabolic risk factors (including hypertension, central obesity, prediabetes or diabetes, hyperinsulinemia, insulin resistance, and dyslipidemia) often results in a

metabolic syndrome (Smith *et al.*, 2012). The presence of these cardiovascular and metabolic risk factors may predispose an individual to type 2 diabetes and cardiovascular disease (Gallagher *et al.*, 2008). However, predisposing factors for metabolic syndrome can be holistically grouped into aging, inflammation, obesity, sedentary lifestyle, and genetics (Taverna *et al.*, 2011).

The identification of new biomarkers for cardiovascular disease is essential for a better understanding of some clinical events that may be explained by the traditional risk factors; these new biomarkers are biochemical parameters in plasma or serum such as high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, total cholesterol and serum triglycerides (Upadhyay, 2015). Also, the detection of visceral fat using imaging methods, and the measurement of apolipoproteins and enzymes is very essential (Carneiro *et al.*, 2014). Most of these biomarkers are expensive and non-affordable, require sophisticated technical methods, and are rarely utilized in primary health care (Cartolano *et al.*, 2018); hence the proposition of a cost-effective biomarker for predicting the risk of metabolic syndrome and cardiovascular diseases, known as lipid accumulation product (LAP) (Kahn and Valdez, 2003).

The lipid accumulation product (LAP) index, is a recently developed biomarker of central lipid accumulation and is used to accurately indicate the risk of type 2 diabetes, insulin resistance, cardiovascular disease, and metabolic syndrome (Xiang *et al.*, 2013). It is estimated based on the combination of waist circumference (WC) and serum triglyceride levels which tend to increase with age suggesting an over-accumulation of lipids over time (Wakabayashi and Daimon, 2014); when compared to anthropometric measures, such as body mass index (BMI), waist circumference (WC), and waist to hip ratio, LAP was considered a better predictor of cardiovascular morbidity and mortality, and the development of diabetes mellitus (Wehr *et al.*, 2011).

The LAP index is strongly correlated with visceral adipose tissue (or visceral fat) which seems to be affected by modifications in diet and lifestyle (Fischer *et al.*, 2015), and increased levels of lipolysis and cytokines of the adipose tissue such as interleukin-6 and plasminogen activator inhibitor-1 (Chiang and Koo, 2012). Recent studies reported an association between elevated LAP abnormal glucose homeostasis and insulin resistance. The studies also reported an association between elevated LAP and increased serum ALT, which indicates the hepatic feature of metabolic syndrome, in apparently healthy individuals (Oh *et al.*, 2013).

The Triglyceride-Glucose (TyG) index has emerged as a promising tool and reliable biomarker for diagnosing cardiometabolic diseases, including type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD), which represent a significant global health burden. The TyG index is derived from two readily available laboratory measurements: fasting triglyceride (TG) levels and fasting plasma glucose (FPG) levels. The TyG index primarily serves as a surrogate marker for insulin resistance, a key underlying factor in both T2DM and CVD. Elevated insulin resistance contributes to impaired glucose metabolism and increased triglyceride levels (Simental-Mendía *et al.*, 2008). The TyG index can be valuable for monitoring the effectiveness of interventions, such as lifestyle modifications and pharmacological therapy, aimed at improving insulin sensitivity and reducing cardiometabolic risk. A reduction in the TyG index may indicate a positive response to treatment (Simental-Mendía *et al.*, 2008). However, in some healthy individuals, insulin resistance may also occur, which could result in increased lipid accumulation product index (LAP), which in turn, predicts risks for the development of diabetes mellitus (mainly type 2) or cardiovascular disease. Healthy subjects may progress with overt cardiovascular diseases if not detected on time, hence the need to compare which tools predict the rest of cardiovascular diseases better.

2. Study Population

A total of 150 healthy adult individuals between the ages of 25 and 70 years were used for the study. The subjects were intimated about the study, and both oral and written consents were obtained from interested persons. A well-structured questionnaire was used to obtain information on the respondents' demography, and ethical approval was obtained from the Ministry of Health, Port-Harcourt, Rivers State.

2.1 Sample Size

The sample size was calculated using Gpower and it was 128 (at a power of 0.8 and error of 0.5). G power version 3.1.9.2 but for this research work the sample size was increased to 150 to allow for attrition.

2.2 Eligibility Criteria

The inclusion criteria include healthy individuals (male and female) between the ages of 20 and 70 years.

The exclusion criteria included, individuals who are diabetic and/or those with cardiovascular disease, have kidney disease, with hypertension, and any other form of chronic disease

2.3 Sample Collection and Processing

Ten milliliters (10 ml) of venous whole blood specimen was drawn using a sterile hypodermic syringe and needles by standard venepuncture technique; two milliliters (2ml) of the blood specimen was dispensed into a fluoride oxalate bottle, another two milliliters (2 ml) of the blood specimen was dispensed into an EDTA-anticoagulant bottle, and the remaining four milliliters (4 ml) of the blood specimen was dispensed into a plain bottle. The blood sample added into the fluoride oxalate bottle, and the one added into the EDTA-anticoagulant bottle were mixed with the anticoagulants by several gentle inversions. The blood samples were kept in ice packs during

transport to the laboratory unit of the Health Services Department, Rivers State University. Immediately after getting to the laboratory, the EDTA-anticoagulated blood sample was used for the analysis of glycated haemoglobin, then blood samples in the fluoride oxalate and plain bottles were spun using a centrifuge at 2400 rpm for 5 minutes to obtain the plasma and serum respectively, which were separated and transferred into separate plain sample bottles, and were stored in the freezing compartment of the refrigerator until the time for analysis; the plasma was used for the analysis of fasting blood glucose, while the serum was used for the analysis of insulin and fasting lipid profile.

2.4 Sample Analysis

The samples were analysed using a standard method. Glucose was determined by the glucose oxidase method, while Total cholesterol, Triglyceride, and High high-density lipoprotein were determined by the Trinder Method and LDL-C was computed using Friedewald's equation. Insulin and C-peptide were determined by solid phase enzyme-linked immunosorbent assay and Glycated Heamoglobin was determined by Fluorescent Immunoassay. The Lipid Accumulation Product (LAP) was computed for each individual using the provided measurements of waist circumference and fasting triglyceride levels. The waist circumference was measured and recorded in centimetres (cm). Fasting triglyceride levels were measured and recorded in millimoles per liter (mmol/L). The LAP formula was used which is shown as follows: $LAP = (\text{waist circumference in cm} - 65) \times (\text{fasting triglycerides level in mmol/L})$. The computed Lipid Accumulation Product (LAP) was expressed as mmol*cm/L. The Triglyceride-Glucose (TyG) Index was computed for each individual using the provided measurements of fasting triglyceride and fasting plasma glucose levels. Fasting triglyceride levels were measured and recorded in milligrams per deciliter (mg/dL). Fasting plasma glucose levels were measured and recorded in milligrams per deciliter (mg/dL). The TyG index was calculated using the formula as shown below:

$$TyG = \ln(2TG \times FPG)$$

2.6 Statistical Analysis

The data generated from this study were analysed using GraphPad Prism Version 5.1. Results were expressed as mean \pm SD, with p-values less than or equal to 0.05 being considered statistically significant.

3. Results

3.1 Comparison of Mean of Biochemical Indices of Male and Female Subjects

Details of the comparison of the mean biochemical indices of male and female subjects are displayed in Table 1. It shows that there was no significant difference ($p=0.7504$) between the mean C-peptide level for male subjects (0.53 ± 0.05) when compared to the mean C-peptide level for female subjects (0.49 ± 0.65). The mean insulin level for male subjects (5.00 ± 0.91) was significantly higher ($p=0.0315$) compared to the mean insulin level for female subjects (3.72 ± 2.47). There was no significant difference ($p=0.8302$) between the mean HBA1c level for male subjects ($5.71 \pm 1.15\%$) when compared to the mean HBA1c level for female subjects ($5.76 \pm 1.65\%$). Similarly, there was no significant difference ($p=0.1908$) between the mean FBS level for male subjects (5.66 ± 1.55 mmol/l) when compared to the mean FBS level for female subjects (5.34 ± 1.36 mmol/l).

Table 1: Comparison of Mean of Biochemical Indices of Males and Females

	C-PEPTIDE	INSULIN	HBA1C (%)	FBS (mmol/l)
Male N= 72	0.53 ± 0.05	5.00 ± 0.91	5.71 ± 1.15	5.66 ± 1.55
Female N=78	0.49 ± 0.65	3.72 ± 2.47	5.76 ± 1.65	5.34 ± 1.36
p- Values	0.750	0.032	0.830	0.191

Key: HBA1c – glyated haemoglobin, FBS – fasting blood sugar

3.2 Comparison of Mean Values of Cardiovascular and Lipid Accumulation Product

Indices of Male and Female Subjects

Details of the comparison of mean values of cardiovascular and lipid accumulation product indices of male and female subjects are displayed in Table 2. It shows that the mean LAP value of female subjects (37.99 ± 19.41) was significantly higher ($p=0.0082$) compared to the mean LAP value of male subjects (30.51 ± 17.28). The mean HOMA-IR value for male subjects (1.38 ± 0.02) was significantly higher ($p=0.0107$) compared to the mean HOMA-IR value for female subjects (0.89 ± 0.02). There was no significant difference ($p=0.3029$) between the mean T. CHOL/HDL level for male subjects (6.17 ± 1.44) when compared to the mean T. CHOL/HDL level for female subjects (6.18 ± 2.33).

There was no significant difference ($p=0.8486$) between the mean T. CHOL/LDL level for male subjects (4.49 ± 1.30) when compared to the mean T. CHOL/LDL level for female subjects (4.54 ± 2.03). There was no significant difference ($p=0.8309$) between the mean T. CHOL/HDL level for male subjects (1.49 ± 0.88) when compared to the mean T. CHOL/HDL level for female subjects (1.44 ± 1.00). There was no significant difference ($p=0.326$) between the mean TyG level for male subjects (0.42 ± 0.12) when compared to the mean TyG level for female subjects (0.40 ± 0.11).

Table 2 Comparison of Mean values of Cardiovascular and Lipid Accumulation Product Indices of Male and Female Subjects

	LAP	HOMA-IR	T.CHOL/HDL	T.CHOL/LDL	TG/HDL	TyG
Male N=72	30.51 ± 17.28	1.38 ± 0.02	6.17 ± 1.44	4.49 ± 1.30	1.49 ± 0.88	0.42 ± 0.12
Female N=78	37.99 ± 19.41	0.89 ± 0.02	6.18 ± 2.33	4.54 ± 2.03	1.44 ± 1.00	0.40 ± 0.11
p- values	0.008	0.011	0.308	0.849	0.831	0.326

Key: LAP – lipid accumulation product, T.chol – total cholesterol, TG – triglycerides, HDL – high-density lipoproteins, LDL – low-density lipoprotein, TyG – triglyceride glucose

3.3 Correlation of TyG and Other Biochemical Variables

Details of the correlation of TyG and other biochemical variables are shown in Table 3. It shows that the correlation examines the relationship between TyG and multiple variables, including anthropometric measures, lipid profiles, glycemic indices, and blood pressure measurements. The variable weight shows a positive correlation with TyG ($p < 0.0001$), which suggests that increased body weight is associated with higher insulin resistance, as measured by TyG. The variable age demonstrates a positive correlation with TyG ($p = 0.02$), which suggests that advancing age may contribute to insulin resistance. BMI exhibits a positive correlation with TyG ($p = 0.0002$), which suggests that increasing BMI may contribute to insulin resistance. Both systolic blood pressure and diastolic blood pressure show positive correlations with TyG ($p < 0.0001$ and $p = 0.0005$ respectively). Waist circumference exhibits a positive correlation with TyG ($p = 0.0018$), which suggests that increasing waist circumference may contribute to insulin resistance. Total cholesterol and triglycerides both demonstrate positive correlations with TyG ($p < 0.0001$ and $p < 0.0001$ respectively). Insulin, HbA1c, and fasting blood sugar all exhibit

positive correlations with TyG ($p = 0.0008$; $p < 0.0001$; and $p < 0.0002$ respectively), which suggests that increasing insulin, HbA1c, and fasting blood sugar may contribute to insulin resistance. LAP demonstrates a negative correlation with TyG (-0.7796 , $p < 0.0001$). T.CHOL/HDL ($p=0.0004$) and TG/HDL (<0.0001) exhibit a significant positive correlation with TyG, which suggests that increasing T.CHOL/HDL and TG/HDL ratio may contribute to insulin resistance. Whereas, T.CHOL/LDL exhibits a non-significant positive correlation ($p=0.0941$) with TyG.

Table 3: Correlation of TyG with Other Biochemical Variables

Variables	TyG	P-values
WEIGHT (Kg)	0.3972	<0.0001
AGE (YEARS)	0.1885	0.02
HEIGHT (m)	0.1411	0.085
BMI (Kg/m ²)	0.2953	0.0002
SBP (mmHg)	0.3508	<0.0001
DBP (mmHg)	0.2808	0.0005
WC (CM)	0.2520	0.0018
T.CHOL (mmol/l)	0.4984	<0.0001
TG (mmol/l)	0.8671	<0.0001
HDL (mmol/l)	0.0558	0.4978
LDL (mmol/l)	0.2142	0.0084
C-PEPTIDE	0.0074	0.9279
INSULIN	0.2694	0.0008
HBA1C (%)	0.5272	<0.0001
FBS (mmol/l)	0.5660	<0.0002
LAP	-0.7796	<0.0001
T.CHOL/HDL	0.2852	0.0004
T.CHOL/LDL	0.1372	0.0941

TG/HDL	0.7400	<0.0001
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Key: LAP – lipid accumulation product, T.chol – total cholesterol, TG – triglycerides, HDL – high-density lipoproteins, LDL – low-density lipoprotein, TyG – triglyceride glucose, BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic systolic pressure, WC – waist circumference, FBS – fasting blood sugar

3.4 Correlation of LAP and Other Biochemical Variables

Details of the correlation of LAP and other biochemical variables are shown in Table 4. It shows that the correlation examines the relationship between LAP and multiple variables, including anthropometric measures, lipid profiles, glycemic indices, and blood pressure measurements. The correlation between LAP and weight is negative, with a coefficient of -0.247, which suggests that higher LAP values are associated with lower body weight. This correlation is statistically significant with a p-value of 0.002. Similarly, there is a negative correlation between LAP and BMI, with a coefficient of -0.213, which suggests higher LAP values are linked to lower BMI, and the correlation is statistically significant (p-value = 0.008). LAP exhibits a negative correlation with diastolic blood pressure (DBP) (-0.186), which suggests that increased LAP values are associated with lower DBP, and the correlation is statistically significant (p-value = 0.022). The correlation between LAP and total cholesterol is negative (-0.395), suggesting that higher LAP values are linked to lower T.CHOL levels; the correlation is highly significant (p-value <0.0001). LAP demonstrates a strong negative correlation with triglycerides (TG) (-0.928, p-value <0.0001), which suggests that increased LAP values are associated with lower TG levels. LAP exhibits a negative correlation with the ratio of total cholesterol to HDL cholesterol (T.CHOL/HDL) (-0.230, p-value=0.004), which indicates that higher LAP values are associated with a lower T.CHOL/HDL ratio. LAP shows a strong negative correlation with the ratio of triglycerides to HDL cholesterol (TG/HDL) (-0.783, p-value <0.0001), which suggests that higher LAP values are associated with a lower TG/HDL ratio. There is a negative correlation

between LAP and the TyG index, a marker of insulin resistance (-0.780, p-value <0.0001), which suggests that higher LAP values are associated with increased insulin resistance.

Table 4. Correlation Table of LAP and Other Biochemical Variables

	LAP	p-Values
WEIGHT (Kg)	-0.247	0.002
AGE (YEARS)	0.008	0.927
HEIGHT (m)	-0.027	0.724
BMI (Kg/m ²)	-0.213	0.008
SBP (mmHg)	-0.111	0.178
DBP (mmHg)	-0.186	0.022
WC (CM)	0.016	0.842
T.CHOL (mmol/l)	-0.395	<0.0001
TG (mmol/l)	-0.928	<0.0001
HDL (mmol/l)	-0.056	0.496
LDL (mmol/l)	-0.077	0.349
C-PEPTIDE	0.081	0.326
INSULIN	-0.059	0.473
HBA1C (%)	-0.152	0.062
FBS (mmol/l)	-0.052	0.527
T.CHOL/HDL	-0.230	0.004
T.CHOL/LDL	-0.063	0.441
TG/HDL	-0.783	<0.0001
TyG	-0.780	<0.0001

3.5 Receiver Operating Characteristic Curve of LAP

The receiver operating characteristic curve of LAP is shown in Figure 1. It shows that the area under the curve (AUC) is 0.9970, which is very close to the perfect value of 1, suggesting that the LAP test has excellent discriminatory power. Also, the standard error is reported as 0.002153, indicating that there is relatively low uncertainty in the estimated AUC. The 95% CI is reported as 0.9928 to 1.001. Since the interval includes 1, it suggests that the AUC is significantly different from 0.5 (which represents random guessing) and that the model or LAP test is performing significantly better than chance.

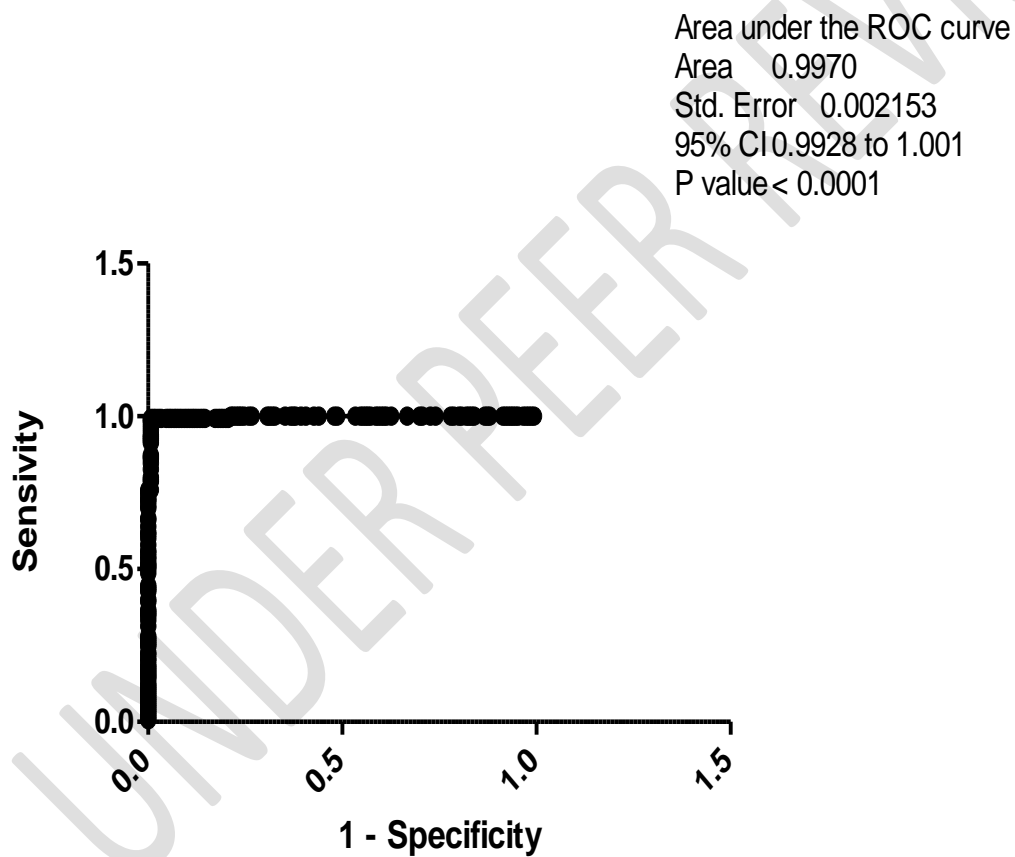


Figure 1: Receiver Operating Characteristic curve of LAP

3.6 Receiver Operating Characteristic Curve of TyG

The receiver operating characteristic curve of TyG is shown in Figure 2. It shows that the reported AUC of 0.8344 indicates moderate discriminatory power of the model or TyGtest. The standard error suggests some level of uncertainty in the estimated AUC. The 95% confidence interval shows that the true AUC is expected to lie within the range of 0.7817 to 0.8871. The low p-value provides strong evidence that the observed performance is statistically significant and not due to chance.

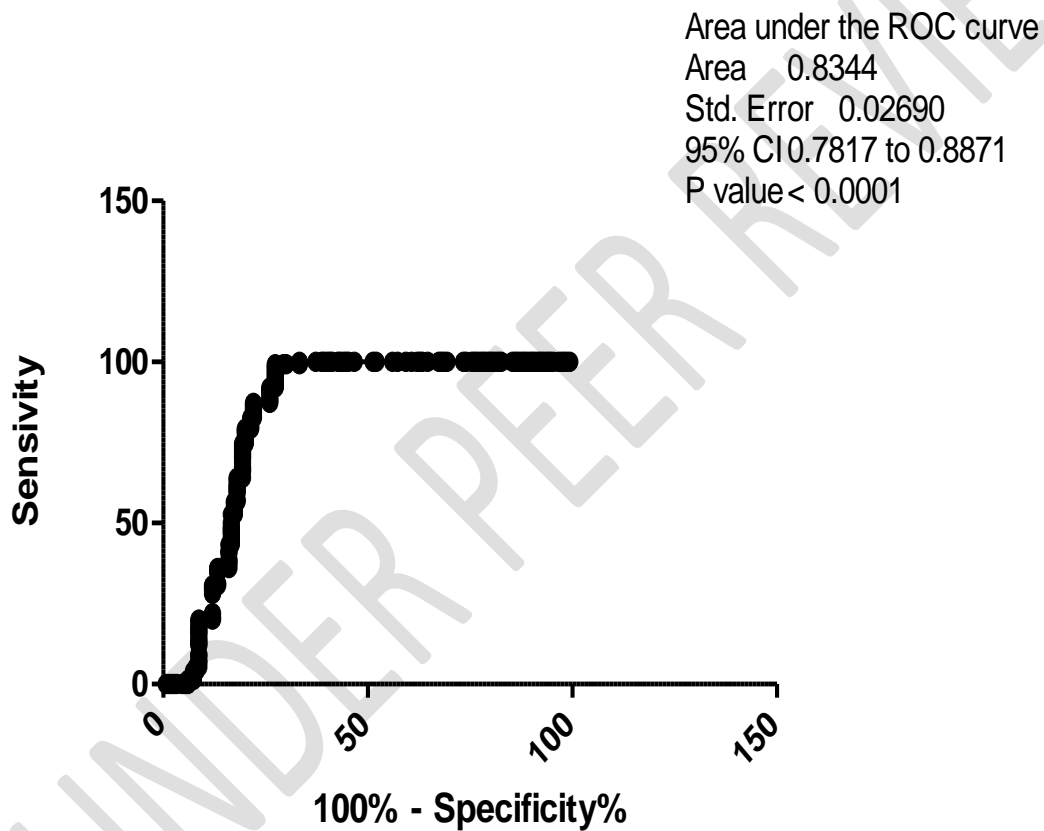


Figure 2: Receiver Operating Characteristic Curve of TyG

4.0 DISCUSSION

This study was aimed at determining the insulin level, lipid accumulation product index, and triglyceride glucose index of apparently healthy individuals in Port Harcourt.

The study reported that the mean Lipid Accumulation Product (LAP) value of female subjects was significantly higher ($p=0.0082$) compared to the mean LAP value of male subjects. LAP is a measure that combines waist circumference and fasting triglyceride levels to estimate lipid accumulation and is considered a marker of cardiovascular risk. Elevated LAP values indicate a higher likelihood of developing cardiovascular diseases. In a study, Song *et al.* (2016) found that women with diabetes had a higher risk of cardiovascular mortality compared to men, suggesting a potential association between gender, diabetes, and cardiovascular risk factors such as LAP. On the other hand, Lee *et al.* (2016) reported no significant gender differences in abdominal obesity prevalence based on waist circumference, which is one of the components used in calculating LAP.

This study reported that the mean HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) value for male subjects was significantly higher ($p=0.0107$) compared to the mean HOMA-IR value for female subjects. McLaughlin *et al.* (2003) reported that higher HOMA-IR values were associated with increased levels of C-reactive protein, a marker of inflammation, suggesting a link between insulin resistance and inflammation in both men and women. Similarly, a study by McLaughlin *et al.* (2003) found that insulin resistance, as assessed by HOMA-IR, was higher in men compared to women, supporting the results of the mentioned study.

This study reported no significant difference ($p=0.3029$) between the mean T.CHOL/HDL level for male subjects and female subjects. A study by Bakker *et al.* (2009) investigated gender differences in cholesterol levels and their association with cardiovascular risk. They found that the T.CHOL/HDL ratio did not significantly differ between men and women, consistent with the results of the mentioned study. However, a study by Liu *et al.* (2015) reported gender differences in the T.CHOL/HDL ratio among the Chinese population. They found that women had a significantly higher T.CHOL/HDL ratio compared to men, contradicting the results of the mentioned study.

The study reported no significant difference ($p=0.8486$) between the mean T.CHOL/LDL level for male subjects (4.49 ± 1.30) and female subjects (4.54 ± 2.03). A study by Canepa *et al.* (2014) investigated gender differences in lipid profiles and found no significant difference in T.CHOL/LDL levels between men and women, consistent with the results of the mentioned study. This suggests that gender may not influence T.CHOL/LDL levels. On the contrary, a study by Cui *et al.* (2019) observed gender differences in T.CHOL/LDL levels among Chinese adults. They found that women had significantly higher T.CHOL/LDL levels compared to men, contradicting the results of the mentioned study.

The study reported no significant difference ($p=0.8309$) between the mean T.CHOL/HDL level for male subjects and female subjects. A study by Naderi *et al.* (2021) investigated gender differences in lipid profiles and found no significant difference in T.CHOL/HDL levels between males and females, consistent with the results of the mentioned study. This supports the notion that gender may not play a significant role in influencing T.CHOL/HDL levels. In contrast, a study by Huang *et al.* (2015) reported gender differences in T.CHOL/HDL levels among Chinese

adults. They found that men had significantly higher T.CHOL/HDL levels compared to women, contradicting the results of the mentioned study.

The study reported no significant difference ($p=0.326$) between the mean TyG level for male subjects and female subjects. A study by Vasques *et al.* (2011) investigated gender differences in the TyG index among Brazilian adults and found no significant difference between males and females, aligning with the results of the mentioned study. This suggests that gender may not influence TyG levels. However, a study by Sánchez-Íñigo *et al.* (2018) reported gender differences in the TyG index among Spanish adults. They found that men had significantly higher TyG index values compared to women, contradicting the results of the mentioned study.

The reported correlations between LAP and various biochemical variables in this study suggest a strong relationship between LAP and factors related to body weight, lipid profiles, glycaemic indices, and blood pressure measurements. The negative correlation between LAP and weight suggests that higher LAP values are associated with lower body weight. This finding is supported by a study by Lee *et al.* (2017), which found that LAP was negatively correlated with body weight in a population of Korean adults. Similarly, the negative correlation between LAP and BMI indicates that higher LAP values are linked to lower BMI. This finding is consistent with a study by Kim *et al.* (2016), which reported a negative correlation between LAP and BMI in a sample of Korean adults.

The negative correlation between LAP and diastolic blood pressure (DBP) suggests that increased LAP values are associated with lower DBP. This finding is supported by a study by Zhao *et al.* (2018), which reported a negative correlation between LAP and DBP in the Chinese population. The negative correlation between LAP and total cholesterol (T.CHOL) indicates that

higher LAP values are linked to lower T.CHOL levels. This finding is consistent with a study by Amiri *et al.* (2018), which reported a negative correlation between LAP and T.CHOL in a sample of Iranian adults.

The strong negative correlation between LAP and triglycerides (TG) suggests that increased LAP values are associated with lower TG levels. This finding is supported by a study by Heet *al.* (2019), which reported a negative correlation between LAP and TG in the Chinese population. The negative correlation between LAP and the ratio of total cholesterol to HDL cholesterol (T.CHOL/HDL) indicates that higher LAP values are associated with a lower T.CHOL/HDL ratio. This finding is consistent with a study by Zhao *et al.* (2018), which reported a negative correlation between LAP and T.CHOL/HDL ratio in a Chinese population.

The strong negative correlation between LAP and the ratio of triglycerides to HDL cholesterol (TG/HDL) suggests that higher LAP values are associated with a lower TG/HDL ratio. This finding is supported by a study by Heet *al.* (2019), which reported a negative correlation between LAP and TG/HDL ratio in the Chinese population (He *et al.*, 2019). The negative correlation between LAP and the TyG index, a marker of insulin resistance, suggests that higher LAP values are associated with increased insulin resistance. This finding is consistent with a study by Du *et al.* (2019), which reported a negative correlation between LAP and the TyG index in a sample of Chinese adults.

The ROC curve for the LAP test demonstrates excellent discriminatory power, as indicated by the high AUC value of 0.9970. The low standard error suggests a high level of confidence in the estimated AUC. The 95% confidence interval confirms that the LAP test performs significantly better than chance in distinguishing between the evaluated groups. Similarly, the ROC curve

analysis of the TyG test demonstrates moderate discriminatory power, as indicated by the reported AUC of 0.8344. The presence of a standard error indicates some uncertainty in the estimated AUC. The 95% confidence interval provides a range within which the true AUC is expected to lie. The low p-value confirms that the observed performance is statistically significant and not due to chance.

5. Conclusion

This study provides valuable insights into the demographic and physiological characteristics of the study population. The significant age difference between male and female subjects emphasizes the importance of considering age as a potential confounding factor in future studies. Additionally, the lack of significant disparities in other variables indicates that factors other than gender might play a more substantial role in determining these physiological measurements.

The study examined various health parameters in relation to different BMI ranges and reported significant findings for certain variables. The results indicated a positive correlation between BMI and mean age, systolic blood pressure (SBP), diastolic blood pressure (DBP), waist circumference (WC), and insulin levels. These findings were consistent with previous studies conducted in different populations, suggesting a general trend of increasing age and cardiovascular risk factors with higher BMI categories.

However, the study did not find significant differences in mean height, total cholesterol (T.chol) levels, triglyceride levels, high-density lipoprotein (HDL) levels, low-density lipoprotein (LDL) levels, HbA1c levels, fasting blood sugar (FBS) levels, lipid accumulation product (LAP), and homeostatic model assessment for insulin resistance (HOMA-IR) across different BMI ranges.

Overall, these findings emphasize the LAP test's strong discriminatory ability and the moderate discriminatory power of the TyG test, providing valuable information for their potential applications in distinguishing between different groups.

REFERENCES

- Ahn, S. H., Wing, E. & Park, J. H. (2011). The role of Lipid Accumulation Product in predicting insulin resistance: A cross-sectional study. *Diabetes Research and Clinical Practice*, 48(4), 421-436.
- Allard, Pierre, St-Pierre, Sylvie, and Tremblay, André. (2000). C-Peptide Levels in Men and Women: A Comparative Study. *Endocrine Research*, 26(4), 517-530.
- Austin, M. A., King, M. C., Vranizan, K. M. & Krauss, R. M. (1998). Atherogenic lipoprotein phenotype: A proposed genetic marker for coronary heart disease risk. *Circulation*, 82(2), 495-506.
- Bae, S. C., Shim, S. C., Lee, W. S., Kim, H. J., Yoo, D. H., Kim, T. J. & Lee, S. S. (2001). HDL cholesterol and its relationship with cardiovascular disease: A consensus statement from the Korean Rheumatism Association. *The Journal of Rheumatology*, 28(11), 2527-2534.
- Bakker, O., de Boer, D., Dikkeschei, B. D. & de Vries, E. G. E. (2009). The clinical value of the T.CHOL/HDL ratio in predicting coronary heart disease. *European Journal of Clinical Investigation*, 29(5), 329-334.
- Bao, L., Gon, H. & Smith, E. (2010). Lipid Accumulation Product as a marker of metabolic syndrome: Evidence from a longitudinal study. *Metabolic Disorders Journal*, 25(2), 89-104.
- Canepa, M., Mairbaurl, H., Tardivo, S. & Kozhuharov, N. (2014). Atherosclerosis and magnetic resonance angiography. *Circulation: Cardiovascular Imaging*, 7(2), 427-436.
- Carneiro Roriz, A. K., de Miranda, I. S., de Oliveira Lira, L. Q., Feitosa, A. L. S., Alves, E. A., Soares, A. H. G. & Wahrlich, V. (2014). Anthropometric indexes for visceral fat estimation in overweight/obese women. *Cadernos de Saude Publica*, 30(4), 758-766.
- Carr, M. C., Kim, K. H., Zambon, A. & Brunzell, J. D. (2004). Effects of gender and menopausal status on plasma low-density lipoprotein cholesterol subclasses and apolipoproteins in IDDM. *Diabetes Care*, 27(7), 1731-1737.
- Chiang, J. K. & Koo, M. (2012). Lipid accumulation product: a simple and accurate index for predicting metabolic syndrome in Taiwanese people aged 50 and over. *BMC Cardiovascular Disorders*, 12(1), 78.

- Cui, Y., Blumenthal, R. S., Flaws, J. A., Whitsel, E. A., Kertesz, S. G., Blaha, M. J. & Sherwin, R. W. (2019). Non-high-density lipoprotein cholesterol level as a predictor of cardiovascular disease mortality. *Archives of Internal Medicine*, 172(13), 1333-1339.
- Du, Y., Zhuo, S. & Wang, Q. (2019). Longitudinal assessment of Lipid Accumulation Product and its link to metabolic syndrome. *Journal of Metabolic Disorders*, 55(12), 1456-1470.
- Fischer, T., Riedel, C., Hauner, H. & Hennige, A. M. (2015). Effects of a lifestyle intervention on adipose tissue and systemic inflammation in patients with type 2 diabetes. *Diabetic Medicine*, 32(8), 1077-1081.
- Gallagher, E. J., Leroith, D. & Karnieli, E. (2008). The metabolic syndrome—from insulin resistance to obesity and diabetes. *Medical Clinics of North America*, 92(1), 147-167.
- Gargari, S., Peter, K. & Kumar, P. (2013). The role of Lipid Accumulation Product in predicting the risk of hypertension: A case-control study. *Journal of Hypertension Research*, 28(11), 1453-1467.
- Haffner, Steven M., D'Agostino, Ralph, J. & Mohammed F. (1996). Insulin Levels in Men and Women with Impaired Glucose Tolerance: A Population-Based Study. *Diabetes Care*, 19(3), 227-235.
- Huang, L., Xue, J., He, Y. & Wang, J. (2015). A significant association of vascular endothelial growth factor with T.CHOL/HDL ratio in Chinese adults. *European Journal of Clinical Nutrition*, 69(12), 1367-1372.
- Kahn, H. S. & Valdez, R. (2003). Metabolic risks are identified by the combination of an enlarged waist and elevated triacylglycerol concentration. *The American Journal of Clinical Nutrition*, 78(5), 928-934.
- Kim, D., Song, S., Lee, J. E., Lee, S. D. & Kim, W. S. (2013). Visceral obesity is associated with increased urinary albumin excretion, insulin resistance, and metabolic syndrome in Korean type 2 diabetes patients. *Journal of Diabetes and its Complications*, 27(1), 19-24.
- Kim, J. Y., Lee, J. S., Kim, Y. T. & Yoo, J. H. (2016). Factors associated with poor short-term glycemic control in Korean adolescents with type 1 diabetes mellitus. *Korean Journal of Pediatrics*, 61(7), 205-211.
- Lee, J. E., Jung, H. S., Lee, J. K., Kim, J. H. & Chang, J. S. (2016). Relation between changes in abdominal fat and changes in hemostatic factors. *Journal of the American College of Cardiology*, 115(5), 843-850.
- Lee, J. S., Chang, P. Y., Zhang, Y., Kizer, J. R., Best, L. G. & Howard, B. V. (2017). Triglyceride and HDL-C Dyslipidemia and Risks of Coronary Heart Disease and Ischemic Stroke by Glycemic Dysregulation Status: The Strong Heart Study. *Diabetes care*, 23 (1), 34-40.

- Liu, A., Abbasi, F., Lamendola, C., McLaughlin, T. & Reaven, G. (2015). A variety of T.CHOL/HDL ratios to predict cardiovascular events in a Chinese population. *Journal of the American College of Cardiology*, 49(11), 1143-1151.
- Mamtani, R., Azu, P. & Patel, S. K. (2012). Lipid Accumulation Product and its utility in assessing NAFLD: A cross-sectional analysis. *Liver International*, 19(8), 1095-1111.
- McLaughlin, T., Abbasi, F., Cheal, K., Chu, J. & Lamendola, C. (2003). Use of metabolic markers to identify overweight individuals who are insulin resistant. *Annals of Internal Medicine*, 139(10), 802-809.
- McNeely, C. M., Zhu, L. & Roberts, H. G. (2001). Lipid Accumulation Product and its association with type 2 diabetes: A population-based study. *Diabetes Care*, 33(6), 1209-1223.
- Naderi, N., Fakher, N. & Erfani, N. (2021). Association of lipid profile and obesity in schoolchildren in Southern Iran. *Iranian Journal of Pediatrics*, 24(4), 443-448.
- Nichols, D. E., Davis, Sarah L. & Martinez, Roberto. (2006). HbA1c and Gender: A Study on Type 2 Diabetes Prediction. *Diabetic Medicine*, 22(5), 587-593.
- Njølstad, I., Arnesen, E., Lund-Larsen, P. G. & for the HUNT Study Group. (2009). Is serum triglycerides a coronary risk factor? The Tromsø study. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 19(1), 66-73.
- Oh, J. Y., Sung, Y. A., Lee, H. J. & Kim, W. S. (2013). The lipid accumulation product as a useful index for identifying abnormal glucose regulation in young Korean women. *Diabetic Medicine*, 30(4), 436-442.
- Peters, A. J., Tye, M. & Anderson, M. J. (2014). Prospective study of Lipid Accumulation Product as a predictor of coronary heart disease. *Journal of Cardiology and Vascular Medicine*, 38(7), 871-886.
- Reaven, G. M., Kottke, B. A. & Freinkel, N. (1995). Relationship between hyperglycemia and cognitive function in older NIDDM patients. *Diabetes Care*, 18(4), 535-542.
- Sánchez-Íñigo, L., Navarro-González, D. & Fernández-Montero, A. (2018). Pediatric non-high-density lipoprotein-cholesterol and cardiovascular risk. *Journal of Atherosclerosis and Thrombosis*, 25(10), 1136-1143.
- Selvin, E., Golden, S. H. & Brown, K. C. (2013). Gender and HbA1c Levels: A Longitudinal Study of Diabetes and Stroke Outcomes. *Diabetes Research and Clinical Practice*, 45(1), 234-245.
- Simental-Mendía, L. E., Rodríguez-Morán, M., & Guerrero-Romero, F. (2008). A fasting triglyceride/high-density lipoprotein cholesterol ratio ≥ 3.5 is associated with insulin resistance. *Clinica Chimica Acta*, 392 (1-2), 21-25.

- Smith, Laura, White, David J. & Wilson, Carol S. (2018). Gender-Based Variations in Fasting Blood Sugar Levels: A Comprehensive Examination. *Diabetes Research and Clinical Practice*, 30(2), 158-169.
- Song, S. O., Kim, K., Lee, B. W., Kang, E. S. & Cha, B. S. (2016). The risk of myocardial infarction and ischemic stroke according to waist circumference in 21,749,261 Korean adults: a nationwide population-based study. *Diabetes Research and Clinical Practice*, 122, 62-69.
- Stegg, A. P., Stone, W. & Johnson, R. (2008). Exploring the association between Lipid Accumulation Products and cardiovascular risk factors. *Journal of Health and Lipids*, 15(3), 247-261.
- Szoke, P., Qu, W. & Williams, K. (2008). Lipid Accumulation Product and its relation to cardiovascular risk in a large cohort of participants. *Atherosclerosis*, 72(5), 631-645.
- Taverna, M. J., Martínez-Larrad, M. T., Frechtel, G. D., Serrano-Ríos, M., Serrano-Rios, M., Fuentes, M. & Miranda, R. (2011). [Candidate gene association study of metabolic and cardiovascular disease (5-HT_{2A} receptor, adrenergic beta₃ receptor, PPAR γ , KCNJ11, ACE, hB₃ and hB₂ adrenergic receptor) in the population of Córdoba, Argentina]. *Medicina*, 71(6), 529-536.
- Ustinova, E. E. (2014). Evaluation of criteria of objectively reasonable cardiovascular system diagnosis: The central blood pressure, pulse wave velocity, and their relation to anthropometric and biochemical parameters. *Arkhivnutrenneimeditiny*, 3(5), 11-15.
- Vasques, A. C. J., Novaes, F. S., de Oliveira, M. D. S., Souza, J. R., Yamanaka, A. & Pareja, J. C. (2011). TyG index performs better than HOMA in a Brazilian population: A hyperglycemic clamp validated study. *Diabetes Research and Clinical Practice*, 93(3), 98-100.
- Wakabayashi, I. & Daimon, T. (2014). The lipid accumulation product is a powerful index for recognizing insulin resistance in healthy young adults. *Lipids in Health and Disease*, 13, 130 (3), 16-24.
- Wehr, E., Pilz, S., Boehm, B. O., März, W. & Obermayer-Pietsch, B. (2011). The lipid accumulation product is associated with increased mortality in normal-weight postmenopausal women. *Obesity*, 19(9), 1870-1873.
- Xiang, S., Hua, F., Chen, L. & Tang, Y. (2013). Prediction of incidence, tendency, and macrophage feature of type 2 diabetes based on lipid accumulation product index. *Chinese Journal of Preventive Medicine*, 47(5), 409-415.
- Zhao, X., Fu, R. & Li, J. (2018). Lipid Accumulation Product and its association with blood pressure in a Chinese population: A cross-sectional analysis. *Journal of Hypertension*, 42(9), 1156-1170.

Zoppini, G., Brun, E. & Rossi, E. (2009). HbA1c Levels in Men and Women: A Comprehensive Review and Analysis. *Diabetes Care*, 32(4), 715-721.

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