Original Article

Association of waist circumference with atherogenic cardiovascular risks in centrally obese Myanmar male subjects

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Abstract

Background and Aim: Central obesity is a major contributor to the development of cardiovascular (CV) risks. Several atherogenic indices had been derived from lipid profiles for predicting the risk of CV disease. The present study assessed atherogenic indices as CV risk in centrally obese men.

Methods: A cross-sectional comparative study was undertaken in 34 apparently healthy centrally obese (waist circumference [WC] >90 cm) and 30 nonobese (WC < 90 cm) men aged between 18 and 35 years. The plasma total cholesterol (TC), triglyceride (TG), high-density lipoprotein-cholesterol (HDL-C) and low-density lipoprotein-cholesterol (LDL-C) were determined using spectrophotometry methods. The following atherogenic indices were calculated: TC/HDL-C, LDL-C/HDL-C, and atherogenic index of plasma (AIP). Insulin sensitivity was assessed by homeostasis model assessment method of insulin resistance (HOMA-IR).

Results: Atherogenic indices and HOMA-IR values increased significantly in the centrally obese subjects than that of nonobese subjects. There was a significant positive correlation between WC and LDL-C/HDL-C (r = 0.46, P < 0.01), TC/HDL-C (r = 0.51, P < 0.01) and AIP (r = 0.66, P < 0.001). Among them, AIP has the strongest and most significant correlation with WC. The risk of developing CV disease (AIP > 0.1) among centrally obese male subjects is 11.72 times (adjusted odds ratio = 11.72; 95% confidence interval = 1.84–72.81) greater than that of nonobese subjects. AIP can only express the association between (HOMA-IR > 2.52) and CV risk (AIP > 0.1) in central adiposity.

Conclusion: AIP is a better indicator of CV risk than other previously used lipid parameters in centrally obese Myanmarese.

Key words: Cardiovascular risk, central obesity, homeostatic model assessment-insulin resistance, lipid profile

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INTRODUCTION

Cardiovascular (CV) diseases are among the major leading causes of death worldwide. Dyslipidemia is recognized as prominent risk factor for the development of CV disease,[1] which may be primary or associated with hypertension, diabetes mellitus and obesity. Dyslipidemia includes hypercholesterolemia, elevated low-density lipoprotein-cholesterol (LDL-C), low high-density lipoprotein cholesterol (HDL-C), hypertriglyceridamia and high atherogenic indices.[2]

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Serum total cholesterol (TC) levels have been shown to be consistently related to coronary heart disease (CHD) risk in many populations.[3,4] Mathematically calculated value of serum LDL-C is commonly used to estimate how much LDL-C is driving progression of atherosclerosis.[5] According to United State National Cholesterol Education Program (NCEP) guidelines,[6] LDL-C concentration should be considered the primary therapeutic target, whereas HDL-C levels, may also be critical in the assessment of CV disease risk. Triglyceride (TG) levels are ignored in the NCEP. LDL-C and HDL-C levels are used to assess risk while

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considering the presence or absence of other important risk factors such as family history of early CHD, age, smoking, hypertension, diabetes mellitus, low physical activity, and obesity. LDL-C/HDL-C ratio is often calculated to estimate CV disease risk. Further, results of the prospective studies[7,8] have suggested high LDL-C/HDL-C ratio in combination with hypertriglyceridemia to be associated with high CV disease risk. This dyslipidemic state (lipid triad) has been described as atherogenic dyslipidemia.[9]

On the other hand, it is reported that the LDL-C/HDL-C ratio may underestimate the magnitude of the dyslipidemic state in these patients since there is more cholesterol in the very low density lipoprotein fraction in individuals with elevated TG concentrations. Therefore, a risk assessment for CV disease is alternatively given by comparing the TC to HDL-C ratio (TC/HDL-C).[10]

Atherogenic index of plasma (AIP) is based on the ratio of the values of TG to HDL-C levels, calculated according to the formula (AIP = Log [TG]/[HDL-C]) where both TG and HDL-C are measured in plasma and are expressed in molar concentration. TG and HDL-C reflect the balance between the atherogenic and protective lipoproteins. High serum TG level stimulates the activity of hepatic lipase, which results in the increase of HDL-C catabolism (degradation of HDL-C). Each degradation of 1 mg HDL-C will correlate with 2% increase in the risk CHD.[11,12] AIP value <0.1 in young children and increases up to 0.4 in men and subjects with other CV risk factors such as hypertension, diabetes and dyslipidemia. Indeed, it has been suggested that AIP values of <0.1 are associated with low risk, 0.1–0.24 with medium risk and above 0.24 with high CV risk.[13]

Although several consensus documents have been reported,[3-13] there is no universal acceptance of how this information should be used and interpreted. Recently, Khazaál[14] studied 119 males with an established diagnosis of acute myocardial infarction and has concluded AIP as an index of highest sensitivity for predicting the acute coronary events. Although this AIP has been used to predict the risk of atherosclerosis in postmenopausal women,[15] type 1 and type 2 diabetes mellitus, beta-thalassemia, hypothyroidism[16] and chronic renal failure,[17] there is paucity of literature on its application to obese subjects especially in Myanmarse population. Therefore, the aim of this study was to assess atherogenic indices in centrally obese men compared with nonobese men. This study also determined the association between atherogenic indices and insulin resistance assessed by homeostasis model assessment of insulin resistance (HOMA-IR).

MATERIALS AND METHODS

Subject selection

This was a cross-sectional study in which a total of 64 apparently healthy male medical students and teaching staff (between 18 and 35 years of age) from the University of Medicine 2, Yangon were recruited. History taking and clinical examination including anthropometric measurement was carried out. Healthy subjects without family history of diabetes mellitus, history of chronic smoking and alcohol drinking were included in the study. A written informed consent was obtained from all subjects individually. Anthropometric data such as height, weight, waist circumference (WC) and hip circumference were taken from all subjects. Those with WC <90 cm were selected for the control group and those with WC >90 cm were selected for centrally obese group.

Measurement of biochemical variables

Fasting blood sample (10 ml) was obtained from the antecubital vein and collected in two separate blood collecting tubes. 1 ml of blood was collected in tube containing 10 mg of sodium fluoride for determination of blood sugar and 9 ml of blood in another tube for serum separation. After the collection of blood sample, serum was promptly separated and stored at (−20°C) until the blood sample analysis. Fasting blood glucose was measured by glucose oxidase method (Glucose Liquicolor, Human, D-65205 Wiesbaden, Germany) and serum insulin level was measured by Insulin ELISA (DSL-10-1600, Diagnostic System Laboratories, Inc., Texas, USA) kit method. Insulin sensitivity was calculated by following formulas.[18]

HOMA-IR = Insulin (μIU/mL) × glucose (mmol/L)/22.5

Reference interval of HOMA-IR has been established between 0.4 and 2.4, and HOMA-IR value > 2.5 is considered as insulin resistance.[19] TC and TG were assayed by enzymatic colorimetric test kits (Pars Azmoon Inc.,) and HDL-C was measured after precipitation of the apolipoprotein B-containing lipoproteins with phosphotungstic acid. LDL-C was calculated from serum TC, TG and HDL-C using the Friedewald formula.[20] The atherogenic indices were calculated as TC/HDL-C, LDL-C/HDL-C, and AIP.[11]

Statistical analysis of data

The data were expressed as mean ± standard deviation. The statistical analysis was performed with SPSS version 16 (SPSS Software Inc., Chicago, IL, USA). Comparison of the diabetes-related parameter, lipid parameter and atherogenic indices between nonobese and centrally obese groups was done by unpaired Student's *t*-test. Skewed data were computed by nonparametric tests,

(Mann–Whittney Signed-Rank test). Correlation studies were done by Pearson's correlation. Chi-squared test was used to determine whether there is a significant association between the insulin resistance and CV risk. Differences were considered significant when $P < 0.05$.

RESULTS

Table 1 shows the baseline characteristics of subjects participated in this study. Comparison of lipid parameter and atherogenic indices between centrally obese group and non obese group were shown in Table 2. Value of fasting blood glucose, fasting serum insulin and insulin resistance (HOMA-IR) were significantly higher in the centrally obese group compared to the non-obese group [Table 2]. Table 3 depicts the correlation between WC, HOMA-IR, lipid profile and atherogenic indices. Figure 1 depicts the HOMA-IR score in low, medium and high risk of CV disease. There is a significant association ($P < 0.001$) between HOMA-IR (insulin sensitive < HOMA-IR 2.5, insulin resistance > HOMA-IR 2.5) and CV risk assessed by AIP (0–0.1 low risk, 0.1–0.24 medium risk and >0.24 high risk).

DISCUSSION

There is a growing body of evidence suggesting that abdominal adiposity rather than general adiposity is a more important risk factor for CV and metabolic disease.[11,21] The intra-abdominal visceral deposition of adipose tissue assessed by WC is a major contributor to the development of hypertension, elevated plasma insulin concentrations and insulin resistance, hyperglycemia and hyperlipidemia (metabolic syndrome).[22,23] According to the international obesity task force reference, overweight is defined as a body mass index (BMI) ≥23, and the recommended WC cutoffs are 90 cm for men and 80 cm for women among Asian populations[24] Therefore, in the present study, WC and BMI of the participants were assessed by Asian criteria.

Table 1: Age, BMI, WC, WHR, SBP and DBP parameters of subjects expressed in mean±SD

Parameters	Nonobese subjects (*n*=30)	Centrally obese subjects (*n*=34)	*P*
Age (years)	22.7±5.7	25.6±6.5	0.067
BMI (kg/m^2)	21.1±2.7	31.6±4.6*	0.009
WC (cm)	73.8±6.6	99.3±6.4*	0.008
WHR	0.81±0.05	0.93±0.04*	0.007
SBP (mmHg)	108.6±6.4	117.7±7.9*	0.006
DBP (mmHg)	70.1±5.7	77.9±7.7*	0.002

Statistical analysis was done by Student's *t*-test. *P*<0.05 was considered significant. BMI: Body mass index, WC: Waist circumference, WHR: Waist hip ratio, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation, **P*<0.01

In the present study, the centrally obese subjects have elevated TC, TG and LDL-C and low levels of HDL-C. The present findings were consistent with previous studies.[25,26] The atherogenic indices TC/HDL-C, LDL-C/HDL-C ($P < 0.01$) and AIP ($P < 0.001$) were found to be significantly increased in the centrally obese group.In addition, the present study also observed that WC was significantly and positively correlated with AIP ($r = 0.66$, $P < 0.001$), TC/HDL-C ($r = 0.51$, $P < 0.01$) and LDL-C/HDL-C ($r = 0.46$, $P < 0.01$). These findings contribute to the development of atherosclerosis, which are among the CV risks in centrally obese subjects. It was noted that CV risk, as assessed by atherogenic indices, increase significantly with a degree of the visceral fat deposition, which is expressed by WC. Among three atherogenic indices studied in the present study, it was found that AIP has the strongest and most significant relationship with WC. These findings also tend to strengthen the link between CV risk and visceral adiposity.

In the present study, it was found that 24 out of 64 subjects (37.5) were low risk, 9 out of 64 subjects (14%) were medium risk and 31 out of 64 subjects (48.5) were high-risk. The risk of developing CV disease in centrally obese male subjects is 11.72 times (age, smoking and physical activity adjusted odds ratio = 11.72; 95%

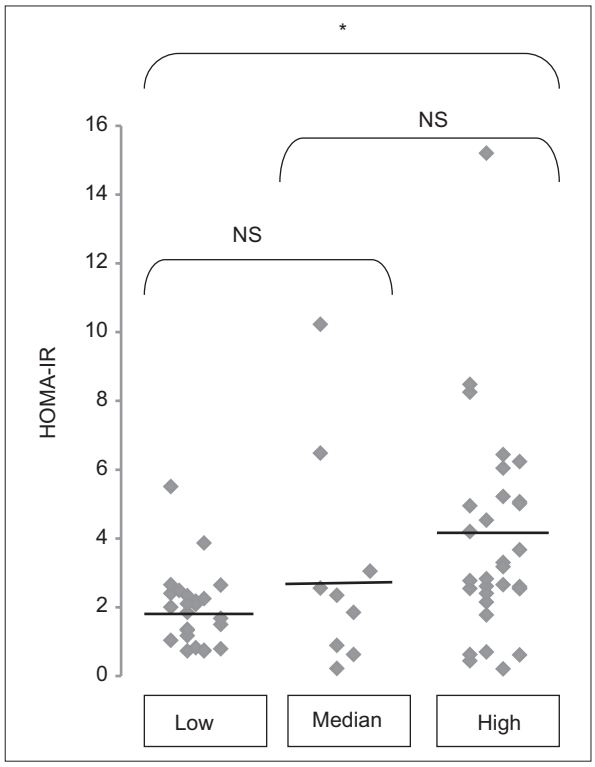

Figure 1: Homeostasis model assessment-insulin resistance score in low, medium and high risk of cardiovascular disease. Solid line indicate mean values. *indicates $P < 0.01$ NS = not significant NB: Comparison was done by using non-parametric test (Mann–Whittney Signed Rank test)

Table 2: Comparison of lipid parameter, atherogenic indices and diabetes-related parameter between two groups

Parameters	Nonobese subjects (*n*=30)	Centrally obese subjects (*n*=34)
Lipid parameter (mean±SD)		
TC (mg/dL)	185.13±43.64	217.33±43.32*
TG (mg/dL)	94.59±28.11	160.04±45.17***
LDL-C (mg/dL)	123.60±41.46	156.36±46.40*
HDL-C (mg/dL)	44.02±13.77	30.08±9.19***
Atherogenic indices (median and interquartile range)		
TC/HDL-C	3.78 (3.4-4.67)	7.78 (6.35-9.96)**
LDL/HDL-C	2.48 (1.99-3.19)	5.72 (4.15-7.81)**
AIP	−0.05 (−0.13-0.15)	0.34 (0.29-0.44)***
Diabetes-related parameter		
FPG (mmol/L) (mean±SD)	4.9±0.5	5.2±0.7*
FSI (μIU/mL) (median and interquartile range)	7.5 (3.5-11)	15 (12-21)**
HOMA-IR (median and interquartile range)	1.7 (0.8-2.38)	3.2 (2.6-5.3)**

*P<0.05, **P<0.01, ***P<0.001. FPG: Fasting plasma glucose, FSI: Fasting serum insulin, SD: Standard deviation, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TC: Total cholesterol, AIP: Atherogenic index of plasma, HOMA-IR: Homeostasis model assessment-estimated insulin resistance, TG: Triglyceride, LDL: Low-density lipoprotein

Table 3: Correlation between WC and HOMA-IR, with lipid profile and AIP

Parameters	*r*	*P*
Correlation with WC		
TC	0.39	<0.001
TG	0.58	<0.001
LDL-C	0.39	<0.001
HDL-C	−0.47	<0.001
HOMA-IR	0.63	<0.001
LDL/HDL	0.46	<0.01
TC/HDL	0.51	<0.01
AIP	0.66	<0.001
Correlation with HOMA-IR		
TC	0.25	<0.05
TG	0.34	<0.05
LDL-C	0.21	NS
HDL-C	−0.17	NS
LDL/HDL	0.16	NS
TC/HDL	0.19	NS
AIP	0.31	<0.05

WC: Waist circumference, HOMA-IR: Homeostasis model assessment-estimated insulin resistance, AIP: Atherogenic index of plasma, TC: Total cholesterol, TG: Triglyceride, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein, HDL: High-density lipoprotein

confidence interval = 1.84–72.8) greater than that of nonobese subjects. Accordingly, the present study indicated that centrally obese subjects are at a high risk of developing CV disease.

Several mechanisms whereby insulin resistance could cause an alteration in lipid metabolism have been described. Hyperinsulinemia is known to enhance hepatic fatty acid esterification, which forms TG, thus may directly contribute to the increased plasma TG.[27] Resistance to the action of insulin on lipoprotein lipase in peripheral tissues may also contribute to elevated TG.[28,29] Moreover, elevated serum TG level also stimulates the activity of hepatic lipase, which results in the increased rate of HDL-C degradation.[30]Accordingly, present study showed that HOMA-IR was significantly and positively correlated with AIP, but not with LDL-C/HDL-C and TC/HDL-C. In addition, it was also noted that high CV risk (AIP > 0.24) was significantly associated with insulin resistance (HOMA-IR > 2.5). Among three atherogenic indices studied in the present study, AIP can only express the linkage between CV risk and development of insulin resistance in centrally obese male subjects.

Limitations of the study

Since dyslipidemia in centrally obese male subjects in the present study are indicative of their susceptibility to atherosclerosis and other CV disorders, a follow-up of these subjects should have been done to find whether, they develop CV diseases in their later life. Future longitudinal studies should be carried out to detect the development of atherosclerosis and CV disease in dyslipidemic subjects.

CONCLUSION

Present study demonstrated decreased insulin sensitivity and dyslipidemia in centrally obese subjects compared to nonobese subjects. Atherogenic indices can significantly add value in assessing the CV risk in centrally obese men. Increasing AIP value was found to be associated with increasing HOMA-IR score in centrally obese subjects. It indicated that the degree of the visceral adiposity seems to worsen insulin resistance and enhance CV risk. The present result also suggests that AIP should be used as a standard risk assessment for CV disease.

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REFERENCES

1. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, *et al.* Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. Lancet 2004;364:937-52.
2. Brunzell JD, Davidson M, Furberg CD, Goldberg RB, Howard BV, Stein JH, *et al.* Lipoprotein management in patients with cardiometabolic risk: Consensus statement from the American Diabetes Association and the American College of Cardiology Foundation. Diab Care 2008;31:811-22.
3. Law MR, Wald NJ. An ecological study of serum cholesterol and ischaemic heart disease between 1950 and 1990. Eur J Clin Nutr 1994;48:305-25.
4. Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? BMJ 1994;308:367-72.
5. Brunzell JD, Davidson M, Furberg CD, Goldberg RB, Howard BV, Stein JH, *et al.* Lipoprotein management in patients with cardiometabolic risk: Consensus conference report from the American diabetes association and the American college of cardiology foundation. J Am Coll Cardiol 2008;51:1512-24.
6. National cholesterol education program. Second report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel II). Circulation 1994;89:1333-445.
7. Assmann G, Schulte H, Funke H, von Eckardstein A. The emergence of triglycerides as a significant independent risk factor in coronary artery disease. Eur Heart J 1998;19 Suppl M: M8-14.
8. Manninen V, Tenkanen L, Koskinen P, Huttunen JK, Mänttäri M, Heinonen OP, *et al.* Joint effects of serum triglyceride and LDL cholesterol and HDL cholesterol concentrations on coronary heart disease risk in the Helsinki Heart Study. Implications for treatment. Circulation 1992;85:37-45.
9. Grundy SM. Small LDL, atherogenic dyslipidemia, and the metabolic syndrome. Circulation 1997;95:1-4.
10. Lamarche B, Moorjani S, Lupien PJ, Cantin B, Bernard PM, Dagenais GR, *et al.* Apolipoprotein A-I and B levels and the risk of ischemic heart disease during a five-year follow-up of men in the Québec cardiovascular study. Circulation 1996;94:273-8.
11. Dobiásová M. Atherogenic index of plasma [log (triglycerides/HDL-cholesterol)]: Theoretical and practical implications. Clin Chem 2004;50:1113-5.
12. Susanti E, Donosepoetro M, Patellong I, Arif M. Differences between several atherogenic parameters in patients with controlled and uncontrolled type 2 diabetes mellitus. Med J Indones 2010;19:103-8.
13. Dobiásová M, Frohlich J. The plasma parameter log (TG/HDL-C) as an atherogenic index: Correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER HDL). Clin Biochem 2001;34:583-8.
14. Khazaál MS. Atherogenic index of plasma (AIP) as a parameter in predicting cardiovascular risk in males compared to the conventional dyslipidemic indices (cholesterol ratios). Karbala J Med 2013;6:1506-13.
15. Nwagha UI, Ikekpeazu EJ, Ejezie FE, Neboh EE, Maduka IC. Atherogenic index of plasma as useful predictor of cardiovascular risk among postmenopausal women in Enugu, Nigeria. Afr Health Sci 2010;10:248-52.
16. Rajab TM. Compaeative study for atherogenic index of plasma (AIP) in patient with type 1 diabetes mellitus, type 2 diabetes mellitus betathalassemia and hypothyroidism. Int J Chem Res 2012;2:1-9.
17. Al-Tai WF, Jaffer EM, Ali ZA. Evaluating the utility of plasma atherogenic index among several atherogenic parameters in patients with chronic renal failure on maintenance hemodialysis. J Fac Med Baghdad 2012;54:259-62.
18. Matthews KA, Rhoten WB, Driscoll HK, Chertow BS. Vitamin A deficiency impairs fetal islet development and causes subsequent glucose intolerance in adult rats. J Nutr 2004;134:1958-63.
19. Yamada C, Mitsuhashi T, Hiratsuka N, Inabe F, Araida N, Takahashi E. Optimal reference interval for homeostasis model assessment of insulin resistance in a Japanese population. J Diabetes Investig 2011;2:373-6.
20. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
21. Rexrode KM, Carey VJ, Hennekens CH, Walters EE, Colditz GA, Stampfer MJ, *et al.* Abdominal adiposity and coronary heart disease in women. JAMA 1998;280:1843-8.
22. Janssen I, Katzmarzyk PT, Ross R. Body mass index, waist circumference, and health risk: Evidence in support of current National Institutes of Health guidelines. Arch Intern Med 2002;162:2074-9.
23. Kopelman P. Health risks associated with overweight and obesity. Obes Rev 2007;8 Suppl 1:13-7.
24. The World Health Organization Western Pacific Region, the International Association for the Study of Obesity, and the International Obesity Task Force. The Asia-Pacific perspective: Redefining obesity and its treatment. Sydney: Health Communications Australia Pty Limited; 2000. Available from: www.wpro.who.int/nutrition/documents/docs/Redefiningobesity.pdf. [Last cited in 2014 Nov 24].
25. Evans DJ, Hoffmann RG, Kalkhoff RK, Kissebah AH Relationship of body fat topography to insulin sensitivity and metabolic profiles in premenopausal women. Metabolism 1984;33:68-75.
26. Krotkiewski M, Björntorp P, Sjöström L, Smith U. Impact of obesity on metabolism in men and women. Importance of regional adipose tissue distribution. J Clin Invest 1983;72:1150-62.
27. Stalder M, Pometta D, Suenram A. Relationship between plasma insulin levels and high density lipoprotein cholesterol levels in healthy men. Diabetologia 1981;21:544-8.
28. Pykälistö OJ, Smith PH, Brunzell JD. Determinants of human adipose tissue lipoprotein lipase. Effect of diabetes and obesity on basal- and diet-induced activity. J Clin Invest 1975;56:1108-17.
29. Sadur CN, Yost TJ, Eckel RH. Insulin responsiveness of adipose tissue lipoprotein lipase is delayed but preserved in obesity. J Clin Endocrinol Metab 1984;59:1176-82.
30. Golay A, Zech L, Shi MZ, Chiou YA, Reaven GM, Chen YD. High density lipoprotein (HDL) metabolism in noninsulin-dependent diabetes mellitus: Measurement of HDL turnover using tritiated HDL. J Clin Endocrinol Metab 1987;65:512-8.

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