

Comparative study of calculated lipid indices viz atherogenic index of plasma, atherogenic coefficient and lipid accumulation product over conventional lipid profile parameters as better predictors of atherosclerosis in obesity: A cross sectional study

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Abstract

Introduction: Rising prevalence of obesity represents rapidly growing threat for Indian subcontinent. Dyslipidemia in obesity accelerates the process of atherogenesis; though its occurrence can't be underestimated in apparently normal individual lipids. This warrants need of precise measures to predict dyslipidemia beyond routine lipid parameters. Atherogenic Index of Plasma, Atherogenic Coefficient & Lipid Accumulation Product have gained attention in this regard.

Aims and Objectives: This cross sectional study aimed at assessing usefulness of calculated lipid indices over individual lipids as potential predictors of atherosclerosis in obesity.

Materials and Methods: The study enrolled 100 apparently healthy overweight & obese cases and 100 healthy controls. Fasting blood sample was collected for lipid profile parameters. Statistical analysis was done by SPSS software.

Results: The levels of TC(211.4± 36.2/173.9±21.4), TAG (162.9±41.5/124.6±26.3), AIP (0.23±0.11/0.08±0.03), AC (4.3±1.4/2.7±1.1) & LAP (31.3±8.6/24.3±6.2) were elevated while HDL (41.7±9.2/ 52.2±8.3) levels were found to be low in cases compared to controls (p<0.05). Lipid indices had strong correlation than individual lipids with WHR & BMI. Cases having raised AIP and LAP outnumbered than those with atherogenic dyslipidemia.

Conclusion: Calculated lipid indices proved to be better than conventional lipid parameters as simple, sensitive & independent tools to screen high risk individuals for atherogenesis in obesity especially in Indian scenario with limited resources.

Keywords: Obesity, Atherogenic index of plasma, atherosclerosis, Lipid accumulation product, Atherogenic coefficient.

Introduction

An alarming rise in prevalence of obesity creates a major medical and public health impact for developed as well as developing nations. This global epidemic has made Indian subcontinent a hub for obesity related cardio metabolic co morbidities. It is evident from the literature that, this cardiometabolic burden is the result of atherogenic processes developing in obese individuals.¹

Atherosclerosis is a multifocal, smoldering, immune inflammatory arterial disease due to gradual lipid deposition leading to intima thickening, lumen occlusion and reduced blood flow. It's a diffuse process which may progress asymptotically as a relatively benign disease or sometimes may culminate in life threatening cardiometabolic event.²

Obesity associated dyslipidemia is supposed to play crucial role in this regard. Obesity triggers a series of lipid disturbances, such as hypercholesterolemia, hypertriglyceridemia, low HDL cholesterol, high small dense lipoprotein particles and so on. Dyslipidemia is known to increase platelets aggregation, fibrinogen levels and platelets activation inhibitor.³ The impact of atherogenic dyslipidemia marked as high Triacylglycerol (TAG) & low High Density Lipoprotein (HDL)⁴ developing in obese individuals severely affects the arterial health leading to atherogenic alterations.

Correlation between atherosclerosis and levels of TAG, LDL and HDL cholesterol has well been confirmed and

widely accepted in diagnostic practice. Presence of frank dyslipidemia makes an identification of high risk individuals absolutely evident. But occurrence of cardiac events and atherogenesis in absence of frank alterations in lipid parameters represent hidden part of iceberg that is potentially under looked. That reflects the gap in screening atherogenic dyslipidemia relying on traditional lipid values alone. This necessitates the need of more precise, sensitive and statistically significant parameters to accurately address and flag high risk profiles and thus offer better prediction of underlying atherogenesis.⁵

Calculated lipid parameters viz Atherogenic Index of Plasma (AIP), Atherogenic Coefficient (AC) and Lipid Accumulation Product (LAP) have gained attention in this regard.^{6,7} There is evidence in previous literature stating that these calculated indices have better predictability in identifying atherogenesis and in turn cardiometabolic risk as compared to individual lipid parameters.

Atherogenic Index of Plasma (AIP) is defined as logarithm of ratio of plasma concentration TAG to HDL. It is proposed as a predictive marker for plasma atherogenicity. Its said to correlate well with the size of HDL and LDL particles and fractional esterification rate of cholesterol by Lecithin Cholesterol Acyl Transferase (LCAT) in plasma.⁸ AIP reflects critical balance between protective and atherogenic lipoprotein.⁹ Depending on its value, individuals are categorized as low risk (<0.10), Moderate risk (0.10 to 0.24) and high risk (>0.24).^{6,10}

Atherogenic Coefficient (AC) calculated as Non-HDL/HDL is yet another ratio relying on the significance of HDL in predicting the risk of CAD. AC is a measure of cholesterol in lipoprotein fractions viz LDL, VLDL, IDL with respect to good cholesterol i.e. HDL. It reflects atherogenic potential of the entire spectrum of lipoprotein fractions. Studies have shown Non-HDLc being similar to Apo-B in assessing atherogenic cholesterol and lipoprotein burden.⁶

Lipid Accumulation Product (LAP) is based on a combination of waist circumference (WC) and plasma TAG levels. It is calculated as $[WC (cm) - 65] \times [TAG (mmol/L)]$ in men, and $[WC (cm) - 58] \times [TAG (mmol/L)]$ in women. The use of TAG levels in combination with waist circumference (WC), termed hypertriglyceridemic waist, has been shown to be able to identify individuals with the greatest amount of visceral fat and to be associated with increased risk of cardiometabolic abnormalities.⁷ Optimal cut-off value for LAP is taken as 34.5.¹¹ Since LAP takes into account both TAG and WC, it is suggested that this index has a stronger correlation with visceral adiposity, higher levels of lipolysis, adipocytokines and plasminogen activator inhibitor-1.¹²

So this study was undertaken at Department of Biochemistry, Government Medical College, Aurangabad, with the objective of assessing usefulness of calculated lipid indices viz AIP, AC & LAP over traditional lipid profile parameters as potential predictors of atherosclerosis in obesity to screen high risk patients for the future development of cardiovascular disease, with a hope that these patients can be targeted for timely interventions and subsequent morbidity and mortality can be largely prevented.

Materials and Methods

Study Population: This OPD based cross sectional Study was conducted by Department of Biochemistry of a tertiary care hospital after approval by institutional ethics committee.

After obtaining written & informed consent, 100 apparently healthy overweight and obese individuals (BMI ≥ 25 kg/meter²) and 100 age & sex matched normal weight (BMI: 18.5 - 24.99 kg/meter²) healthy individuals were enrolled as cases and controls respectively. Participants were in the age group of 15 to 60 years. Exclusion criteria consisted of patients with cardiovascular disease, cerebrovascular accidents, renal impairment, and peripheral vascular disease as well as patients on medications like statins, steroids or antiobesity drugs.

Study Protocol: Study was conducted as per prescribed proforma including detailed history, clinical examination and laboratory investigations.

Detailed history mainly consisted of demographic data, personal habits as well as any past history of medical ailments.

Clinical examination consisted of weight (Kg), Height (meters), Body Mass Index (BMI), Waist circumference

(WC), Hip circumference (HC) and Waist/Hip ratio (WHR). Body weight was taken on a calibrated scale to the nearest 0.1 kg. Height was taken with a wall-mounted stadiometer to the nearest 0.5 cm. Body mass index (BMI) was calculated as body weight (kg) to the squared height (m²). Waist circumference (WC) was measured at the mean point between the lowest rib margin and iliac crest with the participant standing and at the maximum point of normal expiration. Hip circumference was measured at the level of greatest protuberance of buttocks without compression of skin. WHR of >0.9 for men and > 0.85 for women was considered as abnormal.³

After an overnight fast, blood samples were collected from all participants under strict aseptic precautions for lipid profile estimation. Serum was separated after 1 hour by centrifugation at 3000 rpm for 10 minutes. Investigations were done on fully automated chemistry analyzers by Transasia ERBA XL 640 system.

Lipid profile consisted of Serum Total Cholesterol (TC), Triacylglycerol (TAG), High Density Lipoprotein (HDL) and Low density lipoprotein (LDL).

Atherogenic Dyslipidemia was defined as Sr. TAG ≥ 150 mg/dl & Sr. HDL < 40 mg/dl (males) & < 50 mg/dl (females).⁴

Calculated lipid indices were Atherogenic Index of Plasma (AIP),^{6,10} Atherogenic Coefficient (AC)⁶ and Lipid Accumulation Product (LAP).^{7,11} Following formulae were used in their computations:

Atherogenic Index of Plasma (AIP) = $\log (TAG/HDL)$

Atherogenic Coefficient (AC) = $(TC - HDL)/HDL$

Lipid Accumulation Product (LAP) = $(WC (cm) - 65) \times TAG (mmol/l)$ for men

$(WC (cm) - 58) \times TAG (mmol/l)$ for women

Based on AIP values participants were categorized in three groups viz, Low risk <0.10 , Moderate risk 0.10 to 0.24 & high risk > 0.24 .^{6,10} Normal Cut off value for LAP was considered to be <34.5 .¹¹

Statistical Analysis

The results were analyzed using windows SPSS programme (version 25.0). The results were interpreted as mean \pm S.D. for quantitative parameters and as number / percentage for qualitative data. $P < 0.05$ was considered statistically significant. Pearson's Correlation coefficients (r value) were calculated between various parameters to ascertain the strength of association.

Results

100 cases of overweight and obese individuals & 100 age and sex matched healthy controls were enrolled for the study. Demographic and biochemical findings in studied groups are shown in tabular form along with their statistical significance, comparison of various lipid parameters as well as correlation coefficients to establish strength of association is depicted in tabular form.

Table 1: Demographic and clinical characteristics in studied groupsQuantitative data (Mean \pm SD) and qualitative data (number/ percentage)

S. No.	Parameter	Cases (100)	Controls (100)	P value
1	Age (Years)	44.9 \pm 6.2	42.1 \pm 4.8	0.38
2	Sex (Male/ Females)	49/51	57/43	NA
3	Body mass index (BMI)	30.2 \pm 4.1	23.7 \pm 3.3	<0.05 *
4	Waist hip ratio (WHR)	0.99 \pm 0.05	0.81 \pm 0.07	< 0.01 **

*Significant P value, **: Highly significant P value

Table 1 shows that, mean values of age, BMI and WHR are higher in cases as compared to controls. Difference is statistically significant for BMI and WHR while it's non-significant for age.

Table 2: Lipid parameters & calculated lipid indices in studied groups

S. No.	Parameter	Cases (100)	Controls (100)	P Value
1	TC (mg/dl)	211.4 \pm 36.2	173.9 \pm 21.4	<0.05 *
2	TAG (mg/dl)	162.9 \pm 41.5	124.6 \pm 26.3	<0.05 *
3	LDL (mg/dl)	94.9 \pm 16.2	80.2 \pm 18.5	<0.05 *
4	HDL (mg/dl)	41.7 \pm 9.2	52.2 \pm 8.3	<0.05 *
5	VLDL (mg/dl)	32.9 \pm 7.7	27.6 \pm 5.2	0.12
6	AIP	0.23 \pm 0.11	0.08 \pm 0.03	< 0.01 **
7	AC	4.3 \pm 1.4	2.7 \pm 1.1	< 0.01 **
8	LAP	31.3 \pm 8.6	24.3 \pm 6.2	< 0.01 **

From table 2, it can be observed that, Lipid parameters viz TC, TAG & LDL are higher while HDL is lower in cases compared to controls and the difference is statistically

significant. VLDL though higher in cases, the rise is not significant. AIP, AC & LAP are raised in cases compared to controls difference being highly significant.

Table 3: Correlation coefficients of lipids & calculated lipid indices with BMI & WHR

S. No.	Parameter	R value	
		BMI	WHR
1	TC	+ 0.38	+ 0.43
2	TAG	+ 0.48	+ 0.67
3	LDL	+ 0.42	+ 0.45
4	HDL	- 0.51	- 0.62
5	AIP	+ 0.57	+ 0.68
6	AC	+ 0.53	+ 0.61
7	LAP	+ 0.60	+ 0.71

Table 3 represents that, TAG, TC, AIP, AC and LAP show strong positive correlation with BMI and WHR, correlation with WFR being more significant. HDL shows negative correlation with BMI & WHR.

Table 4: Number/ percentage of atherogenic dyslipidemia, AIP and LAP in cases (Total=100)

Parameter	Normal/ Low risk	Moderate/High risk
Atherogenic dyslipidemia	58	42
AIP	39	61
LAP	43	57

Table 4 shows the number/ percentage of atherogenic dyslipidemia, raised AIP and LAP in obese cases. Considering their cutoff criteria, the no. of raised AIP & LAP values has outnumbered the cases with atherogenic dyslipidemia in identifying high risk profiles.

Discussion

Obesity, with increasing worldwide prevalence in the population, not only causes severe harm to individual health but also imposes a considerable burden on healthcare

system. A strong association between obesity and atherogenicity through a highly complex interaction of various lipid derangements has to be addressed on a high priority.

Though conventional lipid profile parameters are the most popular tools to understand lipid derangements in atherogenesis, significant proportion of cases occur without frank lipid derangements and this necessitates the inclusion of newer parameters beyond existing lipid panel. Timely

detection and intervention for this group offers a hope that some or entire atherosclerotic sequel can be prevented.¹³

This study has attempted to assess utility of AIP, AC and LAP over conventional lipid profile measurements as sensitive screening tests of underlying atherogenesis in obese individuals.

100 cases of apparently healthy overweight and obese individuals & 100 age and sex matched healthy controls were enrolled for the study in random manner. Mean values of age, BMI and WHR are higher in cases as compared to controls. Difference is statistically significant for BMI and WHR while it's non significant for age. It can be expected due to the selection of participants on the basis of BMI itself.

TC, TAG & LDL are higher while HDL is lower in cases compared to controls and the difference is statistically significant. Highly significant rise is observed in values of AIP, AC & LAP in cases compared to controls. This finding is in agreement with other studies wherein they have found lipid indices better over individual lipid parameters.⁹

TAG, TC, AIP, AC and LAP show strong positive correlation with BMI and WHR, the strength of association being stronger with WHR as compared to BMI. This reflects an influence of waist circumference i.e. abdominal obesity than BMI in lipid derangements.¹⁴ Lipid indices show stronger correlation with WHR than individual lipid parameters. HDL shows strong negative correlation with BMI & WHR.

Obesity is hallmarked by a series of lipid disturbances, viz hypercholesterolemia, high TAG levels, low HDL cholesterol, high small dense lipoprotein particles and alterations of serum and tissue lipoprotein lipase (LPL) activity.³ Obesity especially of central distribution poses high cardiovascular risk through induced atherogenic dyslipidemia thus leading to increased morbidity and mortality risk in various populations.¹⁵ But occurrence of atherogenesis without frank dyslipidemia reflects a need to look beyond individual lipids. Hence AIP, AC and LAP have been evaluated statistically to accurately address and flag high risk profiles.

Study subjects in case group having raised AIP and LAP is greater than the number of cases showing atherogenic dyslipidemia. This may reflect inability of individual lipid parameters to identify potentially atherogenic profiles which may be achieved by calculated indices. This finding is in agreement with study on lipid ratios and AIP by Nimannapalli HD et al wherein they observed AIP to be a better risk predictor even in normolipidemic settings.⁸ AIP was suggested to be superior to individual lipids in predicting CVD especially in normolipidemic settings and it is proved as potential screening tool.^{6,14} Sushith and his coworkers concluded that AIP has a better prediction of Coronary Artery Disease than triglycerides or High Density lipoprotein alone.¹⁰ As LAP takes into account both TAG levels and WC, its said to have better correlation with visceral adiposity, lipolysis, metabolic syndrome and cardiovascular disease.^{12,16} AC was found to be higher in cases compared to controls. AC is

indeed a measure of non HDL cholesterol i.e. cholesterol present in LDL, VLDL & IDL fractions with respect to HDL. AC which is a ratio based on Non-HDL to HDL reflects atherogenic potential of the entire spectrum of lipoprotein fractions even when there is no statistically significant alteration in Non-HDL. Significant correlation of AC with cardiovascular dysfunction was observed in other studies also.^{6,8}

With reference to above said observations it may be wisely said that, up gradation of existing lipid profile panel with statistically significant indices and its impact on interpretation of dyslipidemia may definitely flash tag high risk cases. It will positively assist diagnostic capability in the simplest way, with a genuine potential to predict atherogenesis and thus cardiovascular risk.

We observed certain limitations for this study with respect to small sample size and cross sectional design. Due to these limitations precise causality can't be established and further follow up studies are necessary to ascertain their usefulness. Still the study has notable strengths. Inclusion of simple indices in conventional lipid profile will increase the potential for early detection and aggressive interventions of high risk individuals. Their utility if assessed and verified on a large scale, it will definitely deliver simple, reliable and cost effective tool for the health care systems.

Conclusion

The present study essentially emphasizes the usefulness of calculated lipid indices viz AIP, AC and LAP beyond individual lipid profile measurements in predicting high risk potential for atherogenesis in obese individuals especially when traditional lipid profile parameters seem to be normal. It is worthy to note that inclusion of these indices to lipid profile interpretation definitely has better existence in Indian clinical settings with limited resources in terms of simplicity, easy applicability and cost effectiveness. Identification and targeted intervention for this high risk group may offer a hope that atherogenesis and its sequel can be largely prevented with considerable inputs from health care professionals and total commitment from the patient.

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Conflicts of Interest: None

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