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Original Research

Correlation between Measures of Obesity and Vascular Ageing in Type 2 Diabetics of Rural Regions of West India with Low Prevailing Obesity: A Pulse Wave Analysis Based Cross-Sectional Study

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Abstract

Background: Obesity and vascular ageing are two facets of type 2 diabetes (T2Ds) to study. The former can be studied by qualitative body fat analysis using bio-electrical impedance (BIA) and later with blood pressure by pulse wave analysis (PWA). We studied the association between BIA and PWA parameters in T2Ds.
Methodology: One hundred and fifty-six T2Ds on treatment were evaluated for BIA (Omron Karada Scan, China) and PWA (IEM, Stolberg, Germany). BIA parameters (weight, BMI, total body fat, visceral fat, subcutaneous fat, skeletal muscle mass) and PWA parameters (arterial stiffness, brachial haemodynamics, aortic blood pressures, central haemodynamics) were studied. Comparison, correlation, risk association, and predictions were done with a p-value < 0.05 as statistically significant.
Results: The mean age was 57.7 years, while the mean BMI was 22.8 kg/m2. The prevalence of hypertension was 50%, while the prevalence of glycaemic control was 10%. The correlation between BIA and PWA parameters in >75% instants was weak and insignificant (especially for aortic parameters and central haemodynamics). Female gender, BMI < 22.5 kg/m2, VF< 10, and low/normal TBF were associated with comparatively high PWA parameters, but inconsistently. High BMI or VF did not impose a significant Odds risk of high aortic pulse wave velocity or central pulse pressure. Visceral fat and aortic pulse wave velocities were not significantly predicted by blood pressure, BMI, and heart rate.
Conclusion: Among rural type 2 diabetics with a mean BMI of 22.8 kg/m2 and poor glycaemic control, there is largely a lack of association between obesity and vascular aging, suggesting differences in time course and pathology of the two entities in type 2 diabetics. Further studies are recommended.
Keywords: Arterial Stiffness; Body Mass Index; Pulse Wave Velocity; Type 2 Diabetes Mellitus; Visceral Fat.

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Introduction

Type 2 diabetes is taking a heavy toll across the globe with India being no different from the rest. Obesity and vascular ageing are two major issues [1] related to T2D. In T2D, obesity can be measured subjectively by body mass index (BMI) and other anthropometric parameters, but there are other objective measures to assess obesity like qualitative body fat analysis [2] that encompasses total body fat (TBF), visceral fat (VF), subcutaneous fat (SCF), and skeletal muscle mass (SKM). Tetrapolar bioelectric impedance (BIA) provides qualitative body fat analysis of these body fat parameters. In diabetics, the altered body composition must be assessed as a preventive measure beyond BMI, for which BIA is a good tool to explore. T2D also augments vascular ageing that can be measured beyond brachial blood pressure discrete parameters. Pulse wave analysis (PWA) provides an objective assessment of the following non-invasive vascular ageing parameters [3],[4], Arterial stiffness AS, brachial haemodynamics BH and central haemodynamics CH (ABC). Mobil-o-graph is one such cuff-based validated, objective, specific, and calibrated tool based on oscillometric PWA. In a recent study [5] in type 2 diabetics not receiving any anti-hypertensives, it was found that these ABC parameters of PWA are related to BMI. In more than 70% of diabetics in our region, hypertension co-exists [6] this justifies the inclusion of hypertensives in studies assessing qualitative body fat and arterial ageing. BMI is a measure of general adiposity which is found to be inferior to qualitative body fat in our type 2 diabetics as revealed by a study [7] as the change in the quality and not the quantity of body fat is what matters in T2D. Using BIA, a wider range of obesity assessments and PWA, a large spectrum of vascular ageing parameters can be derived. Such studies are sparse in the rural population of India with an expected lower prevalence of obesity and contrasting lifestyle. compared to urban dwellers. Following this background, this study aimed to study the correlation between these BIA-derived qualitative body fat parameters and ABC parameters of PWA in a sample rural population with T2D.

Methodology

Study design

A community-based cross-sectional observational study was carried out from January 2019 to April 2019 at a tertiary care teaching hospital in a city in west India.

Study sample

The sample size was calculated using the RaoSoft sample size calculator software, (Raosoft, Inc. free online software, Seattle, WA, USA). A sample of 156 was derived for the current population of a city of 2,000,000 and a prevalence of T2D of 7.33% in an urban area of our state at a 95% confidence interval.

Study subjects

After getting approval from the institutional review board and written informed consent from study participants, the study was carried out among under-treatment ambulatory type 2 diabetics. Subjects were recruited randomly from the medicine outpatient department of a tertiary care teaching hospital attached to the medical college.

Inclusion and exclusion criteria

We included subjects who gave informed consent with known type 2 diabetes, of age ≤ 75 years, of either sex, with or without hypertension, being treated as outdoor patients, taking regular treatment, and having known glycaemic control reports that were ready to give written informed consent. Subjects with known cardiac diseases, dehydration, renal disease, hepatic disease, cancer, indoor patients, and participants taking Insulin (due to complications of uncontrolled diabetes) were excluded. Of 171 participants, we excluded two participants due to an error in body fat analysis, four participants due to arm circumference beyond available cuff size, two participants due to irregular pulse recording, and seven participants due to poor quality of recorded pulse wave, resulting in a final sample of 156.

Research method

Subjects fulfilling the inclusion and exclusion criteria were enrolled for the study, following initial assessment in the form of written informed consent, personal history, disease history, anthropometric measurement, and recent glycaemic control reports. This was followed by body composition analysis and pulse wave analysis.
Body composition analysis was done using the method of previous [2], [7] studies)

A digital, portable noninvasive instrument Omron Karada Scan (Omron Karada Scan HBF-375 Body Fat Analyzer, Omron Health Care PvtLtd.Japan) working on the principle of tetra polar bio-electrical impedance (BIA) was used. The machine passes an electric current of 500 μA at a frequency of 5 kHz to scan the whole body to derive regional body composition. After entering age, gender, and height (taken by stadio-meter) the participants were allowed to stand on the instrument. We enrolled only ambulatory outdoor patients and took all readings in the morning to avoid dehydration and promote the accuracy of this method.

The body composition analysis parameters as used in previous studies [2],[7], included body weight, body mass index (BMI), total body fat (TBF), visceral fat (VF), subcutaneous fat (SCF) – whole body and regional, skeletal muscle mass (SKM)- whole body and regional.

Pulse wave analysis instruments and methods were used in previous [3], [4] studies and measured using a portable, personal computer-attached, validated, calibrated instrument called a Mobil-o-Graph (IEM GMBH, Stolberg, Germany). The Mobil-o-Graph measurement of PWA is based on the principle of oscillometric pressure PWA protocol as designed by the European Society of Hypertension. Pressure oscillations, generated by brachial arterial pulsation are transmitted to the brachial BP cuff and measured by a transducer that is fed into a microprocessor. The computerized PWA software records brachial pulse waves and by a validated generalized transfer factor, derives aortic (central) pulse wave. It further undergoes point-based and area-based PWA by computer software to derive various cardiovascular parameters.

The measurement protocol was based on the format of previous studies [3], [4]. Based on the measured mid-arm circumference, a BP cuff is chosen and applied to the left arm using a standard protocol. All readings were taken after 10 minutes of rest in the post-absorptive phase (at least 2 hours after the last meal) in a calm room without external influences and avoiding arm movement.

The pulse wave analysis parameters that were measured followed that of a previous study in T2Ds [5] and included Heart rate (HR), body mass index (BMI), body surface area (BSA), Brachial blood pressure (bBP)-systolic (bSBP), diastolic (bDBP), pulse (bPP) and mean (bMBP), central blood pressure (cBP) - systolic (cSBP), diastolic (cDBP), pulse (cPP)

The measured central hemodynamics parameters were cardiac output (CO), cardiac index (CI), and peripheral resistance (PR). The derived central hemodynamics included -

Stroke volume (SV) - cardiac output/heart rate

Stroke volume index (SVI) – stroke volume/ body surface area

Stroke work (SW) - (pulse pressure) x (stroke volume) x 0.0144

The measured arterial stiffness parameters were Augmentation pressure (AP), Augmentation index at HR 75/min (AIx@75), Reflection magnitude %, Aortic pulse wave velocity (aPWV)
The derived arterial stiffness parameters were
Total arterial stiffness (TAS) = pulse pressure /stroke volume
Pulse pressure amplification (PPA) = brachial to aortic pulse pressure

Defining cut-off norms

Glycaemic control was defined as per ADA guideline 2014 and fasting plasma glucose (FPG) <126 mg/dl was taken as current glycaemic control.

As per JNC 8 guidelines for the management of hypertension in adults [8], hypertension was defined as systolic blood pressure ≥ 140 and diastolic blood pressure ≥ 90 or the use of antihypertensive medications for 3 months.

For qualitative analysis, we defined standard norms [9] as (1) BMI ≤ 22.5, (2) VF ≤ 10, (3) total body fat (TBF), and skeletal muscle mass (SKM) as per standard guidelines based on age and gender.

Aortic PWV ≥ 10 m/s [10] and central PP ≥ 40[11] were taken as the positive (adverse) outcome for odds risk calculation.

Results

The T2D study group had equal representation of either gender and a mean BMI of 22.8 kg/m2, with half of the total cases having hypertension and the other half having their blood pressure controlled; and one out of 10 having current FPG-based glycaemic control. Females had higher TBF, and SCF while males had higher VF and SKM. As compared to males, females had higher SBP (both aortic and brachial), PP (both aortic and brachial), PPI (pulse pressure index), and HR while lower DBP (aortic and brachial), MBP, and RPP. Amongst AS parameters, females had higher AP, AIx, TAS, Ref (reflection magnitude), and PWV but only the first three parameters (list parameters here) showed statistical significance with the PPA comparable between groups. In CH parameters, females had higher CI, and SW but low SVI.

Table 1: Baseline and study parameters of the whole group and male versus female subgroups

Parameter	**Male (n=74)**	**Female (n=82)**	**P Value**	**Whole (n=156)**
Age, years	57.14±10.59	58.21±10.06	0.53	57.70±10.29
Height, Cm	168.46±2.18	165.88±3.82	***<0.0001****	167.1±3.40
Weight, Kg	70.21±12.84	58.37±11.10	***<0.0001****	63.99±13.31
Body mass index BMI, kg/m^2	24.70±4.38	21.10±4.73	***<0.0001****	22.81±4.90
Hypertension, +/-	36/38	51/31	0.11	87/69
Glycemic Control +/-	5/69	9/73	0.41	14/142
Blood pressure Control +/-	42/32	43/39	0.63	85/71
Body fat parameters, %				
Total body fat TBF	26.32±6.64	29.78±6.024	***0.003****	28.14±6.54

Visceral fat VF	11.48±5.96	5.20±3.56	***<0.0001****	8.19±5.76
Subcutaneous fat thorax SCT	16.59±4.69	20.76±5.925	***0.0013****	18.78±5.75
Skeletal muscle thorax SKT	21.92±3.89	19.98±2.78	***<0.0001****	20.90±3.48
Subcutaneous fat legs SCL	24.93±6.6	32.98±7.46	***<0.0001****	29.17±8.12
Skeletal muscle legs SKL	45.36±5.37	38.04±3.92	***<0.0001****	41.51±5.92
Subcutaneous fat arms SCA	25.76±7.37	38.81±8.036	***<0.0001****	32.62±10.10
Skeletal muscle arms SKA	35.10±3.18	28.58±4.98	***<0.0001****	31.68±5.33
SC WB	18.94±5.17	24.36±5.98	***<0.0001****	21.78±6.22
SK WB	29.42±3.34	26.05±2.705	***<0.0001****	27.65±3.46
bBP(mmHg)				
Systolic blood pressure SBP	134.43±19.15	138.1±20.66	0.21	136.4±19.98
Diastolic blood pressure DBP	89.40±11.46	85±11.44	***0.0157****	87.09±11.62
Mean blood pressure MBP	110.12±13.37	109.9±14.24	0.97	110.0±13.80
Pulse pressure PP	45.70±15.26	54.16±16.06	***0.0004****	50.15±16.19
Pulse pressure index PPI	0.33±0.07	0.39±0.07	***<0.0001****	0.36±0.08
Heart rate HR, bpm	85.70±15.13	88.21±14.78	0.37	87.02±14.96
RPP, mmHg. Bpm	115.35±27.02	121.39±24.8	0.13	118.5±25.99
Art stiffness				
AP, mmHg	8.43±7.22	13.44±8.61	***<0.0001****	11.06±8.34
Ref (%)	64.24±10.28	65.46±7.44	0.27	64.88±8.89
AIx@75 (%)	27.49±12.19	36.64±9.19	***<0.0001****	32.28±11.64
PWV, m/s	8.43±1.51	8.81±1.51	0.25	8.63±1.51
TAS, mL/mmHg	0.73±0.211	0.91±0.25	***<0.0001****	0.83±0.25
PPA	1.37±0.173	1.36±0.17	0.73	1.37±0.17
cBP (mmHg)				
cSBP	124.66±16.99	127.46±19.7	0.36	126.1±18.47

cDBP	90.85±11.82	86.85±11.56	***0.0346****	88.75±11.82
cPP	33.67±11.44	40.36±13.54	***0.0004****	37.19±12.99
Central Hemodynamics				
CO, L/min	5.31±1.012	5.16±0.74	0.66	5.23±0.88
PR, mmHg/ml	1.28±0.18	1.29±0.17	0.63	1.29±0.18
CI, L/min/m2	2.94±0.55	3.14±0.51	***0.0123****	3.05±0.54
SV, ml/beat	63.18±12.19	59.69±11.07	***0.0004****	61.35±11.71
SVI, ml/m2/beat	62.32±12.13	60.65±11.29	0.43	61.44±11.69
SW, g/beat	42.81±19.32	47.88±20.67	0.12	45.48±20.14

SC WB= subcutaneous fat whole body, SK WB=skeletal muscle whole body, RPP=rate pressure product, AP= augmentation pressure, Ref =reflection percentage, AIx@75=augmentation index at heart rate 75 beats per minute, PWV = pulse wave velocity, TAS= total arterial stiffness, PPA=pulse pressure amplification CO=cardiac output, PR=peripheral resistance, CI= cardiac index, SV=stroke volume, SVI= stroke volume index, SW=stroke work, '*' statistical significance.

The univariate correlation was checked between body fat parameters and PWA parameters. Brachial blood pressure, weight, BMI, and BSA correlated only with bDBP; VF correlated with bSBP, bDBP, bPP; SCF and SKM correlated with dBP.HR, bMBP, and RPP had no significant correlation with body fat parameters. Of AS parameters, except PPA, and Ref, most parameters correlated predominantly negatively and mostly significantly with body fat parameters except TBF. Among cBP only PP correlated significantly mainly with VF, SCF, and SKM. For central haemodynamics, most correlations were insignificant except with weight, BMI, VF; and SW with SCF, and SKM.

Table 2: Correlation between body fat measures and pulse wave analysis parameters (rvalues and in bracket p-value)

Parameters	**Weight**	**BMI**	**BSA**	**TBF**	**VF**	**SC WB**	**SK WB**
bBP							
bSBP	0.01 (0.86)	0.04 (0.63)	-0.02 (0.82)	0.09 (0.24)	0.16 ***(0.0451)****	-0.01 (0.90)	-0.14 ***(0.0771)****
bDBP	0.18 ***(0.0285)****	0.15 ***(0.0621)****	0.17 ***(0.0357)****	-0.01 (0.92)	0.18 ***(0.0241)****	-0.02 (0.83)	0.07 (0.36)
bMBP	0.09 (0.28)	0.10 (0.21)	0.11 (0.19)	0.07 (0.01)	0.06 (0.48)	0.14 (0.08)	-0.10 (0.22)
bPP	-0.12 (0.14)	-0.08 (0.32)	-0.14 (0.07)	0.12 (0.14)	-0.18 ***(0.0211)****	0.23 ***(0.0038)****	-0.23 ***(0.0046)****
HR	-0.03 (0.68)	-0.04 (0.63)	-0.06 (0.48)	-0.05 (0.55)	-0.08 (0.32)	-0.06 (0.47)	0.10 (0.22)
RPP	-0.04 (0.63)	-0.01 (0.98)	-0.08 (0.34)	0.02 (0.84)	-0.08 (0.30)	0.04 (0.65)	0.02 (0.80)
Arterial stiffness							

AP	-0.25 ***(0.0015)****	-0.21 ***(0.0077)****	-0.28 ***(0.0004)****	0.08 (0.33)	-0.32 ***(0.0001)****	0.21 ***(0.0074)****	-0.23 ***(0.0035)****
Aix@75	-0.24 ***(0.0031)****	-0.21 ***(0.0076)****	-0.28 ***(0.0003)****	0.06 (0.49)	-0.35 ***(<0.0001)****	0.15 (0.0558)	-0.16 ***(0.0407)****
aPWV	-0.19 ***(0.0158)****	-0.17 ***(0.0304)****	-0.15 (0.06)	0.12 (0.15)	-0.12 (0.1945)	0.08 (0.3420)	-0.28 ***(0.0005)****
Ref	-0.10 (0.23)	-0.08 (0.31)	-0.14 (0.0860)	-0.01 (0.9299)	-0.06 (0.49)	-0.02 (0.8304)	-0.06 (0.46)
TAS	-0.27 ***(0.0007)****	-0.24 ***(0.0029)****	-0.28 ***(0.0004)****	0.04 (0.59)	-0.38 ***(<0.0001)****	0.19 ***(0.0170)****	-0.18 ***(0.0285)****
PPA	-0.07 (0.36)	-0.06 (0.49)	-0.05 (0.50)	0.01 (0.92)	-0.07 (0.42)	0.05 (0.51)	0.01 (0.99)
cBP							
cSBP	0.07 (0.41)	0.08 (0.30)	0.06 (0.43)	0.11 (0.19)	0.03 ***(0.0378)****	0.16 (0.05)	-0.12 (0.12)
cDBP	0.15 (0.06)	0.13 (0.12)	0.14 (0.08)	-0.01 (0.87)	0.16 (0.05)	-0.03 (0.7222)	0.08 (0.32)
cPP	-0.08 (0.29)	-0.06 (0.47)	-0.12 (0.15)	0.13 (0.12)	-0.17 ***(0.0512)****	0.22 ***(0.0062)****	-0.23 ***(0.0036)****
Central hemodynamics							
CO	0.13 (0.10)	0.14 (0.08)	0.08 (0.31)	0.04 (0.59)	0.12 (0.14)	0.02 (0.80)	0.01 (0.99)
SV	0.17 ***(0.0350)****	0.19 ***(0.0192)****	0.13 (0.10)	0.06 (0.42)	0.19 ***(0.015)****	0.06 (0.48)	-0.06 (0.44)
PR	-0.04 (0.61)	-0.04 (0.61)	-0.01 (0.96)	0.02 (0.77)	-0.04 (0.63)	0.08 (0.33)	-0.06 (0.49)
SW	-0.03 (0.96)	0.03 (0.71)	-0.03 (0.76)	0.13 (0.10)	-0.03 (0.72)	0.20 ***(0.0142)****	-0.20 ***(0.0131)****

Abbreviations of parameters and units as per Table 1, '*' indicates statistical significance.

The subgroups stratified by BMI cut-off 23 had comparable BH, CH, and most AS but the group with BMI < 23 had significantly higher AP, Aix, PWV, and TAS than the one with BMI ≥ 23. In subgroups stratified by VF cut-off 10, the group with VF < 10 had significantly higher BP, HR, RPP, and AS than the one with VF ≥ 10.

Table 3: Comparison of AS, BH & CH of diabetics' subgroups, Stratified by BMI and visceral fat

Parameters	**BMI < 23 (n=79)**	**BMI ≥ 23 (n=77)**	**P value**	**VF < 10% (n=99)**	**VF ≥ 10% (n=57)**	**P Value**
bBP						
bSBP	137.34±21.19	135.44±21.19	0.88	137.3±20.45	112±41.16	***0.002****
bDBP	85.58±11.66	88.64±11.46	0.17	85.36	90.09	***0.0328****
bMBP	109.45±14.81	110.60±12.73	0.60	109.3±14.49	111.3±12.51	0.32
bPP	52.44±16.47	47.79±15.66	***0.082****	52.49±16.01	46.07±15.84	***0.0107****
HR	86.91±15.57	87.13±14.40	0.92	87.82±15.38	85.63±14.21	0.42
RPP	119.16±27.21	117.88±24.83	0.76	120.4±26.97	115.2±24.06	0.32

Arterial stiffness						
AP	12.81±9.37	9.27±6.72	***0.0037****	12.37±8.63	8.78±7.33	***0.0003****
Aix@75	34.27±11.43	30.22±11.56	***0.0197****	34.78±10.68	27.94±12.04	***0.0008****
aPWV	8.92±1.54	8.32±1.44	***0.0189****	8.71±1.58	8.50±1.39	0.47
Ref	65.93±9.27	63.80±8.40	***0.0698****	65.10±8.61	64.51±4.42	0.63
TAS	0.87±0.25	0.77±0.23	***0.0081****	0.88±0.26	0.73±0.20	***<0.0001****
PPA	1.36±0.17	1.36±0.17	0.78	1.37±0.16	1.36±0.17	0.44
cBP						
cSBP	126.68±20.42	125.57±16.34	0.82	126±19.62	125.9±16.44	0.83
cDBP	87.44±11.91	90.09±11.64	0.30	87.22±12.06	91.40±11.0	0.09
cPP	38.95±13.94	35.39±11.74	0.12	38.82±13.27	34.37±12.07	***0.0277****
Central hemodynamics						
CO	5.18±0.83	5.28±0.93	0.47	5.19±0.83	5.32±0.97	0.49
SV	61.01±12.03	61.70±11.43	0.71	60.28±11.33	63.21±12.22	0.21
PR	1.28±0.18	1.28±0.16	0.88	1.28±0.18	1.29±0.17	0.65
SW	47.21±20.61	43.70±21.61	0.26	46.61±19.78	43.52±20.79	0.29

Abbreviations of parameters and units as per Table 1, '*' indicates statistical significance.

T2Ds with low/normal TBF had more AS, and BH than those with TBF high/very high. Subgroups stratified by SKM had comparable BH, CH, and AS.

Table 4: Comparison of AS, BH & CH of diabetics' subgroups stratified by TBF, SKM

	TBF Low / Normal (n=77)	**TBF High/Very High (n=79)**	**P value**	**SKM Normal/ High (n=26)**	**SKM Low /Very Low (n=130)**	**P value**
bBP						
bSBP	138.3±20.67	134.2±19.04	0.20	135.9±19.35	150.8±34.12	0.38
bDBP	85.89±12.48	88.49±10.46	0.17	87.07±11.34	87.80±20.33	0.70
bMBP	110±14.96	110±12.40	0.97	109.8±13.33	116±25.50	0.64
bPP	53.8±15.88	46.72±15.99	***0.0048****	49.72±15.98	63±19.46	0.11
HR	88.00±15.45	85.88±14.38	0.38	86.97±14.71	88.60±23.42	0.91
RPP	121.3±25.79	115.3±26.02	0.15	118.2±26.15	128.8±19.87	0.31
Arterial stiffness						
AP	12.83±8.95	9±7.08	***0.0002****	11±8.33	13±9.43	0.62
Aix@75	35.14±11.05	28.94±11.49	***0.0008****	32.21±11.68	34.20±11.10	0.91
aPWV	8.82±1.54	8.41±1.45	0.09	8.63±1.51	8.48±1.54	0.69
Ref	66.01±8.19	63.57±9.58	0.09	65.07±8.96	59.4±3.20	*0.05*

TAS	0.89±0.27	0.75±0.81	***<0.0001****	0.82±0.24	1.03±0.31	0.08
PPA	1.36±0.16	1.37±0.19	0.95	1.36±0.17	1.48±0.14	0.08
cBP						
cSBP	127±19.92	124.8±16.62	0.49	125.9±18.01	132.2±31.73	0.76
cDBP	87.71±12.63	89.96±10.76	0.24	88.74±11.55	89.20±20.36	0.70
cPP	39.33±13.05	37.69±12.55	***0.0134****	37.00±12.94	43.00±14.76	0.37
Central Hemodynamics						
CO	5.20±0.80	5.275±0.97	0.98	5.23±0.89	5.3±0.76	0.84
SV	60.37±11.61	62.49±11.80	0.26	61.30±11.53	63.0±17.98	0.77
PR	1.29±0.19	1.29±0.16	0.96	1.29±0.17	1.36±0.27	0.94
SW	47.15±19.81	43.54±20.48	0.17	45.0±19.46	59.98±35.36	0.38

Abbreviations of parameters and units as per Table 1, '*' indicates statistical significance.

Neither BMI ≥ 23 nor VF ≥ 10 imposed significant odds risk of aPWV ≥ 10 or cPP ≥ 40.

Table 5: Association between high BMI ≥ 22.5 / VF ≥ 10 and high aPWV ≥ 10 / cPP ≥ 40 (odds risk OR with 95% confidence interval)

Parameter	**BMI ≥ 23**	**BMI < 23**	**P Value**	**O R**	**95 % CI**
aPWV≥ 10	09	19	0.06	0.42	0.18 - 0.99
aPWV< 10	68	60			
cPP ≥ 40	23	30	0.31	0.70	0.36 - 1.36
cPP< 40	54	49			
Parameter	**VF ≥ 10**	**VF < 10**	**P Value**	**O R**	**95 % CI**
aPWV≥ 10	7	22	0.14	0.49	0.19 – 1.23
aPWV< 10	50	77			
cPP ≥ 40	14	39	0.08	0.5	0.24 – 1.03
cPP< 40	43	60			

As per multiple linear regressions, age was a significant predictor for aPWV while age, height, and weight were significant predictors of VF.HR and BPs were not significant predictors for both.

Table 6: Multiple linear regression of VF and aPWV to find significant predictors ($r_{partial}$ and p-value)

	VF		**aPWV**	
	r	**P value**	**R**	**P value**
Age	0.06	***0.006****	0.11	***<0.0001****
Height	-0.15	***0.049****	-0.01	0.45
Weight	0.32	***<0.0001****	-0.01	0.92
BMI	0.20	0.19	-0.04	0.74
SBP	0.03	0.39	0.01	0.54

DBP	0.18	0.08	-0.02	0.49
MBP	-0.19	0.78	0.04	0.06
HR	0.01	0.36	-0.01	0.24
PP	0.01	0.80	0.01	0.40

Discussion

Obesity is a combination with diabetes as diabesity [12] that should be studied beyond BMI which has many issues of cut-off [13], [14] and limitation of inferring only generalized obesity [7]. Alike obesity, diabetes accelerates vascular ageing, but vascular ageing is studied in terms of late effects of incident hypertension and blood pressure and not aortic or central haemodynamics. Obesity and vascular ageing both are related to type 2 diabetes [15] and in one previous study [5], a correlation was found between BMI and vascular ageing parameters-ABC (arterial stiffness AS, brachial haemodynamics BH and central haemodynamics CH). Adiposity measurements were extended to qualitative body fat (QBF) analysis to correlate it with ABC parameters of PWA in type 2 diabetics.

The gender-wise difference in the distribution of body fat and vascular ageing was found. Among body fat parameters body mass index, visceral fat, and skeletal muscle mass were higher in males while total body fat and subcutaneous fat were higher in females. This pattern of gender-based differences is in line with other [16],[17] Asian studies. Similarly, gender differences were observed for ABC parameters of PWA in line with previous [3],[4],[5],[18],[19],[20] studies. This reaffirms gender as a strong factor affecting adiposity and hence its aftermaths like cardiovascular ageing in type 2 diabetics.

At more than three fourth instances, QBF with PWA correlation for various study parameters was weak and insignificant. This contrasts with others [15],[20],[21],[22],[23],[24] who found significant correlation between these two studied parameters. Among ABC parameters, it was weakest for CH, followed by BH but strongest for AS parameters. This indicates AS to be a better correlate for body adiposity than haemodynamic parameters especially central and suggests adiposity as a confounder for AS parameters though not as strong as age or gender. In contrast to the literature [15],[25] and our previous study [5] on type 2 diabetics, BMI < 22.5 was weakly associated with more adverse profile of ABC parameters of PWA than BMI ≥ 22.5. Similarly, visceral fat < 10 or total body fat less than normal was weakly associated with higher PWA parameters than visceral fat ≥10 or total body fat high to very high. BMI, VF, and TBF were thus anomalously associated with vascular ageing as studied by PWA. It was further reinforced as an insignificant odds risk for abnormal PWV or cPP by high BMI or VF, as studied using standard cut-offs. Apart from gender, age was only a common significant associate of both VF (most important body fat parameter) and aPWV(most important vascular ageing parameter) and both these were independent of conventional risk factors brachial haemodynamics, duration of disease, and glycaemic control. So, the addition of VF and aPWV gives better risk stratification for cardiovascular health and can be explored further in diabetics beyond mere BMI or brachial blood pressure.

This lack of significant correlation between obesity (as stratified by QBF) and vascular ageing (as reported by ABC parameters of PWA) in chronic type 2 diabetics is in contrast to our previous studies done in type 1 diabetics [26], type 2 diabetics[5], hypertensives[19] and postmenopausal normal women[18]. Possible causes could be 1) the use of beyond BMI study of adiposity as compared to BMI-based studies, 2) the mean BMI was 22.8 which is near the BMI cut of 22.5 indicating that nearly half of the cases had to have BMI near normal, and representation of obese diabetics was less and same can be further studied by choosing group with higher BMI and more severe grades of obesity, 3) use of first-line antihypertensives in many participants, irrespective of class difference[27] can modify PWA parameters to obscure its association with obesity and that can be rectified by a study on Normotensive type 2 diabetics not taking anti-hypertensives. 4) Glycemic control was poor and only 10% had it controlled indicating flaring of effects of type 2 diabetes that affects body fat beyond BMI[24], 5) Indian ethnicity[9] is offering risk of diabetes at lower BMI and

high prevalence of cardiovascular disease in diabetics,6) as per our previous PWA based studies[29],[30] in young aged normal individuals with a family history of diabetes or hypertension, vascular ageing was reported to get amplified even before incident hypertension or diabetes so obesity and vascular ageing may not run the same course and association may be difficult to explain with incident diabetes associated with hypertension in the majority.

There is a surge of non-communicable diseases especially in India [31] with a lack of studies regarding novel risk factors like arterial stiffness and qualitative body fat. Visceral fat is known to lead to insulin resistance, diabetes, arterial stiffness, and hypertension [18] and central obesity is responsible for cardiac remodeling [19] which has an abnormal impact on cardiovascular health. Yet in chronic diabetics, we found a lack of strong association between obesity the forerunner of diabetes, and arterial stiffness the forerunner of hypertension. This suggests different courses of both parameters studied and the fact that they can complement each other together inferring g about different aspects of health. However, vertical studies are needed for studying this association of vascular ageing with obesity over a while from pre-diabetes to diabetes to hypertension, that too in populations with optimum glycaemic and pressure control. As our study population had mean BMI on lower scales of adiposity, it will also be interesting to study the same relation in moderate to severely obese and how it is modified by weight reduction or blood pressure control in diabetics.

The study had its limitations like its transverse nature, baseline data, a small representation of severely obese, and unavailability of HbA1c and other biomarkers of vascular ageing and obesity. It also suffers limitations of lack of adjustment for food intake patterns, sleep quality, tobacco chewing, and other unknown confounders.

Conclusions

Among type 2 diabetics from rural populations with a mean BMI of 22.8kg/m2 and poor glycaemic control, there is largely a lack of association between obesity measured by qualitative fat analysis and vascular ageing measured by pulse wave analysis. It suggests differences in time course and pathology of these two associates of type 2 diabetics and the use of both together supplementing each other inferring about two different aspects of health. It also warrants further study with large-scale, baseline data and follow-up to ascertain the exact relationship between obesity and vascular ageing in type 2 diabetics.

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