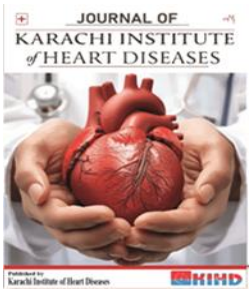

ASSOCIATION BETWEEN OBESITY AND PREMATURE CARDIOVASCULAR DISEASE IN YOUNG FEMALES: A CASE CONTROL STUDY

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ABSTRACT:

Background: Increasing obesity among young females is associated with early-onset of cardiovascular disease (CVD). We accomplished a case control study to examine associations between overweight/obesity and premature CVD among young females aged 18–45.

Methods: This study was case control study total 300 study subjects were enrolled from cardiac hospital out of which 150 was consecutive female cases with first CVD event before age 46 and rest 150 was age-frequency-matched female controls without CVD. Present study mainly focused on key exposures: for instance, BMI categories, central obesity, physical activity, smoking, diabetes, hypertension, dyslipidemia, and history of PCOS and adverse pregnancy outcomes. Logistic regression computed odds ratios (OR) adjusted for controlling confounders.

Results: In adjusted models, obesity (BMI ≥30 kg/m²) was associated with increased odds of premature CVD (adjusted OR 2.84; 95% CI 1.72–4.69). Overweight (BMI 25.0–29.9) had an intermediate effect (adjusted OR 1.52; 95% CI 1.02–2.26). Central obesity (waist circumference >80 cm) and insulin resistance or diabetes double the risk of premature CVD. It was found that gestational hypertension (preeclampsia) and PCOS were more common among cases.

Conclusions: Obesity in young women is a strong independent predictor of premature CVD. Early identification and targeted preventive strategies are essential to control onset of CVD.

Keywords: Obesity; Overweight; Young women; Case control study; Cardiovascular disease; PCOS; Premature CVD

Submitted: 17-01-2026, Revised: 27-01-2026, Accepted: 10-02-2026

INTRODUCTION

Obesity and overweight are strongly associated with increased risk of cardiovascular disease (CVD) and premature mortality in adults. Although CVD is typically considered as a disease of middle-aged and elderly populations, however, a significant shift in epidemiologic trends over the past two decades showed an increase in early-onset cardiovascular events among young adults, particularly young women. While mortality rates from CVD once declined steadily, recent global reports indicate stagnation or even reversal of progress among women under 50. Obesity or overweight in young women is also a potential predictor of CVD and early mortality. Epidemiological research shows that risk factors incidence begins early through metabolic, hormonal, and vascular pathways, and excess body weight in young women carries measurable long-term health consequences. Timely interventions especially related to lifestyle habits, metabolic screening, and reproductive health factors can intensely reduce long-term CVD risk[1]. Obesity contributes directly to cardiovascular risk factors incidence including hypertension (HTN), dyslipidemia, type 2 diabetes (DM II), and systemic inflammation and independently increases the risk of cardiovascular events and mortality. Major scientific statements highlight obesity as a vital, modifiable risk of CVD(1). Epidemiologic studies and meta-analyses have consistently shown that elevated body-mass index (BMI) and central adiposity are associated with increased risks of coronary heart disease (CVD) and all-cause mortality, and these associations are significant across both gender and age groups. BMI is the simplest and most widely indicator for assessing general adiposity, whereas central obesity as measured by waist circumference or waist–hip ratio captures visceral fat distribution more closely associated with cardio-metabolic dysfunction. Numerous large-scale cohort studies have demonstrated that both elevated BMI and central adiposity are

associated with higher risks of HTN, dyslipidemia, insulin resistance, DM II, systemic inflammation, atherosclerosis, and ultimately CVD and premature mortality. The metabolic consequences of excess adipose tissue begin early in life, and even modest elevations in BMI in adolescence or young adulthood predict long-term cardiovascular risk. Evidence also indicates that weight elevated in early adult life and persists from adolescence into adulthood have higher lifetime CVD risk [2]. Young women represent a unique population whose CVD risk markedly differ from men. Premenopausal women have been considered relatively protected from CVD due to hormonal influences, particularly estrogen, which exerts beneficial effects on endothelial function, lipid metabolism, and arterial stiffness. However, as obesity promote chronic inflammation, oxidative stress, endothelial dysfunction, and adverse lipid profiles which contribute in reducing these protective mechanisms. Moreover, obesity also interacts with polycystic ovary syndrome (PCOS) which is commonly associated with insulin resistance, hyper-andro-genism, dyslipidemia, and chronic low-grade inflammation. Women with PCOS often present with the complain of metabolic imbalances which linked to increased cardio metabolic risk later-life. Recent guidelines emphasize early screening and complete risk assessment for women with metabolic imbalance [3]. Despite these associations, risk of CVD among young female is often remain under-recognized, even their symptoms frequently misattributed to anxiety or stress

Pregnancy-related complications such as gestational diabetes mellitus (GDM), preeclampsia and preterm delivery are also well-established markers of future cardio-metabolic disease. These complications are more common in overweight and obese women, which further increase CVD risk later. Epidemiological study set a well-established example, which demonstrated that, the majority of ischemic heart diseases risk increased globally due to central obesity which is modifiable risk factors[4]. On the basis of this approach we conducted a matched case–control study of 150 female cases and 150 controls, because case–control study is an efficient and well-established method to explore both unusual risk factors or rare outcomes such as premature CVD the aim to conduct this study was to quantify the association of overweight/obesity with premature CVD and to examined the relationship between BMI, central obesity and metabolic risk factors in young women with a first cardiovascular event There is a significant need for early diagnosis of CVD risk factors among young women especially those with overweight and obesity, which is prevalent but modifiable.

METHODS

Study design

This was a hospital-based, observational, matched case–control study conducted from 1st October 2023 to 20th December 2024 at Karachi Institute of Heart Diseases, a tertiary care hospital. The study was approved by the Institutional Review Board, and written informed consent was obtained from all participants' prior data collection

Participants

Cases (n = 150): Consecutive female patients aged 18-45 present with a first major cardiovascular event such as acute coronary syndrome(ACS), ischemic stroke, or documented coronary heart disease requiring angiography/PCI during the study period were enrolled in the study till the completion of estimated sample size. Whereas the females those have complained of congenital heart disease, cardio-myopathy unrelated to atherosclerosis, and who were have chronic CVD were excluded.

Controls (n = 150): For the enrolment of control group age-frequency (±2 years) was matched, those women who were attended outpatient clinics but for non-cardiovascular complaints or those who volunteers from community with no history of CVD and had normal resting ECG. Controls were frequency-matched rather than individually matched.

Data collection procedure

Anthropometrics measurements including weight and height were assessed by using standard protocols. Asian BMI categories: underweight <18.5; normal 18.5–22.9; overweight 23.0–24.9; pre obese 25.0-29.9; and obese > 30 kg/m². Waist circumference measured at the iliac crest; central obesity defined as >80 cm for Asian women. Clinical variables involved HTN >130/80mmHg according to ACC definitions or documented history, DM fasting glucose ≥126 mg/dL or prior diagnosed by health care provider, dyslipidemia as per lab cutoffs, smoking current/former/never, family history of premature CVD first-degree relative <55 men / <65 women. PCOS diagnosed by Rotterdam criteria when available in records or patient report confirmed by clinical features; pregnancy complications including GDM and preeclampsia recorded from obstetric history. Physical activity included self-reported moderate/vigorous physical activity (≥150 minutes/week yes or no. Laboratory tests comprised fasting glucose and lipid profile, HbA1c where available.

Statistical analysis

We used open-epi for sample-size computations assuming an exposure prevalence (obesity) in controls of 25% and alpha 0.05, the study has >80% power to detect an OR ≈1.9–2.0. and total sample size come out 300, out of which 150 were cases and rest of the 150 were control. Normally distributed continuous variables are presented as mean ± standard deviation (SD). whereas non-normally distributed continuous variables are reported as medians with inter-quartile ranges (IQR). Categorical variables are expressed as frequencies and percentages. The prevalence of major cardiovascular risk factors, including HTN, DM, and dyslipidemia, BMI categories were evaluated using chi-square tests to assess differences in proportions. Multivariable logistic regression analyses were conducted to examine the association between BMI categories and the presence of premature cardiovascular disease. Normal-weight individuals were used as the reference group. Odds ratios

(ORs) with 95% confidence intervals (CIs) were calculated. The unadjusted model included BMI categories alone, while adjusted models controlled for potential confounders including age, smoking status, HTN, DM, dyslipidemia, and other relevant clinical covariates. Variables such as history of PCOS, GDM preeclampsia, and other pregnancy-related complications were compared between cases and controls. Categorical variables were analyzed using the chi-square or Fisher's exact test, while continuous variables were compared using the independent samples t-test or Mann–Whitney U test, depending on data distribution.

All statistical analyses were performed using IBM SPSS Statistics software (version 29.0; IBM Corp., Armonk, NY). A two-sided p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1. Baseline characteristics of cases and controls (n = 300)

Variable	Cases (n=150)	Controls (n=150)	p-value
Age (years), mean ± SD	39.2 ± 4.1	38.8 ± 4.3	0.34
BMI (kg/m²), mean ± SD	30.1 ± 5.8	24.8 ± 4.9	<0.001
BMI category, n (%)			
Normal	30 (20.0)	65 (43.3)	<0.001
Overweight	50 (33.3)	57 (38.0)	0.39
Obese	70 (46.7)	28 (18.7)	<0.001
Waist circumference >88 cm, n (%)	92 (61.3)	44 (29.3)	<0.001
Hypertension, n (%)	76 (50.7)	35 (23.3)	<0.001
Diabetes, n (%)	42 (28.0)	15 (10.0)	<0.001
Dyslipidemia, n (%)	84 (56.0)	46 (30.7)	<0.001
Current smoker, n (%)	30 (20.0)	18 (12.0)	0.06
Physical activity ≥150 min/wk, n (%)	38 (25.3)	76 (50.7)	<0.001
PCOS history, n (%)	28 (18.7)	12 (8.0)	0.007
GDM history, n (%)	18/110 (16.4)	6/108 (5.6)	0.01
Preeclampsia history, n (%)	14/110 (12.7)	4/108 (3.7)	0.01
Preterm delivery (<37 wks), n (%)	10 (9.1)	6 (5.6)	0.28
Infertility evaluation history, n (%)	22 (20.0)	10 (9.3)	0.02

Table I define differences of multiple variables of the study participant's cases versus controls. There were few variable including age, overweight, smoker and preterm delivery where differences didn't exist, rest of the variables were found to be different in both cases and control.

Table 2. Cardio-metabolic risk factors by BMI category (combined cases and controls, n=300)

BMI category	Hypertension	Diabetes %	Dyslipidemia %	Central obesity%
Normal	12.0	4.0	18.7	8.0
Overweight	32.0	12.0	36.0	40.0
Obese	63.0	38.6	78.6	85.7

Table 2. showed prevalence of HTN, DM, dyslipidemia and central obesity, throughout BMI categories and summarized that the percentage of all risk factors were increasing with the increase of body weight categorized through BMI.

Table 3. Logistic regression: Odds ratios (OR) for premature CVD

Predictor	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	p-value
Overweight normal	1.86 (1.18-2.94)1	1.52 (1.02–2.26)1	0.041
Obese normal	3.76 (2.33-6.07)1	2.84 (1.72–4.69)1	<0.001
Waist circumference >80cm	3.90 (2.45-6.21)1	2.65 (1.62–4.33)1	<0.001
Waist circumference <80cm PCOS history No PCOS history	2.66 (1.31-5.40)1	1.94 (1.01–3.72)1	0.046
GDM Without GDM	3.28 (1.29-8.37)1	2.30 (0.86–6.14)1	0.097

**Adjusted for age, smoking, hypertension, diabetes, dyslipidemia, physical activity, family history*

Table 3 presents logistic regression results for BMI categories vs. normal-weight reference. analysis found that the obesity remained closely associated and have nearly three times higher risk of CVD in adjusted model OR for obese vs normal OR 2.84 (CI 1.72–4.69). All predictors were also remained higher odds of risk of CVD even after adjusted with multiple variables.

DISCUSSION

The present case control study contributes to growing evidence that both type of obesity general and central is significantly and independently predictor of premature CVD among young women. In our study population, nearly half of the cases were obese as compared to controls group which consist almost half number of obese subjects of cases, and BMI remained statistically significant after multivariable adjustment, confirming obesity as an independent predictor of cardiovascular events[5, 6]. Similar findings were observed in a Swedish national cohort of 1.5 million women, where even mild overweight significantly increased myocardial infarction and ischemic stroke in women <40 years old [7]. A pooled JAMA Cardiology analysis supports this, concluding that elevated BMI

in early adulthood predicts earlier onset and greater lifetime CVD risk [8].

Additionally, central obesity was substantially more prevalent in cases than in controls. Recent research revealed that because of hormonal and inflammatory processes connected to the buildup of abdominal fat, visceral adiposity and waist circumference carry a higher cardio-metabolic risk than BMI alone[2, 9]. Recent meta-analyses and systematic reviews emphasize that BMI in early adult life predicts later CVD and that visceral adiposity and cardiorespiratory fitness modulate risk concordant with our observation that physical activity attenuated but did not fully remove obesity-associated risk[10]. Another current meta-analysis confirmed that abdominal obesity is a strong predictor of ischemic heart disease and stroke in women as compared to BMI categories alone[11]. Similarly, our findings also closely align with this data which indicated that adiposity distribution is critically significant in cardiovascular risk assessment particularly among female.

Female-specific endocrine and pregnancy-related factors were also covered in our study. PCOS was significantly highly prevalent in cases than controls. PCOS has been associated with insulin resistance, metabolic syndrome, and endothelial dysfunction, all of them may speed up early CVD development [3, 12]. A Danish cohort reported increased HTN and dyslipidemia rates among PCOS patients [13], while longitudinal studies done in Korea also showed that PCOS women have higher incidence of CVD [14]. Cases with the history of GDM was likewise higher than control. Several studies confirm this evidence that GDM almost doubles the risk of later-life coronary artery disease and metabolic syndrome, even postpartum normalized hyperglycemia [11, 15]. Pregnancy is now widely regarded as a "stress test" that reveals underlying cardio-metabolic vulnerability in women [2]. Our data emphasized that postpartum cardiovascular screening may be essential in young mothers, particularly those with prior GDM or preeclampsia.

CVD risk factors such as HTN, DM, dyslipidemia were significantly more common in cases, global evidence support our study findings that these conditions remain significant cause of ischemic cardiac disease [4, 11, 16], in our results, obesity remained significant even after adjusting for confounding risk factors such as HTN, DM, dyslipidemia, and smoking, but obesity remained strongly associated with early cardiovascular events, these findings are consistent with classic cohort data similar to excess weight to coronary heart disease in women (e.g., Framingham, Nurses' Health Study) and with pooled analyses showing higher all-cause and cardiovascular mortality across increasing BMI categories. The INTERHEART case–control study highlighted modifiable conditions like smoking, lipids, HTN, DM, central obesity and psychosocial factors increase the odds of myocardial infarction globally. This finding emphasized that obesity is not merely a cluster of risk factors but also a major cause of cardio-metabolic dysfunction which have direct or indirect effects on vascular health [8, 17].

All of these results point to overweight and obesity as early cardio-metabolic warning signs rather than benign conditions in young women. Adolescents and women of reproductive age are becoming more obese worldwide [1, 18, 19]. Therefore, in order to prevent premature CVD, early lifestyle interventions should focus on managing weight, encouraging physical activity, screening for insulin resistance or diabetes, managing pregnancy-related risk factors, and implementing policy-level public health measures. Furthermore, integrating PCOS and pregnancy-related metabolic complications into cardiovascular screening would allow better early detection of young-at-risk females [7]. In the end, this study emphasises the significance of reproductive factors in cardiovascular risk assessment and supports the crucial role of obesity as a modifiable risk factor for premature CVD in young women. It is possible to prevent CVD as well as unfavourable pregnancy and metabolic outcomes by lowering obesity and enhancing cardio-metabolic health at a young age [5, 9]. Future prospective cohort study focus on young women, mechanistic studies of adiposity-associated vascular changes, and randomized trials of targeted preventive measures (lifestyle and pharmacologic) in women with obesity and reproductive risk markers are needed.

Strengths

There are much strength present in our study, first it mainly focused on young women (understudied group for premature CVD) start with diagnosed cases rather than following thousands of participants over time. This allows researchers to focus directly on the association between obesity and early CVD without requiring follow up, compared with longitudinal cohort, case–control study is less expensive and quicker to complete as it depends on existing medical records or recalled information. Secondly adequate sample size, inclusion of female-specific variables (PCOS, pregnancy complications), and possible to examine several potential risk factors and confounders (e.g., smoking, hypertension, dyslipidemia) together with obesity, provide a broad understanding of early CVD contributors. Additionally, use of both BMI and waist circumference both are useful in assessing obesity and central adiposity respectively. Furthermore, our study provides locally relevant evidence in a demographic under-represented in cardiovascular literature South Asian women who traditionally have higher chance of premature cardio-metabolic disease [20]. Findings from current study can help generate hypotheses for future prospective research or intervention trials. Observed associations between obesity and CVD will add valuable evidence to justify larger longitudinal study.

Limitations

A number of limitations were also taken into account, such as the fact that a case-control study evaluates exposures after the onset of the disease, making it challenging to verify that obesity contributed to the development of risk factors. Causal inferences are constrained in the absence of clear temporal sequencing. Body Mass Index (BMI) or obesity status assessed at one point in time may not reflect long term weight patterns or central

adiposity, which could offer better insight into cardiovascular risk. Lack of repeated measures can underestimate true exposure effects. Self-reported history of body weight, lifestyle factors e.g., physical activity or PCOS diagnosis may be subject to recall or classification. Residual confounding is possible despite multivariable adjustment. Because PCOS diagnosis was based partly on self-report or available records (misclassification possible). Hospital-based recruitment like subjects with premature CVD are selected based on disease status, there is a risk that they may not be representative of the general population of young females which may limit generalizability and may introduce selection bias.

CONCLUSION

The present study demonstrates that both general obesity and central adiposity are significant and independent predictors of premature CVD in young women. Early diagnosis through female-specific risk assessment (including history of PCOS and pregnancy complications), and timely interventions are essential to reduce future CVD burden. Understanding these relationships is essential to develop gender-specific strategies for early detection, intervention, and prevention.

Conflict of interest

Authors declare no conflict of interest.

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