Int J Biol Med Res. 2013; 4(1): 2952-2957

BioMedSciDirect Publications

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International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Original Article

Role of MAP and AIP in prediction of CVD risk in type 2 diabetic patients with and without metabolic syndrome.

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ARTICLE INFO

Keywords:
Type 2 Diabetes Mellitus
Metabolic syndrome
Mean Arterial pressure(MAP)
Atherogenic Index of plama(AIP)
Cardiovascular disease (CVD)

ABSTRACT

Abstract: Metabolic stress is associated with increased risk of cardiovascular morbidity and mortality. Aim: To analyze the role of MAP and AIP in predicting CVD risk in type 2 diabetic patients with metabolic syndrome and inclusion of these parameters in defining MS. Materials and Methods: 120, Type 2 diabetic patients aged between 40-60 yrs were included in this study. They are categorized as diabetic patients with metabolic syndrome (n=60) and diabetic patients without metabolic syndrome (n=60) by fulfilling at least 3 criteria of NCEP (ATP) III. Their anthropometric characteristics were measured and MAP was calculated. FBS, lipid profile were estimated and atherogenic index of plasma was calculated. Result: A significant increase was observed in waist circumference, BP, MAP, lipid profile and AIP of diabetic patients with metabolic syndrome when compared to diabetic patients without metabolic syndrome. Hence the study suggests that MAP and AIP may serve as a better indicator in assessing metabolic syndrome among type 2 diabetes mellitus.

1. Introduction

Evidence shows the presence of metabolic syndrome increases cardiovascular risk and mortality. Studies have also shown metabolic syndrome and diabetes had the highest prevalence of cardiovascular disease when compared to those with neither MS nor diabetes (Alexander 2003). Metabolic syndrome is a multifactorial disorder characterized by abdominal obesity, atherogenic dyslipidemia, increased blood pressure, insulin resistance, proinflammatory and prothrombotic state (Das UN 2007). Based on the definitions proposed by several organizations MS can be assessed by a fasting blood glucose of >110mg/dl, central obesity measured as waist hip ratio or BMI or WC, triglycerides >150mg/dl, HDL < 35 mg/dl (male) and<40 mg/dl (female) and blood pressure >140/90mm Hg by WHO and EGIR and >135/85 by NCEP ATP III criteria (Expert panel Detection-third report NCEP ATP III 2001, Albert KG 1998, Balkau B 1999).Studies also suggest the inclusion of the inflammatory marker CRP in the definition of metabolic syndrome. However less data are available regarding the use of MAP and AIP in relation to metabolic syndrome. The mean arterial pressure (MAP) is the average over a cardiac cycle and is determined by the cardiac output (CO), systemic vascular resistance (SVR), and central venous pressure (CVP) (Klabunde, RE 2007). It is so important that it reflects the hemodynamic perfusion pressure of the vital organs. MAP = [(2 x diastolic) + systolic] / 3 (Zheng L etal 2008). Diastole counts twice as much as systole because 2/3 of the cardiac cycle is spent in diastole. A MAP of about 60 is necessary to perfuse coronary arteries, brain, kidneys. Usual range is 70-110 mm Hg.

Several studies have reported the possibility that newly addressed lipid ratio like T-C/HDL-C, TGLHDL-C, and LDL-C/HDL-C be more useful than the traditional ones used for CVD prediction (Kimm H, 2010). The Atherogenic Index of Plasma (AIP) has recently been proposed as a marker of plasma atherogenicity because it is increased in people at higher risk for coronary heart disease and is inversely correlated with LDL particle size (Tan MH 2004). Universally, atherogenic index of plasma (AIP) calculated as log (TG/HDL-C) has been used by few practitioners as a significant predictor of atherosclerosis (Dobiasova M, 2001, Tan MH, 2004).

At this scenario the present study is aimed to analyze the role of MAP and AIP in predicting CVD risk in type 2 diabetic patients with metabolic syndrome and inclusion of these parameters in defining metabolic syndrome.

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2. Materials and Methods

The study involved 120, Type 2 diabetic patients aged between 40-60 yrs. They are categorized as diabetic patients with metabolic syndrome (n=60) and diabetic patients without metabolic syndrome (n=60) by fulfilling at least 3 criteria of NCEP (ATP) III. Their anthropometric characteristics like height, weight, waist circumference, Blood pressure, were measured and Mean Arterial Pressure (MAP) was calculated using the formula MAP = [(2 x diastolic) + systolic] / 3. The following parameters are estimated in a fasting blood sample.

— FBS and PPBS - Glucose oxidase Peroxidase method

— HbA1C – Ion exchange resin method Trivelli L., 1971

— Total Cholesterol – Cholesterol oxidase peroxidase method

— Triglycerides – Glycerol 3 phosphate oxidase method

— HDL cholesterol – Phosphotungstate method

— LDL and VLDL using Friedewald's formula. VLDL = TGL/5, LDL = Total cholesterol – (HDL+VLDL).

— AIP= log TGL/HDL using Czech online calculator

Statistical tool: Student's t- test and linear regression analysis.

Inclusion criteria:

Age between 30-60 yrs, type 2 diabetes mellitus

Exclusion criteria:

Smokers, Alcoholics, liver diseases, kidney disease, patients on antioxidant therapy. or hypolipaedemic drugs

Ethical isssues: The purpose of the study was explained to all the participants and their consent was obtained. The requisite clearance of institutional human ethics committee was obtained.

3. Results

Table 1 showed the comparison of anthropoemetric measures among the type 2 diabetic patients with and without metabolic syndrome. A significant increase in WC and BP was seen in Type 2 diabetic patients with metabolic syndrome when compared to Type 2 diabetic patients without metabolic syndrome. The Mean arterial pressure was also found to be significant in diabetic patients with metabolic syndrome when compared to diabetic patients without metabolic syndrome.

Table: 1. Comparison of Anthropometric measures

Parameters	Type 2 Diabetic patients with out metabolic syndrome	Type 2 Diabetic patients with metabolic syndrome	p value	Significance
Age	58.1 ± 11.03	54.2 ± 8.68	0.2216	NS
WC	77.68 ± 6.8	98.03 ± 10.11	0.0001	Significant
BMI	24 ± 3.6	31.5 ± 4.7	0.0001	Significant
Systole	127.5 ± 12.3	152.35 ± 14.7	0.0001	Significant
Diastole	81.25 ± 6.7	97 ± 11	0.0001	Significant
MAP	97± 7.8	118 ± 10.98	0.0001	Significant

Table 2 compares the fasting blood sugar, HbA1C and lipid profile among the diabetic patients with and without metabolic syndrome. A significant increase was observed in HbA1C, cholesterol, TGL, VLDL and a significant decrease in HDL was observed in diabetic patients with metabolic syndrome when compared to diabetic patients without metabolic syndrome.

Table: 2 Comparison of Fasting blood sugar and lipid profile

Parameters	Type 2 Diabetic patients with out metabolic syndrome	Type 2 Diabetic patients with metabolic syndrome	p value	Significance
FBS	191 ± 97	146 ± 43	0.0654	NS
HbA1C	7.3 ± 1.2	8.0 ± 1.5	0.0056	S
Cholesterol	179 ± 34	223 ± 34	0.0001	S
Triglycerides	136 ± 32	210 ± 64	0.0001	S
HDL	42.25 ± 5.0	38.0 ± 4.2	0.0001	S
LDL	109 ± 35	143 ± 39	0.0001	S
VLDL	27 ± 6.5	42 ± 14	0.0002	S

Table 3 showed the atherogenic risk parameters among the diabetic patients with and without metabolic syndrome. A significant increase was observed in TGL/HDL, LDL/HDL and AIP in diabetic patients with metabolic syndrome when compared to diabetic patients without metabolic syndrome.

Table: 3 Risk parameters for CVD

Parameters	Type 2 Diabetic patients with out metabolic syndrome	Type 2 Diabetic patients with metabolic syndrome	p value	Significance	Low risk
LDL/HDL	2.6 ± 0.9	3.8 ± 1.02	0.0001	S	3.3-4.4
TGL/HDL	3.3 ± 0.8	5.3 ± 1.7	0.0001	S	1.57-3.5
AIP(log TGL/HDL)	0.15 ± 0.09	0.38 ± 0.13	0.0001	S	<0.11

Table 4 showed the linear regression analysis of the metabolic characters, HbA1C, MAP, AIP among the diabetic patients with and without metabolic syndrome. A significant increase was observed in WC, systole, MAP and AIP in diabetic patients with metabolic syndrome when compared to diabetic patients without metabolic syndrome.

Table 4: Linear regression analysis of the variables in relation to Diabetic patients with metabolic syndrome.

Parameters	Beta Coefficient	Significance	CI (lower)	CI (upper)
WC	0.182	0.005	0.002	0.012
SYS	-1.663	0.031*	-0.085	-0.004
DIAS	-1.819	0.056	-0.152	0.002
MAP	3.523	0.032*	0.011	0.246
HbA1C	0.022	0.505	-0.015	0.031
TGL	-2.229	0.153	-0.047	0.008
HDL	-0.055	0.538	-0.023	0.012
LDL/HDL	-0.304	0.147	-0.306	0.046
TGL/HDL	0.145	0.515	-0.090	0.178
AIP	0.148	0.047*	0.006	0.972

4. Discussion

Our study showed a significant increase in WC in Type 2 diabetic patients with metabolic syndrome when compared with the Type 2 diabetic patients without metabolic syndrome Studies have shown increased waist circumference is associated with CVD risk. (Shen W etal 2006, Yusuf etal 2005). A study by Huxley et al 2010 reported that measures of abdominal obesity is associated with CVD risk factors. Thus central obesity is found to play a key role in the pathogenesis of metabolic syndrome, it promotes inflammation, hypertension and dyslipidemia and leads to the development of type 2 diabetes mellitus and atherosclerosis.

Our study also showed an increase in BP in diabetes with MS which is one of the metabolic components. The reason may be the interaction between the effects of insulin resistance located primarily in muscle and adipose tissue and the adverse impact of the compensatory hyperinsulinemia which in turn induce blood pressure leading to the metabolic abnormalities (Low Wang C, 2004).

It has also been suggested that chronic increases in portal venous fatty acid levels may be responsible for hypertension that accompanies visceral obesity. Subjects with visceral obesity deliver a FFA load to the liver that, in turn, activates hepatic afferent pathways that may lead to sympathetic activation and contribute to insulin resistance (Bergman et al., 2001). Increased visceral fat accumulation is a strong predictor of arterial hypertension (Rahmouni K, 2005).

In the present study the MAP was found to be significantly increased in diabetic patients with metabolic syndrome when compared to diabetic patients without MS. The MAP of diabetic patients with and without metabolic syndrome was 118 mmHg and 97 mmHg respectively. The measure of MAP gives the average arterial blood pressure during a single cardiac cycle. It is a vital sign to monitor anytime the patient has a potential problem with perfusion of his organs. Hence the findings of this study suggest that the measure of MAP may also be useful in predicting CVD in metabolic syndrome. In a CVD risk patient a lesser value may represent ischemic injury due to insufficient blood flow and a higher MAP might reflect the excess blood flow and may result in raising arterial pressures.

A recent study has included the measure of MAP instead of BP as one of metabolic component. (M. Solera-Martı´nez et al, 2011). Carethers M (1989) reported that higher SBP reflects the progressive stiffening of the arterial wall, changes in vascular structure and the development of atherosclerosis. Cruickshank JM, (1988) demonstrated that decreased DBP may indicate poor coronary flow reserve and coronary perfusion of the myocardium. MAP reflects the steady flow of blood through the aorta and its arteries and equals the cardiac output multiplied by vascular resistance (Safar ME, 1989).

Linear regression analysis among the study group showed systolic pressure was significant but not diastolic pressure in diabetic patients with metabolic syndrome when compared to diabetic patients without metabolic syndrome. But the mean arterial pressure was found to be significant in diabetic patients with metabolic syndrome when compared to diabetic patients without metabolic syndrome. These data also suggest MAP may be more useful than systole and diastolic blood pressure. The cutoff of BP based on NCEP criteria is 130/85 mmHg. The Mean Arterial Pressure for 130/85 is 100 mmHg. Hence when considering MAP as a metabolic component for MS, a cutoff value above 100 mmHg which is equivalent to 130/85 can be used. An increase in MAP above 100 mm Hg suggests an increased CVD risk.

Though the FBS of diabetic patients were higher than normal a significant decrease was observed in diabetic patients with metabolic syndrome when compared to diabetic patients without metabolic syndrome. The decrease in FBS in metabolic syndrome may be due to the effect of hypoglycemic drugs. A significant increase observed in HbA1C of diabetic patients with metabolic syndrome suggests a CVD risk in them. Levels of HbA1C are not influenced by daily fluctuations. Thus it serves as a useful indicator of how well the blood glucose level has been controlled in the recent past and may be used to monitor the effects of diet, exercise, and drug therapy on blood glucose in diabetic patients. It has been demonstrated that the complications of diabetes can be delayed or prevented if the HbA1C level can be kept close to 7%. Hence the above results suggest T2 DM with metabolic syndrome are more prone to CVD.

A significant increase was seen in cholesterol, triglyceride, LDL and VLDL of diabetic patients with metabolic syndrome when compared with the diabetic patients without metabolic syndrome. Triglycerides play the role of regulator of lipoprotein interactions. Increased plasma triglyceride is associated with 1. increased incidence of CAD 2. an increased population of LDL 3. enhanced cholesterol esterification.

In the present study a significant increase was observed in LDL/HDL, TGL/HDL in diabetic patients with metabolic syndrome when compared to diabetic patients without metabolic syndrome. Table 5.3 shows the LDL/HDL ratio of diabetic patients without MS and with MS are 2.6 ± 0.9 and 3.8 ± 1.02 respectively and the expected low risk is 3.3-4.4. The TGL/HDL ratios of diabetic patients without MS and with MS are 3.3 ± 0.8 and 5.3 ± 1.7 respectively and the low risk is between1.5 and 3.5. These results suggest that LDL/HDL ratio and TGL/HDL ratio are significantly increased in diabetic patients with metabolic syndrome. The LDL/HDL ratio predicts that patients with metabolic syndrome are at low risk while TGL/HDL ratio predicts that this group is under moderate risk.

Earlier reports suggest, the measure of lipid ratios as the potent predictor of heart disease (Grover SA, 1999, Gotto AM, 1998 Kimm H (2010), McLaughlin T (2003) ,(Ryuichi Kawamoto etal, 2011). In the present study the atherogenic index of plasma (AIP) is 0.15 ± 0.090 in diabetic patients without metabolic syndrome and 38 ± 0.13 in diabetic patients with metabolic syndrome. Previous studies suggest that AIP values of -0.3 to 0.1 are associated with low CAD risk, 0.1 to 0.24 medium and above 0.24 high risk. AIP can be easily calculated from the standard lipid profile. As a marker of lipoprotein particle size it adds predictive value beyond that of the individual lipids, and/or TC/HDL-C ratio (Dobiasova M.2004).Hence our report suggests atherogenic index of plasma which is a better predictor of CVD and is significantly increased in diabetic patients with metabolic syndrome. This is in agreement with the study by Tan et al. (2004)

Though dyslipidemia was found in diabetic patients with MS, linear regression analysis results shows no significance in both TGL and HDL. These results suggest that even diabetic patients without MS have dyslipidemia, Studies have shown the presence of dyslipidemia in diabetic subjects (Turner RC, 1998). Linear regression analysis of the atherogenic risk parameters showed no significance in LDL/HDL, TGL/HDL among the study groups. But a significant increase was observed in AIP in diabetic patients with MS when compared to diabetic patients without MS. The p value of AIP is more significant when compared to other ratios. Hence the present study suggests AIP has a higher efficiency of indicating atherogenic lipid abnormality and is a more reliable indicator of CVD.

The importance of AIP as an indicator of the atherogenesis has been demonstrated in hypertensive postmenopausal women (Nwagha UI 2005, VA Josephs 2011) smokers (Veerendra Kumar et al 2011). According to Usoro et al (2006) lower atherogenic index is protective against coronary heart disease. However less data are available regarding AIP between diabetic patients with and without metabolic syndrome.AIP is calculated as log (TG/ HDL-C), with TG and HDL-C expressed in molar concentrations (Dobiasova M, 2001). Dyslipidemia involves the triad of increased triglyceride, decreased HDL and a preponderance of LDL in metabolic syndrome. AIP represents the logarithmatically transformed ratios of TGL and HDL and inversely correlates the LDL size. Hence the present study suggests that AIP can be included as a component of metabolic syndrome, as it is the best marker for cardiovascular risk.

5. Conclusion

A significant increase in WC, BP, MAP TGL, and AIP was observed in diabetic patients with metabolic syndrome when compared to diabetic patients without metabolic syndrome. Metabolic syndrome is an added factor which increases the risk for CVD among the diabetics. The results of the study suggest MAP and AIP may be useful in diagnosing the CVD risk among diabetic patients with metabolic syndrome. The study also suggests the use of MAP and AIP in defining metabolic syndrome. However the study has limitations viz cross sectional study and only one criteria was followed to define metabolic syndrome.

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