VISCERAL ADIPOSITY INDEX IN TYPE 2 DIABETES MELLITUS AND ITS RISK FOR CARDIOVASCULAR DISEASE

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Abstract:

Back ground: *The Visceral Adiposity Index (VAI) is an empirical mathematical model, gender-specific, based on simple anthropometric (BMI and WC) and functional parameters (triglycerides (TG) and HDL cholesterol (HDL)), and indicative of fat distribution and function.*

Methods: *This is a Cross sectional study. It was carried out in the department of Biochemistry, BSMMU from July 2015- June 2017. Type 2 Diabetes Mellitus patients attending in outpatient Department of Endocrinology and Metabolism, BSMMU were our study population. The cutoff value for VAI was considered as 3.*

Results: *We enrolled 105 participants in this study. Among them 41 were male and 64 were female. There was significant difference between male and female in terms of height, weight and BMI. Male had greater height (p =0.01) and weight (p =0.01) than female. Female had greater BMI (p =0.01) than male. The majority of male and female scored above the cut off value of VAI which were 63.4% and 59.4% respectively. The mean value of biochemical parameters TG, FBG and HbA1c were significantly different on the basis of cutoff point of VAI (d"3 and > 3). There is increased TG, FBG and HbA1c and decreased HDL-C with the cut off value more than 3 in VAI. We found significant strong positive correlation with HbA1c with FRS (r= +.631, p=<0.001) and VAI (r= +.596, p=<0.001)*

Conclusion: *High Visceral Adiposity Index is associated with Type 2 diabetes mellitus and increased cardiovascular risk*

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Introduction:

The Visceral Adiposity Index (VAI) is an empirical mathematical model, gender-specific, based on simple anthropometric (BMI and WC) and functional parameters (triglycerides (TG) and HDL cholesterol (HDL)), and indicative of fat distribution and function. It does not originate from theoretical assumptions, rather from observation in a healthy normal/ overweight population of a linear relationship between BMI and CV, from which a linear equation has been extrapolated. At first a model of adipose distribution (MOAD) was created based on this linear equation (which shows a strong correlation with visceral fat mass determined by MRI. Subsequently MOAD was corrected for triglyceride and HDL cholesterol levels, determining the VAI (Amato et al. 2013).[1]

$$\text{Females : VAI} = \left(\frac{\text{WC}}{36.58 + (1.89 \times \text{BMI})}\right) \times \left(\frac{\text{TG}}{0.81}\right) \times \left(\frac{1.52}{\text{HDL}}\right)$$

$$\text{Males : VAI} = \left(\frac{\text{WC}}{39.68 + (1.88 \times \text{BMI})}\right) \times \left(\frac{\text{TG}}{1.03}\right) \times \left(\frac{1.31}{\text{HDL}}\right) \quad (1)$$

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Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces (WHO 2009). There are mainly two types of diabetes; Type 1 diabetes is immune-mediated and requires daily administration of insulin. The other common type is T2DM and characterized by insulin resistance or relative insulin deficiency (WHO 2009). T2DM is the most common form and comprises of 90% of people with diabetes around the world (WHO 2009). T2DM increases the risk of a myocardial infarction two times and the risk of suffering a stroke two to four times. It is also a leading cause of blindness, limb amputation and kidney failure (International Diabetes Federation 2006). Although trials of secondary prevention after myocardial infarction show as good or better short term effect of interventions in patients with diabetes as in patients without, patients with diabetes have not had a similar reduction in longer-term case fatality rates of CVD.[2] Population based studies of CVD risk factor trends among subjects with and without diabetes show differing trend in disfavor of those with diabetes.[3] Studies of adherence to guidelines for CVD prevention targets in patients with diabetes in general practice have shown that only 13% reach all the targets.[4] Previous studies have found appropriate lifestyle intervention and/or drug treatment are effective in delaying or preventing both diabetes and its complications.[5] Accordingly, simple, sensitive and acceptable tools for identification of subjects at risk are warranted. The world prevalence of diabetes in 2010 among adults aged 20-79 years is estimated to 6.4%, affecting 285 million adults.[6] Between 2010 and 2030, there is an expected 70% increase in numbers of adults with diabetes in developing countries and a 20% increase in developed countries.[6] Each year more than 231,000 people in the United States and more than 3.96 million people worldwide die from diabetes and its complications.[3]

Various methods exist for accurate measurement of the amount and distribution of body fat. Traditional methods, such as underwater weighing (densitometry) and isotope dilution (hydrometry), calculate body composition based on a two-compartment model that divides body weight into fat mass and fat-free.[7] Multi-compartment models that directly measure bone mineral, fat, protein and other components provide more accurate measurement of body composition. For instance, the Dual-Energy X-Ray Absorptiometry (DXA) is a frequently used technique to estimate body composition in clinical studies [8]. It provides accurate measurements of the three components (fat mass, fat-free mass and bone mineral density) for the whole body, as well as for specific body regions. Imaging methods are considered the most accurate technique for measuring body composition and ascertaining fat distribution at the tissue-organ level.[9] Computed tomography and magnetic resonance imaging produce high resolution images of selected tissue and organs to accurately quantify percentage body fat, and visceral and subcutaneous fat.[10] Although these techniques are highly reproducible and accurate, they are very expensive and time consuming and therefore may not currently suitable for clinical settings and most large-scale epidemiological studies (although UK Biobank, a prospective study of 500,000 people, may be an exception). For this reason, most studies measure weight, height and other anthropometric variables to assess amount and distribution of body fat.

BMI, defined as the ratio of weight in kilograms to the square of height in meters, represents a simple, but crude index that is widely used to indirectly estimate overall or general adiposity (without taking into account fat distribution). Overall adiposity has been generally expressed as a percentage of body fat.[11] The validity of BMI has been demonstrated by various studies, as BMI correlates with percentage body fat that was assessed by superior techniques.[12] BMI values are considered age and sex independent. BMI is recommended as the most useful epidemiological measure of obesity by the World Health Organization. Their guidelines define BMI between 18.5 and 24.9 kg/m2 as normal, 25 kg/m2 or higher as overweight and 30 kg/m2 or higher as obese (WHO 2000). Although BMI correlates well with body fat and predicts cardiovascular outcomes, the measure itself has

some major limitations. BMI cannot distinguish between fat mass and lean (fat-free) mass, leading to potentially substantial differences in percentages of fat mass between individuals with similar BMI.[13] BMI values do not correspond to the same degree of fatness across the different populations because of ethnic variation in body composition. For instance, the percentage of body fat is generally higher in Asian than in Caucasian populations for a given. Asians have been shown to be at increased risk of type II diabetes and cardiovascular disease at BMI values lower than the existing WHO cut-off point for overweight (i.e., e"25 kg/m2) (WHO 2004).

Location of body fat or body fat distribution has been recognized to be associated with several obesity-related diseases.[14] There is growing evidence that android obesity (i.e, excess fat mass in the upper part of the body, such as the abdomen) is more strongly linked with metabolic abnormalities, which could subsequently lead to cardiovascular disease, than gynecoid obesity (i.e, fat accumulation in the lower part of the body, such as the hips and thighs).[16] Particularly, visceral adipose tissue in the abdominal region is believed to be more metabolically active than other fat depots, such as abdominal subcutaneous fat AND family history.[17]

Throughout the world the burden of non-communicable disease (hypertension, diabetes mellitus, collagen vascular disease, asthma etc.) are increasing alarmingly. Therefore, the overall morbidity and mortality rate are also increasing due to the increasing prevalence of such diseases. When visceral adiposity increases, the risk of non-communicable diseases also increases. VAI is a simple but yet a useful clinical marker of adipose tissue dysfunction. The objective of the study was to evaluate the relationship between Visceral Adiposity Index (VAI) in type 2 Diabetes Mellitus (T2DM) and Cardiovascular Disease (CVD) risk on the basis of Framingham Risk Score (FRS). The association of VAI with diabetes mellitus has not been studied in Bangladesh. Therefore, we designed the current study, finding of which could be helpful for the evaluation of visceral adipose tissue dysfunction and its associated cardiovascular risk in various patient populations in near future.

Methodology:

This is a Cross sectional analytical study. It was carried out in the department of Biochemistry, BSMMU from July 2015- June 2017. T2DM patients attending in outpatient Department of Endocrinology and Metabolism, BSMMU were our study population. Our calculated sample size was 105 at 5% level of significance or 95% confidence level with acceptable error of 0.05. We enrolled the participants by non-probability purposive convenient sampling technique. Data collection sheet was prepared which included all the variables of interest and it was validated for data collection. A research protocol was approved by the ethical review committee of BSMMU before starting this study. We included Type 2 diabetic patients of both male and female with age between 30 to 70 years. We excluded the patients having organ dysfunctions (Liver, Kidney, Heart), patients having history of previous myocardial infarction, history of any form of allergy and acute infections, Pregnancy, Patients taking lipid lowering medications (e.g. statins, fibrates etc.) and steroids. Before data collection purpose and procedure of the study was explained in details and informed written consent was taken from all the study subjects. Anthropometric measurements of all the study subjects which include their height, weight and waist circumference, was recorded. Then their BMI was calculated. Systolic and diastolic blood pressures of the study subjects were recorded in sitting position. Then fasting blood samples were collected from them to estimate FBG, TG, HDL-C and TC. Whole blood was collected to estimate HbA1c without centrifuged. The biochemical test was performed at the Department of Biochemistry & Molecular Biology, BSMMU, Dhaka. Visceral Adiposity Index (VAI) was calculated for detecting visceral obesity in the study subjects. The outcome variable was VAI and Key variables were Weight (Kg), Height (cm), WC (cm), Body Mass Index (kg/m^2). Collected data were checked and edited and then processed with the help of the software Statistical Package for Social Sciences (SPSS) version 24 and analyzed. Quantitative variable was analyzed by Unpaired t-test between male

and female respondents and expressed mean, standard deviation. Qualitative variable was analyzed by Chi-square test and expressed frequency and percentage. P value d" 0.05 was considered as statistically significant. Cut of value of VAI was determined from previous study.

Result:

We enrolled 105 participants in this study. Among them 41 were male and 64 were female.

There was significant difference between male and female in terms of height, weight and BMI. Male had greater height (p =0.01) and weight (p =0.01) than female. Female had greater BMI (p =0.01) than male. There was also significant difference between male and female in terms of HDL-C, SBP and DBP. Male had higher SBP (p =0.03) and DBP (p=0.02) than female. Female had higher HDL-C (p =0.01) than male (Table I).

Study showed 56.1% respondents were smoker among male and 4.7% among female. Smoking is significantly higher in male patients (p<0.001) than that of female patients. The majority of male and female scored above the cut off value of VAI which were 63.4% and 59.4% respectively. Below the cut off value, there were 37.6 % male and 40.6 % female. There is no significant association between gender and VAI (Table II).

Table-I

Comparison of Demographic, Anthropometric and Biochemical characteristics between male and female study subjects (N=105)

Parameters	Total (n=105)	Male (n=41)	Female (n=64)	*p* value
Age (years)	47.2±10.58	49.2±10.37	46.5±9.31	0.81
Weight (kg)	63.83±8.02	66.97±6.78	61.81±8.16	0.01*
Height (feet)	5.90±2.22	5.5±0.21	5.0±0.34	0.01*
WC (cm)	35.37±3.67	34.77±2.55	35.75±4.21	0.11
BMI (kg/m^2)	25.33±3.47	23.45±1.97	26.52±3.69	0.01*
TG (mg/dl)	197.0±101.0	199.90±103	194.10±100.95	0.81
HDL-C (mg/dl)	36.34±15.38	34.07±5.85	38.6±9.53	0.01*
TC (mg/dl)	231.1±41.82	237.14±41.97	224.96±41.67	0.16
FBG (mg/dl)	8.69±3.91	8.12±2.92	9.25±4.90	0.15
HbA1c (%)	9.29±1.68	8.15±1.83	10.42±1.53	0.38
SBP (mmHg)	128.0±9.52	130±9.53	126±9.50	0.03*
DBP (mmHg)	79.71±10.02	82.44±9.62	77.96±9.94	0.02*

Results are expressed in mean ±SD. Unpaired t-test was done.. S, BP = Systolic blood pressure , DBP = Diastolic blood pressure.

Table II

Distribution of the sex on the basis of cut off value of VAI (N=105)

VAI parameter	Total		Male		Female		P
	n(%)	Mean±SD	n(%)	Mean±SD	n(%)	Mean±SD	value
VAI ≤ 3	41(39.05%)	1.38±0.51	15 (37.6%)	1.49±0.48	26 (40.6%)	1.32±0.53	0.679^{ns}
VAI > 3	64(60.95%)	4.23±1.30	26 (63.4%)	4.18±1.51	38 (59.4%)	4.27±1.16	
Total	105(100.0%)	3.12±1.75	41 (100%)	3.19±1.79	64(100.0%)	3.07±1.74	

Data were expressed as frequency and percentage, P value reached from Chi-square test, ns=not significant

The mean value of biochemical parameters TG, FBG and HbA1c were significantly different on the basis of cutoff point of VAI (≤3 and > 3). There is increased TG, FBG and HbA1c and decreased HDL-C with the cut off value more than 3 in VAI. Mean value of FRS is significantly higher in VAI cut off value more than 3 (Table III).

Above the cut off value of VAI, percentage of study subjects in LCR, ICR and HCR were 23.8%, 21.9% and 15.2% respectively. In contrast, below cut off value of VAI, the percentage of study subjects in LCR, ICR and HCR were 12.3%, 12.3% and 14.2% respectively. This result represents that majority of the study subjects (60.9%) above the cut off value of VAI are in risk of CVD i.e. higher VAI increases the risk of CVD. There is no significant difference between VAI and different risk group of FRS (p>0.05) (Table IV).

Table III

Comparison of biochemical parameters and FRS between VAI cut off point d" 3 and > 3 (N=105)

Biochemical parameter	Visceral adiposity index		*p* value
	≤3 (n=41)	>3 (n=64)	
	Mean±SD	Mean±SD	
TG	111.20±71.35	200.28±100.85	0.001[s]
HDL-C	49.80±10.98	37.45±8.48	0.002[s]
FBG	7.08±1.22	8.72±2.38	0.039[s]
HbA1C	8.72±2.38	9.60±12.59	0.600[ns]
FRS	8.90±3.81	20.26±5.03	<0.001[s]

Data were expressed as mean ±SD. P value reached from Unpaired student t-test, ns=not significant, s= significant. LCR = Low Cardiovascular Risk, ICR = Intermediate Cardiovascular Risk, HCR = High Cardiovascular Risk, FRS=Framingham Risk Score

Table IV

Distribution of the different risk group by using FRS and its relation to VAI (N=105)

Parameter	LCR (FRS <10%) n (%)	ICR (FRS 10-<20%) n (%)	HCR (FRS >20%) n (%)	Total n (%)	*P* value
VAI d" 3	13 (12.3%)	13 ((12.3%)	15 (14.2%)	41(39.0%)	0.440
VAI > 3	25 (23.8%)	23 (21.9%)	16 (15.2%)	64(60.9%)	
Total	38 (36.1%)	36 (34.2%)	31 (29.5%)	105(100%)	

Results are expressed in numbers and percentages. Chi-square test was done to find out the level of significance. LCR = Low Cardiovascular Risk, ICR = Intermediate Cardiovascular Risk, HCR= High Cardiovascular Risk, FRS=Framingham Risk Score

There was significant strong positive correlation with VAI and FRS in male (r=0.748, p<0.001) and female (r=0.826, p<0.001) patients. In total population FRS score had strong positive correlation with VAI (Fig 1).

We found significant strong positive correlation with HbA1c with FRS (r= +.631, p=<0.001) and VAI (r= +.596, p=<0.001) (Figure 2)

Discussion:

Visceral Adiposity Index (VAI) is a mathematical model based on simple anthropometric (BMI and WC) and metabolic (TG and HDL-C) parameters and is considered as a simple surrogate marker of visceral adipose dysfunction.[18] VAI is strongly associated with visceral adiposity measured using magnetic resonance imaging and cardiovascular and cerebrovascular events [18]. Recent data also indicate that hypertriglyceridemia and low HDL-C are key components of the metabolic syndrome and are strongly predictive of coronary artery disease.[19,20] The TG/HDL-C ratio is another practical marker of atherosclerosis and insulin resistance and an independent predictor of cardiovascular risk.[21,22] The role of TG/HDL-C ratio in predicting cardiometabolic risk has been tested in several metabolic disorders, such as diabetes mellitus, hypertension, chronic kidney disease, and nonalcoholic fatty liver disease.[23] This cross sectional study was conducted in order to elucidate the relationship between VAI with type 2 DM patients and to assess their cardiovascular risk (on the basis of Framingham Score Risk).

The average age of male and female participants was different in our study. There was significant difference between male and female in terms of weight, height and BMI. Male had higher weight and height but BMI was higher in female. SBP was higher in male and HDL-C was higher in female. No significant difference was observed in WC, TG, TC, FBG and HbA1c between male and female. But for VAI, we found male were more likely to have higher VAI than female. These findings of our study were not consistent with Chen et al. (2014) study.

Our study showed strong positive correlation between VAI and FRS score in T2DM patients of male, female and total population. These results were in agreement with.[24]

In present study a strong positive significant correlation was found with HbA1c with FRS and VAI. These findings suggested that VAI may be better in identifying diabetes risk. However, the ability of VAI in identifying diabetes risk among people. This difference might be attributed to different study populations. It has reported that compared with Caucasians, Asians may have significantly higher risk of type 2 diabetes and CVDs despite substantially lower BMI.[25]

VAI could be easily conducted in large-scale epidemiological studies and has been suggested as a useful surrogate marker of cardiovascular disease. VAI includes physical (BMI and WC) and metabolic (TG and HDL-C) parameters, it may indirectly reflect other non-classical risk factors, i.e. altered production of adipokine, increased lipolytic activity and plasma-free fatty acids. Recently reported by[26], VAI was negatively related with adiponectin value, this was the first report for the direct relations of VAI with adipose tissue secretion. Some researchers have proved that VAI could be used to predictive individual risk of IR, MS, acromegaly, cardiovascular disease (CVD) and diabetes.[27-29] Consistent with previous researches[27,28], our study also indicated that VAI is a useful surrogate marker to identify the risk of diabetes; individuals with high VAI were accompanied with increased risk of cardiovascular disorders and diabetes. The risk of getting diabetes at the highest VAI group was >3 higher as compared to the lowest VAI group.

Limitation of the study

The main limitation of this study was small sample size. Only 105 patients were considered in this study within a limited time frame and using limited resources. Moreover, the study subjects were not selected randomly rather those who attended OPD, BSMMU were selected for the study. Therefore, the patient pool is not devoid of selection bias. All the patients were enrolled in this study from a single tertiary level hospital. Therefore, the current study lacks multi-centric different ethnic category of patients.

Conclusion:

High Visceral Adiposity Index is associated with Type 2 diabetes mellitus and increased cardiovascular risk. We suggest that VAI could be an easy tool for the evaluation of the risk for cardiovascular disease in patients with T2DM.

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