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Determination of the best anthropometric measurements for early discovery of atherosclerosis in adolescent type 1 diabetic patients

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To evaluate anthropometric measurements for early assessment of atherosclerosis in type 1 diabetic patients. One hundred thirty five adolescent type 1 diabetic patients and 100 healthy volunteers of age and sex matched were included in the study. Blood samples were collected for measurement of oxidized low density lipoprotein (OxLDL), glycosylated hemoglobin (HbA1c), and lipid profile. Urinary albumin/creatinine ratio were assessed. Carotid intimal medial thickness (cIMT) and aortic intimal medial thickness (aIMT) were also assessed via ultrasound.HbA1c, urinary albumin./ creatinine ratio , lipid profile, OxLDL, cIMT and aIMT were significantly higher in diabetic patients. A significant positive correlation was found between body mass index (BMI) and age of diabetic patients, insulin dose, waist/ height ratio, blood pressure, LDL-c and cIMT. A significant positive correlation was found between waist/hip ratio and duration of diabetes, insulin dose/ kg, waist/ height ratio and urinary albumin/ .creatinine ratio. A significant positive correlation was found between waist/ height ratio and HbA1c, lipid profile and cIMT. Waist/ height ratio, BMI, waist/ hip and midarm circumference/ height ratio are useful for early discovery of atherosclerosis. Waist / height ratio is the best anthropometric measurement for assessment of atherosclerosis and glycemic control in diabetic patients.

Keywords: anthropometric measurements, atherosclerosis, type 1 daibetic patients

INTRODUCTION

The major etiology of morbidity and mortality in the United States and around the world is atherosclerosis. A number of clinical, laboratory, and non cardiac tests are routinely used to detect cardiovascular disease (CVD) and to determine patient risk of future cardiac events (Kolluru et al., 2013).

Childhood atherosclerosis occur in the form of intimal fatty streaks as lipids accumulate in the aorta in children more than 3 years of age (Holman et al., 1958). Postmortem of age between 15 to 34 years revealed that atherosclerosis occur in the dorsolateral wall of abdominal aorta proximal to its bifurcation (. McGill et al., 2008), on the other hand, coronary and carotid arteries had atherosclerotic lesions after aorta, and they have a strong association between each other (. McGill et al., 1968; Soha M. Abd El Dayem et al ., 2016).Increased carotid intima media thickness (cIMT) is an evidence of subclinical atherosclerosis and leads to coronary artery disease and stroke (Burke et al., 1995; O'Leary et al., 1999; O'Donnell et al., 2008). Obesity, one of the modifiable risk factors, is associated with increased coronary risk through its indirect effects mediated by its relationship to traditional coronary risk factors.

From our knowledge no previous study examine the relationship of anthropometric measures and CVD risk factors in young type 1 diabetic patients. There are a number of ways to assess obesity, but these different methods have not been compared in terms of their association with atherosclerosis. The objective of our study was to evaluate different anthropometric measurements for early detection of atherosclerosis in type 1 diabetic patients.

MATERIALS AND METHODS

Patients:

The study included 135 type 1 diabetic patients among those attending the endocrine clinic, National Research Centre, Center of Excellence, Cairo, Egypt. One hundred healthy volunteers with age and sex matched was included as a control group.

Inclusion criteria:

Adolescents type 1 diabetic patients, duration of diabetes > 5 years, diabetic age > 14 and < 19 yrs. old.

Exclusion criteria were:

Patients during diabetic ketoacidosis (DKA) or hypoglycemia, patients suffering from cardiac diseases and patients on metformin or multivitamins.

Study design and protocol:

It is a cross-sectional observational study done after obtaining approval from the ethical committee of the National Research Centre, Cairo, Egypt. Registration number is 11052. Written informed consent was obtained from all diabetic patients and controls or their parents after full discussion about the objective of this work.

Methods:

Full clinical examination was done for all diabetic patients and controls including general, Danilova LA, Lopatina Blood pressure was assessed three times for diabetics and controls after rest in the sitting position on both upper limbs with the use of automatic manometer (Omron M4 Plus, Omron Health care Europe, Hoof drop, and Holland).

Anthropometric measurements in the form of weight, height, waist circumference (WC), hip circumference (HC) and midarm circumference were taken for each participant. The weight and height of the participants were measured up to 0.01 kg and 0.1 cm using a Seca Scale standing balance and a Holtain Portable anthropometer (Holtain, Ltd, Crymmych, Wales, U.K.). Body mass index (BMI) (kg/m^2) was calculated according to the standard formula BMI = weight (kg)/ [height (m)]^2 .Waist circumference was measured at the level of the umbilicus with the participant standing and breathing normally; hip circumference was measured at the level of the iliac crest, using non stretchable plastic tape to the nearest 0.1 cm. The waist / hip ratio and waist / height ratio (cm/ cm) were calculated. Mid upper arm circumference was measured using a flexible tape at the midway between the olecranon and acromial process on the upper right arm (Lu et al., 2014). The Arm-to-Height Ratio was calculated as arm circumference / height ratio (9).Each measurement was taken as the mean of three consecutive measurements, using standardized equipment (Cameron I., 1986; Tanner et al., 1969).

Laboratory investigation:

All patients and controls underwent the following tests: venous blood was sampled after a 12-h fast for measurement of serum levels of lipid profile [total cholesterol (mg/dL), high density lipoprotein (HDL) cholesterol (HDL-C, mg/dL), and triglycerides (mg/dL)] was performed on automated clinical chemistry analyzer (OLYMPUS AU400) . Low density lipoprotein cholesterol (LDL-C) level was calculated using Friedewald formula: LDLc=TC-HDLc-TG/5 mg/dl (Friedewald et al., 1972).

Venous blood samples were obtained from each subject in a sterile EDTA vacutainer tubes for measuring glycated haemoglobin (HbA1c). It was measured using The NycoCard READER II (Alere Technologies AS, Kjelsåsveien 161, P.O. Box 6863 Rodeløkka, NO-0504 Oslo, Norway) (Danilova and Lopatina., 1986). Glycated hemoglobin (HbA1c) was done every 3 months and the mean value was calculated per year.

Urinary albumin/ creatinine ratio was assessed. Urinary albumin was measured by NycoCard READER II (Alere Technologies AS, Kjelsåsveien 161, P.O. Box 6863 Rodeløkka, NO-0504 Oslo, Norway) (Mogensen., 1984). Urinary creatinine was assayed using automated clinical chemistry analyzer (OLYMPUS AU400) after dilution in ratio of 1:50.

Serum concentration of oxidized low-density lipoprotein (OxLDL) was detected by commercially available solid phase two-site enzyme immunoassay kit (Mercodia AB, Uppsala, Sweden). Assessment of OxLDL levels in the sera were performed according to the recommendations of the manufacturer. The intra and interassay coefficients of variations were 5.5% – 7.3% and 4.0% – 6.2%, respectively, and the sensitivity was < 1 mU/L..

Carotid intima-media thickness (cIMT) assessment:

General electric medical ultrasonographic machine model: Vivid 7 Pro, GE Vingmed ultrasound AS-Nl90, Horton-Norway equipped with 7.5–10 MHz linear-array transducer was used for evaluation of cIMT. A longitudinal section of the common carotid artery 1 cm proximal to the carotid bulb was imaged to achieve consistent site of measurement, and a resolution box function was used to magnify this part of the artery. Three maximal IMT measurements of the far wall of the artery at 3-mm intervals were obtained starting at 1 cm proximal to the bulb and moving proximally. The reported IMT for each side is the average of these 3 measurements and the reported IMT for each subject is the average of the 6 measurements (3 measurements from the right and 3 from the left common carotid artery). Magnification of the vessel wall allows easy identification of the intimal-medial complex, defined by the border between the echolucent vessel lumen and the echogenic intima and the border between the echolucent media and echogenic adventitia. Image frames are selected on the basis of areas where the intima-media complex is best visualized and appears the thickest, irrespective of the cardiac cycle, with manual assessment by the sonographer using electronic calipers online (Singh et al., 2003).

Aortic intimal medial thickness (aIMT):

Abdominal aorta was first identified in the upper abdomen using a 7.5 MHz pediatric phased array transducer, and it was then followed distally until the aortic bifurcation appear. The depth (antro posterior direction) and location (cranio-caudal direction) of the distal 15 mm of the abdominal aorta was measured from these images and used as an aid to locate the aortic intima-media complex using a 10 MHz linear array transducer. The image was focused on the far wall (dorsal arterial wall of the most distal 15 mm of the abdominal aorta) (McGill et al., 2000). At least 3 measurements of aIMT was done, followed by averaging the three measurements of each patient.

Statistical Analysis:

Statistical analysis was conducted using Statistical Package for Social Science (SPSS) program version 17.0 (Chicago, Illinois, USA). t – test or Mann Whitney-U (for non-symmetrically distributed data) for independent variables was done. Pearson's or spearman correlation was done. Receiver Operating Characteristic curve (ROC curve) was used for different anthropometric measurements and its relation to carotid intimal medial thickness.

RESULTS

Table1, showed that HbA1c, urinary albumin/ creatinine ratio, lipid profile, OxLDL, cIMT and aIMT were significantly higher in diabetic patients.

Body mass index had a significant positive correlation with age of diabetic patient, insulin dose/ kg, waist/ height ratio, blood pressure, LDL-c and cIMT. A positive significant correlation was found between waist to hip ratio and duration of the diabetes, insulin dose/kg, waist to height ratio and urinary. albumin./ .creatinine ratio. Also a positive significant correlation of waist/ height ratio was found between HbA1c, lipid profile and cIMT (table 2). Midarm circumference and midarm / height ratio had a significant positive correlation with cIMT (table 3). ROC curve of different anthropometric measurements and its relation to carotid intimal medial thickness (table 4). Waist / height ratio had the best specificity for early diagnosis of atherosclerosis , on the other hand, midarm circumference / height ratio had the highest specificity.

Table 1 : Demographic, anthropometric, laboratory data, carotid and aortic intimal medial thickness of diabetic patients and controls

Variables	Patients		Controls		P-value
	Mean	SD	Mean	SD	
Demographic data:					
Systolic blood pressure (mmHg)	118.872	12.919	118.214	14.415	0.8
Diastolic blood pressure (mmHg)	79.060	10.003	78.571	6.506	0.8
Blood pressure:					
BMI (kg/m^2)	24.738	4.072	22.472	6.478	**0.03**
Waist/ hip ratio	0.893	0.075	0.869	0.058	0.4
Waist/ height	0.513	0.069	0.499	0.082	**0.0001**
Midarm circumference (mm)	75.884	382.263	25.786	4.405	0.7
Midarm cirumference/ height ratio	0.471	2.365	0.179	0.032	0.8
Laboratory data:					
HbA1c %	9.332	1.908	4.783	0.585	**0.0001**
Albumin/ creatinine ratio (µg/ g creatinine)	75.193	88.038	16.499	8.394	**0.0001**
Total Cholesterol (mg/dl)	191.385	63.795	146.875	21.582	**0.005**
Triglyceride (mg/dl)	104.876	65.484	82.000	27.028	**0.0001**
HDL-c (mg/dl)	50.422	18.442	47.125	11.261	0.4
LDL-c (mg/dl)	114.089	38.227	82.208	21.480	**0.0001**
OxLDL (mg/dl)	17.56	6.45	9.06	3.92	**0.0001**
Image study:					
Rt carotid intimal medial thickness(mm)	0.508	0.074	0.405	0.052	**0.0001**
Lt carotid inimal medial thickness(mm)	0.509	0.076	0.410	0.039	**0.0001**
Carotid intimal medial thickness(mm)	0.509	0.069	0.411	0.029	**0.0001**
Aortic intimal medial thickness (mm)	0.722	0.108	0.458	0.046	**0.0001**

BMI : body mass index, HBA1c : glycosylated hemoglobin, HDL-c : high density lipoprotein , LDL: low density lipoprotein, OxLDL: oxidized low density lipoprotein

Table 2 : Correlation between body mass index, waist/ hip ratio , waist / height ratio with demographic, laboratory data, carotid and aortic intimal medial thickness of diabetic patients

Variables	BMI		Waist/ hip ratio		Waist / height	
	r	P-value	r	P-value	r	P-value
Demographic data:						
Age (yrs)	0.20	**0.02**	0.06	0.49	0.07	0.44
Duration of disease (yrs)	0.03	0.75	0.18	**0.04**	0.06	0.48
Age of onset of disease (yrs)	0.12	0.18	0.14	0.11	0.11	0.19
Insulin dose (U/kg)	0.27	**0.0001**	0.18	**0.04**	0.02	0.84
Blood pressure:						
Systolic blood pressure (mmHg)	0.19	**0.03**	0.01	0.90	0.01	0.90
Diastolic blood pressure (mmHg)	0.19	**0.03**	0.08	0.34	0.09	0.33
Anthropometric measurements:						
BMI (kg/m2)			0.12	0.18	0.68	**0.0001**
Waist/ hip ratio	0.12	0.18	0.00		0.54	**0.0001**
Waist/ height ratio	0.68	**0.0001**	0.54	**0.0001**	1.00	
Mid arm circumference (cm)	0.18	0.15	0.05	0.67	0.20	0.10
Arm/ height ratio	0.18	0.15	0.06	0.65	0.20	0.10
Laboratory data:						
HbA1c (%)	0.01	0.95	0.15	0.09	0.19	**0.04**
Albumin/ creatinine ratio (µg/ g creatinine)	-0.06	0.53	0.19	**0.04**	0.09	0.37

Cholesterol (mg/dl)	0.14	0.14	0.03	0.76	0.22	**0.01**
Triglyceride (mg/dl)	0.07	0.44	0.13	0.17	0.29	**0.0001**
HDL-c (mg/dl)	0.00	0.96	-0.05	0.63	0.03	0.76
LDL-c (mg/dl)	0.24	**0.01**	0.08	0.38	0.33	**0.0001**
OxLDL (mg/dl)	0.04	0.62	0.11	0.20	0.02	0.84
Image study:						
aIMT	0.11	0.36	0.09	0.47	0.16	0.18
cIMT	0.17	**0.04**	0.13	0.15	0.27	**0.0001**

BMI : body mass index, HBA1c : glycosylated hemoglobin, HDL-c : high density lipoprotein , LDL:low density lipoprotein, OxLDL: oxidized low density lipoprotein;cIMT: carotid intimal medial thickness;aIMT: aortic intimal medial thickness

Table 3 : Correlation between arm circumference , arm circumference / height ratio with demographic, laboratory data, carotid intimal medial thickness and resistivity index

Variables	**Midarm circumference**		**Midarm circumference/ height ratio**	
	r	**P-value**	**r**	**P-value**
Demographic data:				
Age (yrs)	0.04	0.75	0.04	0.73
Duration of disease (yrs)	0.13	0.29	0.13	0.28
Age of onset of disease (yrs)	0.11	0.37	0.11	0.37
Insulin dose (U/kg)	0.23	0.07	0.23	0.07
Blood pressure:				
Systolic blood pressure (mmHg)	0.20	0.11	0.19	0.11
Diastolic blood pressure (mmHg)	0.21	0.09	0.21	0.09
Anthropometric measurements:				
BMI (kg/m2)	0.18	0.15	0.18	0.15
Waist/ hip ratio	0.05	0.67	0.06	0.65
Waist/ height ratio	0.20	0.10	0.20	0.10
Laboratory data:				
HbA1c (%)	0.07	0.57	0.08	0.53
Albumin/ creatinine ratio (µg/ g creatinine)	0.13	0.37	0.18	0.21
Total cholesterol (mg/dl)	0.09	0.50	0.09	0.50
Triglyceride. (mg/dl)	0.11	0.41	0.11	0.41
HDL.-c (mg/dl)	0.01	0.95	0.01	0.94
LDL.-c (mg/dl)	0.15	0.29	0.15	0.29
OxLDL. (mg/dl)	0.01	0.92	0.01	0.91
Image study:				
aIMT .(mm)	0.08	0.50	0.08	0.50
cIMT.(mm)	0.25	**0.04**	0.25	**0.04**

BMI : body mass index, HBA1c : glycosylated hemoglobin, HDL-c : high density lipoprotein , LDL: low density lipoprotein, OxLDL: oxidized low density lipoprotein
cIMT: carotid intimal medial thickness, aIMT: aortic intimal medial thickness

Table 4: ROC curve of different anthropometric measurements and its relation to carotid intimal medial thickness

Variables	Cut off	Area under the curve	SE	95% Confidence intervals	Sensitivity	Specificity	+ LR	_ LR
BMI (kg/m²)	24.2	0.58	0.067	0.5 – 0.7	55.6	62.5	1.46	0.73
Waist / height ratio	0.48	0.66	0.065	0.57 – 0.74	36.1	91.7	4.33	0.70
Waist / hip ratio	0.9	0.60	0.066	0.51 – 0.68	59.6	66.7	1.76	0.61
Midarm circumference / height ratio	0.19	0.79	0.17	0.4 – 0.60	64.1	66.7	1.87	0.56

ROC curve: Receiver Operating Characteristic curve , BMI : Body mass index
+LR : Positive likelihood ratio, - LR: Negative likelihood ratio

DISCUSSION

Cardiovascular disease (CVD) is a risk factor for morbidity and mortality in type1 DM. Therefore, it is essential to recognize factors affecting subclinical atherosclerosis to be able to early diagnose, treat, and prevent the occurrence of CVD (Rosane et al.,2017) .

In the current study, diabetic patients had a significantly higher BMI, waist/ height ratio, HbA1c, albumin/creatinine ratio, lipid profile, aIMT and cIMT.

Atherosclerotic heart disease is a preventable disease. Primary prevention can occur when factors leading to disease are detected and eliminated. Therefore, early prediction by using non-invasive easy methods is crucial in diseases leading up to atherosclerosis, such as diabetes (Ersoy et al., 2015).

Risk factor of cardiometabolic disorder (hypertension, dyslipidemia, glucose intolerance and cardiovascular disease) is obesity. Abdominal obesity is markedly associated with risk of disease than general obesity. Previous studies revealed that waist circumference or waist-to-hip ratio as diagnostic of abdominal obesity, may be the best predictors of the risk of disease than the BMI, a predictor of general obesity (Yusuf et al., 2005; Pischon et al., 2008). Anuradha et al., (2013), revealed that several anthropometric and body composition measures were significant predictors of subclinical atherosclerosis, even after controlling for traditional risk factors. Although the gold standard definition of obesity is considered an excess of body fat (Physical status., 1995), clinicians and epidemiologists usually rely on BMI as a means of defining the presence of adiposity or obesity. BMI has shown many advantages as a surrogate for body fat mass, including simplicity and reproducibility. Epidemiologic studies have shown an association between extreme values of BMI and increased mortality (Pischon et al., 2008;Calle et al., 2003, Flegal et al.,2007, Whitlock et al., 2009).

A significant positive correlation of body mass index with age of patients, insulin dose/kg, waist to height ratio, blood pressure, LDL-c and cIMT was found in the present study.

The effect of obesity on atherosclerosis has generally been thought to be a result of associated risk factors, hypertension, diabetes, and high cholesterol. In our study, a positive correlation was found between waist to hip ratio and duration of the disease, insulin dose/kg, waist/ height ratio and urinary albumin/ .creatinine ratio. Also waist/ height ratio had a significant positive correlation with HbA1c, lipid profile and cIMT. This coincide with the result of Ferreira – Hermosillo et al., (2014), who reported that waist-to-height ratio (WHtR) is a better indicator of cardiac and metabolic risk factors. Midarm circumference and midarm / height ratio had a significant positive correlation with cIMT. Waist / height ratio had the best specificity for early diagnosis of atherosclerosis, on the other hand, midarm circumference / height ratio had the highest specificity.

Although BMI is useful for diagnosis of obesity, it can't differentiate between excess adiposity and muscle mass (Hall et al., 2008) and it cannot be used for diagnosis of abdominal obesity. Ferreira – Hermosillo et al., (2014), reported that the cut-off values used to diagnose obesity not useful for diagnosis of metabolic syndrome (MS). On the other hand, waist circumference (WC) can be used for diagnosis of abdominal adipose tissue and cardiovascular risk factors (Ness-Abramof et al., 2008). Waist circumference misdiagnose cardiac risk factors in patients with small stature, as it is important in many groups (Hsieh and Yoshinaga 1999). Highly sensitive screening tools are selected because of the reduced chance of false negative results and they are very useful when screening open populations. On the contrary, patients who need to be referred for further evaluation need a measurement of higher specificities (Ferreira-Hermosillo et al., 2014).

Accumulation of fat tissue in the Abdomen had an increased risk of atherosclerotic cardiovascular disease (CVD) (Nissen et al., 2008). Central obesity as a result of excess Visceral fat leads to metabolic disorders in the form of insulin resistance (Goodpaster et al., 2003; Tulloch-Reid et al., 2004; Wagenknecht et al., 2003), type 2 diabetes (Goodpaster et al., 2003; Boyko et al., 2000; Kanaya et al ., 2004), and metabolic syndrome (Lemieux et al., 2000). Anthropometric measurement is convenience , non-invasiveness and easy in clinical practice (Dahlén et al., 2013). The waist-to-height ratio (WHtR) is an important anthropometric index of central obesity that has no limitations of waist circumference (WC) (Ashwell et al., 2005). Because of the including of height into the ratio, any contribution of cardiometabolic risk by height is avoided. A prospective study (Ashwell et al., 2012) revealed that different measures of abdominal obesity [WHtR > WC > waist-to-hip ratio (WHR)] were strong predictors of stroke. WHtR is best than WC for diabetes, dyslipidaemia, hypertension and CVD risk in both sexes in populations of various nationalities and ethnic groups (Ashwell et al., 2012; Ren et al., 2014).

Previous studies reported that WHtR and WC were the best predictors of CVD, diabetes and related disorders (Browning et al., 2010). Gelber et al. (2008), reported that WHtR was severally associated with CVD, compared with WC, WHR and BMI. Anthropometric measurement is useful for early diagnosis and intervention of risk factors of CVD. cIMT is an early predictor of CVD (Bots et al., 2007; Williams et al., 2003) and BMI is recognized as an index of general fat distribution. Many previous studies (Kotsis et al., 2006; Bigazzi et al., 2006; Karason et al., 1999; Park et al., 2012) have shown the association between obesity and carotid atherosclerosis. However, studies evaluating the relationship between WHtR or VFA and cIMT are limited (Ren et al., 2014).

Waist to height ratio was reported to be the best measurement for diagnosis of obesity-related cardiometabolic risks compared with BMI by a systematic review and meta-analysis (Ashwell et al., 2012), and that WHtR is a more useful clinical screening method than WC (Browning et al., 2010).

CONCLUSION

We conclude that, waist/ height ratio, BMI, waist/ hip and midarm circumference/ height ratio are useful for early discovery of atherosclerosis in type 1 diabetic patients. waist / height ratio is the best anthropometric measurement for assessment of atherosclerosis and glycemic control in diabetic patients. Waist / height ratio had the best specificity for early diagnosis of atherosclerosis , on the other hand, midarm circumference / height ratio had the highest specificity.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

SMA, AAB, AEME put the design of the research and methodology. SMA and SAH choose the patients, collect the clinical data. AAB and AEME did all the image analysis. SMA did the statistics. All authors wrote the manscript , read it and approved the final version

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