Original Article

Effect of Gender on Cardiovascular and Metabolic Risk Profile in Young Adult Indian Population

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Abstract

Background and Aim: Gender difference has been documented in the cardiovascular (CV) morbidity and mortality associated with obesity. Therefore, the aim of the present study was to determine the gender difference in CV and metabolic risk profile in apparently healthy young adult preobese and obese individuals. **Methods:** Obesity indices, body composition, blood pressure variability, and autonomic function test parameters were recorded in 270 individuals divided into control (male n = 43; female n = 47), preobese (male n = 48; female n = 42), and obese (male n = 44; female n = 46) groups. Homeostatic model assessment-insulin resistance, atherogenic index, leptin, adiponectin, and inflammatory and oxidative stress parameters were measured. The gender difference in CV and metabolic profile between the control, preobese, and obese groups was performed by one-way ANOVA. **Results:** The abdominal adiposity was more in females as compared to males in both preobese and obese individuals. However, the increased CV risk (decreased heart rate variability) was observed in obese male compared to obese female individuals, which is supported by the increased inflammatory profile (increased interleukin-6) in males compared to females. There was no much gender difference in most of the CV and metabolic parameters in control, preobese, and obese individuals. **Conclusion:** In the present study, we could not assess much difference in gender between the preobese and obese groups as CV risks and metabolic derangements have not been significantly established in these younger individuals who were in their early phases of preobesity and obesity.

Keywords: Cardiovascular risks, gender, metabolic profile, obesity, preobese, sympathovagal imbalance

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Introduction

Prevalence of obesity is globally amplified with about 38% (2.1 billion) of world's population being either overweight or obese.[1] India ranks third among the global capitals of obesity.[1] Chronic obesity has been observed to be associated with adverse cardiovascular (CV) events.[2,3] Recently, it has been reported that even a mild increase in body weight (BW) is progressively associated with the increase in the incidence of heart failure.[4] Several studies have reported gender difference in metabolic responses to dietary challenges, weight gain, weight loss, and pharmacological interventions.[5,6] Moreover, it has also been documented that the CV morbidity and mortality associated with obesity is gender dependent.[7,8]

Obesity has been reported to increase sympathetic activity, which is established to be the major pathophysiological mechanism for CV morbidities in this condition.[9,10] Sympathovagal imbalance (SVI) in the form of sympathetic overactivity and vagal inhibition[10-12] and established CV risks such as insulin resistance, retrograde inflammation, dyslipidemia, and oxidative stress have been reported in preobesity and obesity.[13-15] However, the contribution of gender on SVI, CV, and metabolic risk profile has not been studied yet. Further, to the best of our knowledge, no study has assessed the association of SVI to CV risk in preobesity and

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obesity. Therefore, in this study, we have analyzed the gender difference in SVI and cardiometabolic risks in preobese and obese Indian population.

Materials and Methods

Subjects

This is a cross-sectional study conducted in the Department of Physiology, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India. After obtaining approval of the project plan from Research and Ethics Committees of JIPMER, 223 healthy young adults aged between 18 and 40 years were recruited from the Medicine Outpatient Department, JIPMER. Height and weight were measured to calculate body mass index (BMI). Based on the BMI classification of WHO for Asian population,[16] these individuals were divided into following three groups:

- Control group: Normal healthy individuals having BMI 18.5–22.9 (*n* = 72)
- Preobese group: Healthy individuals having BMI 23–27.4 (*n* = 77)
- Obese group: Healthy individuals having BMI 27.5 or above (*n* = 74).

Written informed consent was obtained from all the participants before initiation of the study. A brief medical and personal history was obtained from the individuals. Individuals on antihypertensive therapy or receiving any medication, with history of smoking and/or alcoholism, with acute or chronic ailments and known cases of diabetes mellitus, hypertension, cardiac diseases, kidney disease, or any endocrinal disorder were excluded from the present study. As the level of physical fitness is a major determinant of vagal tone, individuals performing regular athletic activities, body-building exercises, and yoga[17,18] were also excluded from the study.

Brief procedure

All the participants reported to the polygraph laboratory between 8.30and 10.30 am while they were fasting.

Obesity indices

For anthropometric measures, all the individuals were assessed with barefoot and minimal clothing. Height was measured to the nearest millimeter by a wall-mounted stadiometer and weight was measured with a digital weight balance to the nearest 0.1 kg. Waist circumference (WC) was measured as the circumference of the abdomen at its narrowest point between the lower costal (10th rib) border and the top of the iliac crest. BMI was calculated using the formula weight in kilograms divided by square of height in meters. Obesity indices such as waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) were also calculated as described previously.[19]

Autonomic functions tests

Following 10 min of supine rest in polygraph laboratory (room temperature maintained at 25°C), the spectral analysis of heart rate variability (HRV) and the conventional autonomic function tests (CAFTs) were recorded.

Baseline cardiovascular parameters

After 10 min of supine rest, baseline CV parameters were recorded by oscillometric method using automated blood pressure (BP) monitor Omron MX3 (Omron Healthcare Co. Ltd, Kyoto, Japan). Rate pressure product (RPP), a determinant of myocardial oxygen consumption and workload, was calculated using the formula, RPP = (basal heart rate [BHR] × systolic BP [SBP]) $\times 10^{-2}$.[20] Mean arterial pressure (MAP) was calculated.

Continuous beat-to-beat blood pressure variability parameters

The baroreflex sensitivity (BRS) and other CV parameters such as BHR, SBP, diastolic BP (DBP), MAP, RPP, interbeat interval, left ventricular ejection time (LVET), stroke volume (SV), cardiac output, and total peripheral resistance (TPR) were measured by continuous BP variability method using Finapres (Finometer version 1.22a; Finapres Medical Systems BV, Amsterdam, the Netherlands). It is a noninvasive continuous hemodynamic CV monitor based on the principle of measurement of finger arterial pressure with the volume clamp technique of Penaz and the physical criteria of Imholz *et al*.[21] In this method, the brachial artery pressure measured was the reconstructed pressure from the finger pressure estimated by generalized waveform inverse modeling and generalized level correction. The individuals were asked to lie down, the brachial cuff of Finapres was tied around the midarm about 2 cm above the cubital fossa, and the finger cuff of either the small, medium, or large size was tied around the middle phalanx of the middle finger depending on the finger width. For the height correction, two sensors were placed, one at the heart level and another at the finger level. The recordings were obtained after connection of cables of the cuffs to the Finometer after 10 min of supine rest. The reconstructed brachial pressure was acquired by a PC-based data acquisition system (Finapres Medical Systems BV).

Recording and heart rate variability

For recording of short-term HRV, recommendation of the Task Force on HRV was followed.[22] For this purpose, electrocardiogram (ECG) electrodes were connected and Lead II ECG was acquired at a rate of 1000 samples/second during supine rest using BIOPAC MP 100 data acquisition system (BIOPAC Inc., USA). The data were transferred from BIOPAC to a Windows-based PC with Acqknowledge software version 3.8.2. Ectopics and artifacts were removed from the recorded ECG. RR tachogram was extracted from the edited 256 s ECG using the R-wave detector in the Acqknowledge software and saved in ASC-II format, which was later used offline for short-term HRV analysis. HRV analysis was done using the HRV analysis software version 1.1 (Biosignal Analysis group, Finland). Mean RR was measured in second (s). Variance, defined as power in a portion of the total spectrum of frequencies, was measured in milliseconds squared (ms^2). Different frequency domain indices such as total power (TP), low-frequency (LF) component expressed as normalized unit (LFnu), high-frequency (HF) component expressed as normalized unit (HFnu), and LF/HF ratio and

time domain indices (TDI) such as mean RR, square root of the mean squared differences of successive normal to normal intervals (RMSSD), standard deviation of normal to normal interval (SDNN), the number of interval differences of successive NN intervals <50 ms (NN50), and the proportion derived by dividing NN50 by the total number of NN intervals (pNN50) were recorded.

Other autonomic functions tests

Three CAFTs were performed following the standard procedures.[23]

Lying to standing test

In this test, heart rate (HR) and BP response to standing were assessed. The BP and ECG were recorded in the supine position. The subject was instructed to attain standing posture in 3 s. The ECG was continuously recorded during the procedure. The BP was recorded every 40 s by automatic BP monitor (Omron, SEM-1, Kyoto, JAPAN) till 5th min. 30:15 ratio (ratio of maximum RR-interval at 30th beat to minimum RR interval at 15th beat following standing) was calculated.

Deep breathing test

In sitting posture, the HR and respiration monitoring was done from ECG recording and stethographic respiratory tracings were recorded on the polygraph (Nihon-Kohden, UK). A baseline recording of ECG and respiration was taken for 30 s. The individual was asked to take slow and deep inspiration, followed by slow and deep expiration such that each breathing cycle lasted for 10 s, consisting of six breathing cycles per minute. E:I ratio (ratio of average RR interval during expiration to average RR interval during inspiration in six cycles of deep breathing) was calculated from ECG tracing.

Isometric handgrip test

The baseline BP was recorded. The individual was asked to press handgrip dynamometer at 30% of maximum voluntary contraction for 2 min. The BP was recorded at 1st min and 2nd min of contraction. $DDBP_{IHG}$ (maximum rise in diastolic BP above baseline) was noted.

Assessment of body composition

Body composition was determined by bioelectrical impedance analysis (BIA), a method which involves the measurement of bioelectrical resistive impedance (R). This method is regarded as safe and reliable[24] and based on the principle that the electrical conductivity of the fat-free tissue mass is far greater than that of fat. Measurements at 5/50/100/200 kHz were obtained using the multiple frequency BIA instrument Bodystat® (Model QuadScan 4000®, Isle of Man, United Kingdom).[25,26] Individuals were instructed to avoid eating or drinking for 4 h before the test and to avoid exercise and alcohol for 24 h before the test. Individuals were placed in the supine position with no parts of the body touching another for at least 10 min in standardized conditions (quiet environment and ambient temperature). The electrodes were placed on the dorsal surfaces of the hand and foot proximal to metacarpal-phalangeal and metatarsal-phalangeal joints, respectively. BIA included body fat (BF), lean body mass, body cell mass (BCM), total body water (TBW), intracellular water (ICW), and extracellular water (ECW). The current range of 50–100 kHz displays BF, BF mass %, BF mass index (BFMI), lean body mass, basal metabolism (BM), and activity metabolism (AM).

Measurement of biochemical parameters

Ten milliliters of fasting blood sample was collected. Fasting blood glucose (FBG) was estimated by colorimetric, enzymatic method with glucose oxidase and peroxidase, (Genuine Biosystem; Chennai). Insulin was measured using enzyme linked immunosorbent assay (ELISA) (Dia.Metra, Italy). For determination of insulin resistance, homeostatic model assessment-insulin resistance (HOMA-IR) was calculated (HOMA-IR = FBG [mMol] × insulin [μIU/L]/22.5), and for insulin sensitivity, HOMA 2%S was calculated using HOMA2 computer model, which takes into account variations in hepatic and peripheral glucose resistance.[27] Lipid profiles such as total cholesterol (TC), triglycerides (TG), high-density lipoproteins (HDL), serum total proteins, serum albumin, and globulin were assessed using fully automated analyzer (AU400, Olympus, USA). Low-density lipoproteins (LDLs) and very LDL (VLDLs) were calculated using Friedewald equation. Atherogenic index (AI) was calculated using the formula: $AI = (TC - HDL)/HDL$.

ELISA was used for the quantification of high-sensitive C-reactive protein (hsCRP) using the commercial kits available from Diagnostics Biochem Canada Inc., Canada. Interleukin-6 (IL-6), tumor necrosis factor-α (TNFα), leptin, and adiponectin were estimated using ELISA kits from Orgenium, Tiilitie, Finland.

Oxidative stress was assessed by estimating thiobarbituric acid reactive substance (TBARS) using ELISA kit (Cayman Chemical Co., Ann Arbor, Michigan).

Statistical analysis

SPSS version 13 (SPSS Software Inc., Chicago, IL, USA) was used for statistical analysis. All the data were presented as mean ± standard deviation. Normality of data was tested by Kolmogorov– Smirnov test. The level of significance between the groups was tested using one-way ANOVA and *post hoc* by Tukey-Kramer test. $P < 0.05$ was considered statistically significant.

Results

The mean age did not differ significantly between the control (male $n = 43$; female $n = 47$), preobese (male $n = 48$; female $n = 42$), and obese (male $n = 44$; female $n = 46$) groups [Table 1].

The BW was significantly more in males than females in all the three groups. However, the BMI was not different between the male and female individuals across the control, preobese, and obese groups [Table 1].

Table 1: Age and anthropometric indices of individuals of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (*n*=43)	Female (*n*=47)	Male (*n*=48)	Female (*n*=42)	Male (*n*=44)	Female (*n*=46)
Age (years)	29.56±6.17	27.51±8.71	30.58±8.98	28.68±7.54	28.15±9.26	30.37±5.99
BW (kg)	59.94±6.23	49.87±5.15***	69.51±6.14	61.92±6.03***	80.71±10.83	72.16±5.72***
BMI (kg/m2)	20.98±1.22	20.70±1.78	25.72±1.22	25.30±1.26	31.11±2.40	30.30±2.46
Circumferences						
NC (cm)	30.20±1.99	30.63±3.05	32.72±4.46	35.19±3.77*	35.20±4.50	36.28±3.25
WC (cm)	80.78±6.00	79.61±6.62	85.05±6.46	86.48±8.67	91.23±7.48	96.16±8.47***
WHR	0.85±0.06	0.82±0.07	0.89±0.07	0.86±0.08	0.95±0.08	0.92±0.06
WHtR	0.47±0.04	0.51±0.04***	0.50±0.04	0.55±0.06***	0.56±0.05	0.59±0.04***
Chest (cm)	84.87±3.28	76.22±13.14***	90.58±11.62	87.98±8.67	91.28±11.49	88.06±4.57
MAC (cm)	27.34±1.69	25.46±9.29	28.68±2.51	31.66±1.98*	31.11±2.11	32.58±2.63
MCC (cm)	31.98±1.83	30.96±3.57	34.40±2.74	35.62±1.79	36.96±2.20	37.64±2.60
CI	1.18±0.08	1.20±0.09	1.22±0.07	1.27±0.12	1.29±0.09	1.33±0.11**
Biepicondylar distance						
Humerus (mm)	6.77±0.28	5.73±0.39***	7.04±0.73	7.18±1.30	7.11±1.24	7.73±1.13**
Femur (mm)	9.17±0.39	8.32±0.42***	9.34±0.49	8.94±0.69***	9.66±0.42	9.18±0.53***
Skinfold thickness						
Biceps (mm)	19.82±9.79	18.94±7.74	25.58±9.94	27.17±7.92	32.87±8.74	33.55±6.71
Triceps (mm)	24.92±7.20	24.69±6.41	31.48±5.95	32.26±6.06	37.51±4.72	38.14±6.15
Subscapular (mm)	26.16±8.75	26.43±8.54	30.45±7.23	33.11±7.13	40.68±8.94	40.94±7.63
Suprailiac (mm)	18.51±7.28	20.92±5.70	28.00±5.99	26.02±7.30	32.46±7.79	31.55±7.29
Lateral abdomen (mm)	28.83±11.04	28.55±7.80	38.94±7.25	35.85±9.71	43.13±7.98	43.02±7.05
Anterior thigh (mm)	41.26±13.69	41.09±10.82	45.77±11.02	48.73±7.89	52.46±8.68	54.52±7.38
Medial-calf (mm)	16.57±5.92	22.72±5.01***	24.41±6.65	27.10±5.46	31.56±9.23	31.86±6.03

The values are expressed as mean±SD, statistical analysis was done by one-way ANOVA. The $P<0.05$ was statistically considered significant. The * mark indicates comparison between the male and female group: *$P<0.05$, **$P<0.01$, ***$P<0.001$. BW: Body weight, BMI: Body mass index, NC: Neck circumference, WC: Waist circumference, WHR: Waist-to-hip ratio, WHtR: Waist-to-height ratio, MAC: Mid-arm circumference, MCC: Mid-calf circumference, SD: Standard deviation, CI: Conicity index

Neck circumference (NC) was not significantly different between male and female individuals in the control group [Table 1]. In preobese group, the NC was significantly high in female compared to males, but this gender difference was not observed in obese group [Table 1]. The WC was not significantly different between male and female individuals in the control and preobese groups, whereas in obese group, the WC was significantly higher in females compared to males [Table 1]. WHR was not significantly altered between males and females across three groups [Table 1]. However, the WHtR was significantly high in females than their male counterparts across the three groups [Table 1]. The chest circumference was significantly high in males compared to females in the control group, but such gender differences were not observed in preobese and obese groups [Table 1]. Mid-arm circumference (MAC) was not significantly different between male and female individuals in the control group [Table 1]. In preobese group, the MAC was significantly high in female compared to males, but this gender difference was not observed in obese group [Table 1]. Mid-calf circumference was not significantly altered between male and female across the three groups [Table 1]. The confidence interval (CI) was not significantly different between male and female individuals in the control and preobese groups, whereas in obese group, the CI was significantly higher in females compared to males [Table 1].

The biepicondylar humerus distance was higher in males compared to females in the control, and such gender difference was not observed in preobese group. However, in the obese group, females had higher biepicondylar humerus distance than the males [Table 1]. The biepicondylar femur distance was higher in males compared to females across the three groups [Table 1]. The skinfold thickness (SFT) at different anatomical sites such as biceps, triceps, subscapular, suprailiac, lateral abdomen, and anterior thigh was not significantly altered between male and female across the three groups [Table 1]. The medial calf SFT in females was significantly higher than males in the control group, whereas such gender difference was not observed in preobese and obese groups [Table 1].

BF and BFMI were significantly high in females compared to their male counterparts in all the three groups [Table 2]. However, the other body composition indices (except ECW) such as fat-free mass (FFM), FFM index, dry lean, BCM, TBW, and ICW were significantly high in males compared to female counterparts in all the three groups [Table 2]. Metabolic indices such as BM and AM were significantly high in males than the females in control, preobese, and obese

groups [Table 2]. However, BM/BW was significantly reduced in females compared to their male counterparts in all the three groups [Table 2].

BHR, SBP, and RPP were not significantly different between the male and female in the control, preobese, and obese groups [Table 3]. DBP was significantly high in males compared to females in the control group, but such gender difference was not observed in preobese and obese groups [Table 3]. The other BP variability parameters such as SV, cardiac output, LVET, TPR, and BRS were not significantly altered between the genders in the control, preobese, and obese groups [Table 3].

There was no significant difference in TP between male and females in the control and preobese groups [Table 4]. However, in the obese group, TP was significantly reduced in males compared to females [Table 4]. Further, the LFnu was significantly higher and HFnu was significantly less in males compared females in the control group [Table 4]. However, such gender difference was not seen in preobese and obese groups [Table 4]. LF:HF ratio was not significantly altered between male and female across three groups [Table 4]. All the TDIs of HRV such as RMSSD, SDNN, NN50, and pNN50 were not significantly decreased in males compared to females in all the three groups [Table 5]. The CAFT parameters such as 30:15 ratio, E:I ratio, and ΔDBP_{IHG} were not significantly altered between the genders across the control, preobese, and obese individuals [Table 6].

The FBG, insulin concentration, and HOMA-IR were not significantly altered in males compared to females in control, preobese, and obese groups [Table 7]. HOMA β was significantly less in males compared to their female counterparts in all the three groups [Table 7]. HOMA 2%S was significantly more in males compared to their female counterparts in control

Table 2: Body composition indices of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (*n*=43)	Female (*n*=47)	Male (*n*=48)	Female (*n*=42)	Male (*n*=44)	Female (*n*=46)
BF (%)	15.97±3.63	25.24±5.62***	19.70±6.24	28.91±8.30***	22.27±4.96	28.15±8.46***
FFM (%)	84.26±3.63	74.76±5.31***	79.38±7.71	70.45±11.93***	79.24±11.32	68.59±8.45***
Dry lean (kg)	13.82±3.85	10.48±2.36***	16.01±3.79	13.44±3.62**	20.01±3.86	14.24±2.55***
BCM (kg)	28.39±3.04	19.87±4.29***	28.95±3.54	24.80±4.74***	33.36±4.34	26.24±3.38***
TBW (%)	61.83±4.76	54.13±4.19***	55.25±5.34	50.48±5.13***	54.42±4.65	48.29±5.38***
ECW (%)	26.39±1.81	25.42±1.65	24.27±1.78	23.14±1.75	24.56±8.51	22.68±2.07
ICW (%)	34.52±2.50	27.44±2.91***	30.67±3.88	27.23±3.29***	31.04±2.45	26.32±2.68***
BM (kcal/day)	1524.26±197.19	1323.89±108.89***	1734.88±200.23	1474.11±192.74***	1887.14±229.17	1566.11±258.64***
BM/wt (kcal/kg)	26.43±1.12	25.57±1.35*	25.02±1.64	23.81±1.98*	23.39±1.51	21.73±2.36***
AM (kcal/day)	2199.60±589.43	2023.89±190.95	2592.98±299.19	2186.00±295.74***	2785.50±361.74	2336.05±221.90***
BFMI	2.92±0.94	5.27±1.24***	4.87±2.11	7.03±2.74***	5.10±1.74	8.35±3.03***
FFMI	16.43±1.64	14.83±1.08***	18.68±1.92	17.53±1.72*	21.27±1.68	19.61±2.36***

The values are expressed as mean±SD; statistical analysis was done by one-way ANOVA. The $P<0.05$ was statistically considered significant. The * mark indicates comparison between the male and female group: *$P<0.05$, **$P<0.01$, ***$P<0.001$. BF: Body fat, FFM: Free fat mass, BCM: Body cell mass, TBW: Total body water, ECW: Extracellular water, ICW: Intracellular water, BM: Basal metabolism, BM/Wt: Basal metabolism to body weight ratio, AM: Activity metabolism, BFMI: Body fat mass index, FFMI: Free fat mass index, SD: Standard deviation

Table 3: Blood pressure variability parameters of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (*n*=43)	Female (*n*=47)	Male (*n*=48)	Female (*n*=42)	Male (*n*=44)	Female (*n*=46)
BHR (/min)	72.08±9.43	68.106±9.77	76.05±8.55	74.67±12.30	78.94±11.92	78.70±7.93
SBP (mmHg)	107.97±5.40	105.69±8.32	113.89±8.03	109.93±8.29	121.64±8.09	117.95±10.48
DBP (mmHg)	70.41±7.75	64.27±5.79**	74.40±5.56	72.02±7.63	80.16±7.98	80.03±9.30
RPP (mmHg/min)	77.82±10.58	71.93±13.12	86.61±16.67	82.08±11.67	96.02±16.22	92.83±18.55
SV (mL)	68.54±14.21	67.06±13.12	76.05±11.92	73.47±17.64	89.41±15.55	81.08±18.05
CO (L/min)	4.94±1.67	4.56±1.14	5.78±1.30	5.48±1.82	7.05±1.84	6.38±1.68
LVET (ms)	203.51±66.84	197.81±76.22	272.95±78.05	251.89±102.31	305.33±44.56	299.91±55.99
TPR (mmHg/min/L)	0.84±0.15	0.85±0.19	1.11±0.31	1.05±0.32	1.12±0.45	1.12±0.68
BRS (ms/mmHg)	28.62±7.12	0.24±12.96	20.76±9.91	22.98±10.15	14.53±6.30	15.02±6.27

The values are expressed as mean±SD; statistical analysis was done by one-way ANOVA. The $P<0.05$ was statistically considered significant. The * mark indicates comparison between the male and female group: *$P<0.05$, **$P<0.01$, ***$P<0.001$. BHR: Basal heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, RPP: Rate pressure product, SV: Stroke volume, CO: Cardiac output, LVET: Left ventricular ejection time, TPR: Total peripheral resistance, BRS: Baroreceptor sensitivity, SD: Standard deviation

Table 4: Frequency domain indices of heart rate variability indices of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (*n*=43)	Female (*n*=47)	Male (*n*=48)	Female (*n*=42)	Male (*n*=44)	Female (*n*=46)
TP (ms^2)	918.82±364.74	992.68±462.17	876.13±308.14	799.54±186.06	469.53±201.58	664.00±198.52*
LFnu	45.01±15.31	33.98±15.57*	56.94±18.07	48.71±15.20	63.95±13.43	57.31±16.8
HFnu	54.80±15.31	66.25±15.57*	43.06±18.07	51.29±15.20	36.06±13.45	42.68±16.86
LF:HF	0.67±0.43	0.64±0.38	1.16±0.72	1.04±0.65	1.63±0.71	1.49±0.68

The values are expressed as mean±SD; statistical analysis was done by one-way ANOVA. The *P*<0.05 was statistically considered significant. The * mark indicates comparison between the male and female group: **P*<0.05, ***P*<0.01, ****P*<0.001. TP: Total power, LFnu: Normalized low-frequency component, HFnu: Normalized high-frequency component, LF: HF: Ratio of the low-frequency component to the high-frequency component of HRV, SD: Standard deviation, HRV: Heart rate variability

Table 5: Time domain indices of heart rate variability indices of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (*n*=43)	Female (*n*=47)	Male (*n*=48)	Female (*n*=42)	Male (*n*=44)	Female (*n*=46)
RMSSD (ms)	64.96±26.38	69.87±42.60	46.24±27.84	50.09±18.74	36.83±21.20	40.88±16.62
SDNN (ms)	56.98±20.72	58.87±21.55	37.24±14.62	42.05±18.41	36.03±9.47	41.23±18.44
NN50	75.37±26.90	81.63±34.11	64.87±25.38	72.90±28.18	55.85±32.38	59.89±24.85
pNN50 (%)	29.15±11.86	31.81±17.72	20.71±11.96	26.40±16.65	10.54±8.16	13.97±10.48

The values are expressed as mean±SD; statistical analysis was done by one-way ANOVA. The *P*<0.05 was statistically considered significant. The * mark indicates comparison between the male and female group: **P*<0.05, ***P*<0.01, ****P*<0.001. RMSSD: The square root of the mean of the sum of the squares of differences between adjacent NN intervals, SDNN: Standard deviation of the averages of NN intervals in all 5 min segments of the entire recording, NN50: Number of interval differences of successive NN intervals greater than 50 ms, pNN50: Proportion derived by dividing NN50 by the total number of NN interval, SD: Standard deviation

Table 6: Conventional autonomic function test parameters of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (*n*=43)	Female (*n*=47)	Male (*n*=48)	Female (*n*=42)	Male (*n*=44)	Female (*n*=46)
30:15 ratio	1.53±0.18	1.55±0.19	1.46±0.20	1.47±0.18	1.35±0.17	1.37±0.18
E:I ratio	1.41±0.18	1.46±0.18	1.30±0.15	1.31±0.14	1.26±0.13	1.29±0.14
ΔDBP_{IHG}	19.44±3.42	17.94±2.44	20.90±5.24	19.97±4.87	24.22±7.33	22.60±6.84

The values are expressed as mean±SD; statistical analysis was done by one-way ANOVA. The *P*<0.05 was statistically considered significant. The * mark indicates comparison between the male and female group: **P*<0.05, ***P*<0.01, ****P*<0.001. 30:15 ratio: Ratio of maximum RR-interval at 30th beat to minimum RR interval at 15th beat following standing from supine, E:I ratio: Ratio of maxizmum RR interval during expiration to minimum RR interval during inspiration following deep breathing, ΔDBP_{IHG}: Maximum rise in diastolic BP above baseline following sustained handgrip, BP: Blood pressure, SD: Standard deviation

Table 7: Fasting blood glucose and insulin-related profile of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (*n*=43)	Female (*n*=47)	Male (*n*=48)	Female (*n*=42)	Male (*n*=44)	Female (*n*=46)
FBG (mg/dL)	74.91±7.75	74.78±7.33	78.20±8.80	82.31±11.52	85.53±9.14	85.83±8.90
Insulin (μU/mL)	10.04±3.49	10.59±3.92	13.53±6.57	14.72±3.75	17.30±5.88	18.15±4.23
HOMA-IR	1.89±0.64	2.01±0.73	2.60±1.43	2.73±0.84	3.63±1.39	3.87±0.86
HOMA β	167.82±5.65	181.51±5.63***	167.80±7.68	193.91±7.43***	182.51±7.52	188.63±6.54***
HOMA 2%S	77.93±5.68	70.41±5.66***	59.20±7.44	54.73±7.34*	47.94±7.49	44.58±6.49

The values are expressed as mean±SD; statistical analysis was done by one-way ANOVA. The *P*<0.05 was statistically considered significant. The * mark indicates comparison between the male and female group: **P*<0.05, ***P*<0.01, ****P*<0.001. FBG: Fasting blood glucose, HOMA-IR: Homeostatic model assessment of insulin resistance, HOMA β: Homeostatic model assessment of beta cell function, HOMA 2%S: Homeostatic model 2 assessment of insulin sensitivity, SD: Standard deviation

and preobese groups, but such difference was not observed in obese group [Table 7].

In lipid profile, TC was not significantly increased in males compared to females in all the groups [Table 8]. TG was significantly increased in males compared to females in the control group, but this gender difference was not observed in preobese and obese groups [Table 8]. There was no significant gender difference in HDL, LDL, and VLDL in all the three groups [Table 8]. Among the lipid risk factors, AI was significantly more in males than the females in the control group, but such gender difference was not seen in preobese and obese groups [Table 8]. The other lipid risk factors such as TC/HDL, TG/HDL, and LDL/HDL were not significantly increased [Table 8] in males compared to females in all the three groups. There was no significant gender difference in protein profile parameters such as total protein, albumin, globulin, and A:G ratio across the three groups [Table 8]. The free triiodothyronine, free thyroxine, and thyroid-stimulating hormone levels were also not significantly different between the genders across the group [Table 9].

Pro-inflammatory cytokines such as hsCRP, TNF-α, and IL-17 were not significantly different [Table 10] between the males and females in all the three groups. Serum IL-6 was significantly increased in males compared to females only in the obese group [Table 10]. All the adipocytokines such as leptin, adiponectin, and resistin were not significantly altered between the genders in control, preobese, and obese group individuals [Table 11]. Marker of oxidative stress, TBARS, was not significantly higher [Table 12] in males compared to females in the control, preobese, and obese groups. However, total antioxidant (TAO) was significantly higher in males compared to females in the preobese and obese groups [Table 12]. Interferon gamma and neopterin were not significantly altered [Table 13] between the genders in control, preobese, and obese groups.

Discussion

Previous studies have examined the role of gender in obesity,[6,7,28,29] and a few studies have reported the influence of gender in preobese individuals.[30,31] However, most of these studies were not conducted in Indian population and also did not categorize individuals based on the revised WHO BMI classification for Asian population. Further, these studies did

Table 8: Lipid and protein profile of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (n=43)	Female (n=47)	Male (n=48)	Female (n=42)	Male (n=44)	Female (n=46)
Lipid profile						
TC (mg/dL)	170.87±26.59	162.67±28.41	184.26±36.00	175.89±39.35	193.20±43.59	189.67±40.94
TG (mg/dL)	107.34±30.60	85.00±22.06*	115.66±34.95	107.89±34.16	129.70±32.59	125.86±32.86
HDL (mg/dL)	36.14±5.79	39.05±7.86	35.32±7.89	34.43±6.49	28.19±5.14	30.05±5.87
LDL (mg/dL)	113.70±32.39	106.70±33.79	122.50±27.35	114.82±23.72	149.10±34.83	139.68±26.89
VLDL (mg/dL)	19.37±6.08	17.84±4.26	21.30±10.10	20.14±5.83	25.10±7.64	24.71±7.19
TC/HDL	4.93±1.47	4.26±1.15	5.30±1.43	5.16±1.03	6.85±1.83	6.31±1.65
TG/HDL	2.97±0.93	2.19±0.80	3.42±1.77	3.26±1.19	4.63±2.01	4.34±1.57
LDL/HDL	3.02±1.42	2.54±1.14	3.67±1.22	3.34±0.90	5.30±1.45	4.65±1.46
Atherogenic index	4.16±1.47	3.24±1.15**	4.35±1.43	4.16±1.03	5.79±1.83	5.38±1.65
Protein profile						
Total protein (g/dL)	7.70±0.43	7.64±0.37	7.61±0.38	7.51±0.39	7.42±0.35	7.37±0.42
Albumin (g/dL)	4.44±0.37	4.34±0.25	4.52±0.30	4.29±0.24	4.32±0.24	4.25±0.36
Globulin (g/dL)	3.26±0.25	3.31±0.36	3.17±0.30	3.21±0.38	3.07±0.37	3.12±0.32
A:G ratio	1.37±0.17	1.33±0.20	1.41±0.19	1.36±0.20	1.43±0.23	1.38±0.27

The values are expressed as mean±SD; statistical analysis was done by one-way ANOVA. The P<0.05 was statistically considered significant. The * mark indicates comparison between the male and female group: *P<0.05, **P<0.01, ***P<0.001. TC: Total cholesterol, TG: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, A:G ratio: Albumin-globulin ratio, SD: Standard deviation

Table 9: Thyroid profile of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (n=43)	Female (n=47)	Male (n=48)	Female (n=42)	Male (n=44)	Female (n=46)
fT3 (pg/mL)	2.86±1.08	3.09±1.37	3.36±1.28	3.49±1.39	4.17±1.44	4.22±1.92
fT4 (ng/dl)	1.02±0.42	1.29±0.53	1.28±0.72	2.52±0.83	1.49±0.87	1.57±0.75
TSH (µlU/mL)	2.64±1.74	2.70±1.28	2.39±2.04	2.57±1.11	2.21±1.41	2.15±1.47

The values are expressed as mean±SD; statistical analysis was done by one-way ANOVA. The P<0.05 was statistically considered significant. The * mark indicates comparison between the male and female group: *P<0.05, **P<0.01, ***P<0.001. fT3: Free triiodothyronine, fT4: Free thyroxine, TSH: Thyroid stimulating hormone, SD: Standard deviation

Table 10: Inflammatory markers of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (*n*=43)	Female (*n*=47)	Male (*n*=48)	Female (*n*=42)	Male (*n*=44)	Female (*n*=46)
hsCRP (ng/mL)	773.08±352.78	746.71±216.77	1469.46±413.86	1455.35±493.84	1672.42±833.87	1719.06±895.88
TNF-α (pg/mL)	99.96±22.17	97.65±37.89	214.67±55.87	195.53±57.38	287.31±72.74	284.43±76.52
IL-6 (pg/mL)	31.08±12.74	29.17±15.32	62.94±20.71	61.75±17.44	111.39±24.98	98.02±29.51*
IL-17 (pg/mL)	16.26±10.77	12.86±8.55	30.81±8.22	26.64±10.23	40.34±17.21	39.58±19.22

The values are expressed as mean±SD; statistical analysis was done by one-way ANOVA. The *P*<0.05 was statistically considered significant. The * mark indicates comparison between the male and female group: **P*<0.05, ***P*<0.01, ****P*<0.001. hsCRP: High sensitive C-reactive protein, TNF-α: Tumour necrosis factor alpha, IL-6: Interleukin 6, IL-17: Interleukin 17, SD: Standard deviation

Table 11: Adipocytokines of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (*n*=43)	Female (*n*=47)	Male (*n*=48)	Female (*n*=42)	Male (*n*=44)	Female (*n*=46)
Leptin (ng/mL)	15.75±5.88	14.92±4.55	31.12±12.18	30.79±11.66	50.58±20.59	54.26±13.86
Adiponectin (ng/mL)	11.31±3.22	12.58±2.55	8.84±2.04	8.42±1.79	6.65±1.52	6.36±1.11
Resistin (pg/mL)	0.23±0.05	0.21±0.02	0.29±0.07	0.27±0.03	0.34±0.06	0.32±0.07

The values are expressed as mean±SD; statistical analysis was done by one-way ANOVA. The *P*<0.05 was statistically considered significant. The * mark indicates comparison between the male and female group: **P*<0.05, ***P*<0.01, ****P*<0.001. SD: Standard deviation

Table 12: Oxidative stress parameters of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (*n*=43)	Female (*n*=47)	Male (*n*=48)	Female (*n*=42)	Male (*n*=44)	Female (*n*=46)
TBARS (µM/L)	2.18±0.47	2.14±0.87	3.11±0.89	3.15±0.96	4.71±1.59	4.58±0.86
TAO (mM/mL)	0.07±0.03	0.05±0.02	0.20±0.07	0.17±0.04***	0.24±0.11	0.23±0.10***

The values are expressed as mean±SD; statistical analysis was done by one-way ANOVA. The *P*<0.05 was statistically considered significant. The * mark indicates comparison between the male and female group: **P*<0.05, ***P*<0.01, ****P*<0.001. TBARS: Thiobarbituric acid reactive substance, TAO: Total antioxidant

Table 13: Immunological markers of control (male and female), preobese (male and female), and obese (male and female) groups

Parameters	Control group		Preobese group		Obese group	
	Male (*n*=43)	Female (*n*=47)	Male (*n*=48)	Female (*n*=42)	Male (*n*=44)	Female (*n*=46)
IF-γ (pg/mL)	9.26±3.10	8.02±2.71	17.98±8.84	14.76±8.32	45.14±31.79	41.97±14.11
Neopterin (ng/dL)	7.37±2.73	6.58±1.22	16.59±10.10	15.34±6.06	22.86±15.08	18.83±12.32

The values are expressed as mean±SD; statistical analysis was done by one-way ANOVA. The *P*<0.05 was statistically considered significant. The * mark indicates comparison between the male and female group: **P*<0.05, ***P*<0.01, ****P*<0.001. IFN-γ: Interferon gamma, SD: Standard deviation

not recruit apparently healthy preobese and obese individuals without any associated comorbid conditions; instead, gender difference was assessed in diabetic[31] and hypertensive[32] preobese and obese individuals. Therefore, in the present study, we investigated the effect of gender on anthropometric, physiological, CV autonomic function and cardiometabolic risks in apparently healthy young adult Indian population.

Measures of abdominal adiposity (WC, WhtR, and CI) was significantly increased [Table 1] in obese females compared to obese males, suggesting the increased visceral fat accumulation in females. This is further supported by the increased BF and BFMI in females compared to males [Table 2]. The decreased insulin sensitivity in females compared to males in control and preobese group could be due to increased abdominal adiposity in females as observed in our study [Table 7]. However, there was no significant difference in insulin sensitivity in obese group.

High basal metabolic rate has been reported as a risk factor for mortality.[33,34] Therefore, the increased BM in males compared to females indicates that the CV morbidity and mortality could be more in males [Table 2].

The sympathetic overactivity (increased LFnu) and vagal withdrawal (decreased HFnu) was observed in control males

compared to control females [Table 4]. This male-female difference was not observed in preobese and obese individuals, suggesting that the gender difference disappears with increase in BW [Table 4]. The similar difference was observed for DBP, i.e., the gender difference in DBP (less in females compared to males) in control group disappeared in preobese and obese groups [Table 3], suggesting that DBP increases more in females compared to males once they become obese.

In addition, increased TG and AI, which were reported to be independent CV risks,[35,36] were found to be more in males compared females in controls, but such a difference in CV risk profile was not observed between the males and females in both preobese and obese group individuals, suggesting that the increased CV risk is similar in both males and females with progressive increase in BW [Table 8]. However, the more decrease in TP in obese males [Table 4], which is a known CV risk,[37,38] suggests that obese males are at increased risk of future cardiac morbidities compared to females. This is further supported by the increased IL-6 levels in obese males [Table 10] compared to obese females as the previous report links increased serum IL-6 levels to CV diseases (CVD) risks.[39] IL-6 secretion has been reported to be regulated by catecholamines through β-adrenergic receptors.[40] Therefore, the increased IL-6 concentration in males could be due to increased sympathetic activity in males compared to females. Thus, the increased IL-6 might contribute to the higher SVI in obese males.

Further, studies have reported that IL-6 production is negatively affected by estrogens.[41] Evidence suggests that increased concentration of IL-6 and hs-CRP has been considered as an independent marker of morbidity and mortality in patients with CVD.[42,43] Therefore, estrogen exerts beneficial effects in female and protects them from CV mortality by partially decreasing the IL-6 production. However, in the present study, we have not assessed the estrogen levels in females. Nevertheless, findings of the present study suggest that among all the inflammatory markers, IL-6 could play an important role in the increased CV risks in obese males.

Although the inflammatory markers (hs-CRP, TNF-α, and IL-17) and oxidative stress (TBARS) were not significantly [Tables 10 and 12] different between males and females in both preobese and obese groups, the increased TAO status in both preobese and obese males [Table 12], suggesting the increased complementary mechanism to counteract the chronic inflammatory state observed in males. As the individuals in the present study were young adults, we could not note significant gender difference, which could be due to the active compensatory mechanisms that are initiated to counteract the inflammatory condition associated with preobesity and obesity.

Limitations of the study

Due to our moderate sample size of males and females in the present study, we could not clearly elucidate the possible influence of gender CV and metabolic risk profile in this study population. Therefore, future studies should assess the gender difference in cardiometabolic risk profile in a larger population of preobese and obese individuals.

Conclusion

In the present study, we could not assess much difference in gender between the preobese and obese group as our study population was predominantly young adults. Therefore, from the findings of the present study, we could assume that gender-specific influences on SVI, CV risks, and metabolic derangements have not been established in these younger individuals who were in their early phases of preobesity and obesity.

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Conflicts of interest

There are no conflicts of interest.

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