

Original Research Article

Unravelling obesity linked cardio-metabolic risk heterogeneity among young adults residing in middle India: a prevalence and comparative study across diverse phenotype

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ABSTRACT

Background: Obesity is a complicated metabolic state with diverse phenotypic expressions; which linked with distinct cardio-metabolic risk profiles. Knowing prevalence of those phenotype and understanding cardio-metabolic risks across phenotypes is essential for developing effective public health care strategies. Objective of this study was to assess the prevalence and compare cardio-metabolic risk profiles among different phenotypes.

Methods: 403 young adult (aged 18-25 years) of both genders were included for this cross-sectional study. Participants were classified into obesity phenotypes based on body mass index (BMI) and metabolic health status. Under ethical consideration demographic, anthropometric measurements and cardio-metabolic risk factors were assessed by using standard protocol.

Results: Overall prevalence of metabolically unhealthy normal weight (MUNW), metabolically unhealthy obese (MUO) and metabolically healthy obese (MHO) phenotypes were 3.47%, 8.44% and 5.56% respectively, with slightly higher prevalence in males than females. MUO individuals exhibited the highest metabolic risk markers with the lowest HDL levels. MHO individuals demonstrated relatively better metabolic profiles. MUNW showed intermediate levels for most parameters.

Conclusions: The study highlights significant metabolic differences among obesity phenotypes, with MUO showing the highest risk and MHNW presenting the most favorable metabolic health. These findings emphasize the importance of distinguishing between different obesity phenotypes for effective management and intervention strategies.

Keywords: Metabolically healthy normal weight, Metabolically healthy obese, Metabolically unhealthy normal weight, Metabolically unhealthy obese

INTRODUCTION

Obesity is a widespread public health risk, with its gradually rising prevalence since last few decades.¹ Increasing prevalence of obesity among young population is alarming, as early-onset obesity is a leading cause of chronic cardio-metabolic complications. Currently over

650 million adults are affected globally and obesity linked cardio-metabolic disorder such as cardiovascular disease, type 2 diabetes, and dyslipidemia became foremost cause of morbidity and mortality among distinct population.¹ Conventionally, body mass index (BMI) is the determining factor of obesity, a simple measure that classifies individuals based on their weight in relation to height. But

BMI is not adequate to understand the complexity and heterogeneous character of obesity.² Recent study report has recognized diverse obesity phenotypes, each characterized by different cardio-metabolic profiles and health risks. Distinct phenotypes are metabolically healthy obese (MHO), metabolically unhealthy obese (MUO), metabolically unhealthy normal weight (MUNW), metabolically healthy normal weight (MHNW). Though obesity can be classified based on BMI, MHO are protected from typical metabolic disturbances associated with obesity, such as insulin resistance, hypertension, and dyslipidemia.^{3,4} In contrast, MUO individuals are suffering from metabolic syndrome, including elevated blood pressure, fasting glucose, and triglycerides, along with reduced HDL cholesterol.⁴ Astonishing fact is that, MUNW phenotype, individuals with normal BMI exhibit metabolic abnormalities typically associated with obesity. MUNW phenotype challenges the assumption that normal weight individual always protected from cardio-metabolic risk and emphasize the importance of other cardio-metabolic risk predictor beyond BMI.^{5,6} These phenotypes confront the conventional understanding of obesity as a homogeneous cardio-metabolic state and highlight the need for a more nuanced approach to its diagnosis and management.³ Young adulthood symbolizes a crucial phase where lifestyle habits are build, and early manifestations of obesity can have profound implications for future health. Identifying obesity phenotypes and their prevalence during this formative stage provides insights into the underlying metabolic mechanisms and potential avenues for early intervention. This study aims to be familiar with the prevalence and cardio-metabolic profiles of obesity phenotypes in young adults. Identification of these diverse obesity phenotypes has noteworthy implications for public health and clinical practice. By identifying the prevalence and cardio-metabolic profiles of these phenotypes among young adult, can develop more targeted interventions that address the unique needs of each group from early stage. This approach is essential for reducing the burden of obesity-related diseases and improving overall population health.⁷

METHODS

Study design and target population

This cross-sectional study was aimed to evaluate the prevalence and cardio-metabolic profiles of different obesity phenotypes among young adult from Rajnandgaon, Chhattisgarh. In this study 403 college going young adult both males and females aged 18-25 years were included. Individuals pre-diagnosed with metabolic disorder, history of chronic diseases, recent surgical intervention and pregnant or lactating women were excluded.

Study duration and study setup

This study was conducted over a period of 24 months, from March 2021 to February 2023, including the phases of

recruitment, data collection, analysis, and interpretation. Data collection was carried out between March 2021 and February 2022. Data collection, anthropometric and biochemical analysis were performed at Department of Physiology and Biochemistry, BRLSABVM (government) Medical College and associated hospital, Rajnandgaon, Chhattisgarh. Data processing, statistical analysis and interpretation of result were done at Department of Physiology, Sikkim Manipal Institute of Medical sciences, Gangtok, Sikkim.

Sampling method

A multistage sampling technique was employed to select participants.

Sample size calculation

The sample size was determined based on the expected prevalence of obesity phenotypes among young adults. Assuming a 95% confidence level and a 5% margin of error, a minimum sample size of 403 participants was calculated to ensure adequate statistical power.

Data collection technique

Demographic and lifestyle data were collected using a standardized questionnaire. Anthropometric measurements such as height and weight were measured using a calibrated stadiometer and digital scale, respectively, to calculate body mass index (BMI). Waist circumference was measured using a non-stretchable tape measure to evaluate central obesity.

Cardio-metabolic risk factor measurements

Blood Pressure was measured by using a standardized sphygmomanometer after the participant had rested for at least 5 minutes. Fasting blood glucose and lipid profile was analyzed from venous blood samples collected after an overnight fast of 8-12 hours by using auto analyzer (Beckman Coulter-Au680). Metabolic syndrome is assessed based on the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, including elevated fasting glucose, triglycerides, blood pressure, and decreased HDL cholesterol levels.⁸

Cardio-metabolic risk linked obesity phenotype classification

Obesity was classified according to the Indian Council of Medical Research (ICMR) guidelines for Asian Indians: normal weight: BMI 18.5-22.9 kg/m², overweight: BMI 23.0-24.9 kg/m², obese: BMI ≥ 25.0 kg/m².⁹ Participants were further classified into cardio-metabolic risk related obesity phenotypes based on BMI and metabolic health status (Figure 1): metabolically healthy obese (MHO): individuals with obesity (BMI ≥ 25.0 kg/m²) without metabolic syndrome. Metabolically unhealthy obese (MUO): individuals with obesity and metabolic syndrome.

Metabolically unhealthy normal weight (MUNW): normal BMI individuals (BMI ≤ 25.0 kg/m²) with metabolic syndrome.

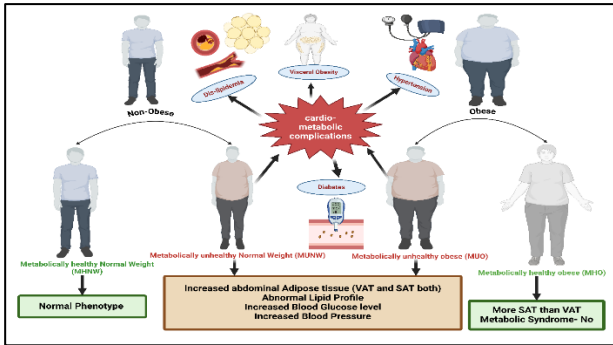


Figure 1: Classification of obesity phenotypes and their association with cardio-metabolic risk factors. This figure illustrates the relationship between different obesity phenotypes [metabolically healthy normal weight (MHNW), metabolically unhealthy normal weight (MUNW), metabolically healthy obese (MHO), and metabolically unhealthy obese (MUO)] and cardio-metabolic health outcomes. The pathways emphasize the varying cardio-metabolic risks across these phenotypes. (VAT: visceral Adipose tissue, SAT: subcutaneous adipose tissue).

Statistical analysis

Descriptive Statistics was used to summarize demographic, anthropometric, and clinical characteristics of the study population. Differences in cardio-metabolic profiles among phenotypes were assessed using ANOVA for continuous variables.

Ethical considerations

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. It was approved by the Institutional Ethic committee. Participants provided written informed consent, and confidentiality of their data was strictly maintained throughout the study.

RESULTS

Among 403 participants 45.66% were male and 54.34% were female with mean age of 23.34 years. Overall results are represented in tabulated and graphical form (Tables 1-5 and Figure 2) as follows:

Table 1 represent demographic data of study participant.

Table 2 represents the frequency and prevalence of various cardio-metabolic linked obesity phenotypes among male and female young adults in the study sample.

Table 1: Demographic characteristics of study participants.

Characteristics	N (%) or mean±SD
Total participants	403 (100)
Gender	
Male	184 (45.66)
Female	219 (54.34)
Age (years)	23.34±3.45
Residence type	
Urban	250 (62.03)
Rural	153 (37.97)
Socioeconomic status	
Low	120 (29.78)
Middle	200 (49.63)
High	83 (20.59)
Religion	
Hindu	300 (74.44)
Muslim	80 (19.85)
Christian	15 (3.73)
Other	8 (1.98)

This table represents the demographic data of the 403 study participants, including gender, age, residence type, socioeconomic status, and religion. The percentages are based on the total number of participants (n=403). The data is provided as frequencies (n) and corresponding percentages (%) or mean±standard deviation (SD) where applicable.

Table 2: Prevalence of cardio-metabolic linked obesity phenotypes among male and female young adults.

Phenotypes	Overall (n=403)		Male (n=184)		Female (n=219)	
	Frequency	Prevalence	Frequency	Prevalence	Frequency	Prevalence
MHNW	331	82.13%	141	34.99%	190	47.15%
MUNW	14	3.47%	8	1.99%	6	1.49%
MUO	34	8.44%	18	4.47%	16	3.97%
MHO	24	5.56%	17	4.22%	7	1.74%

This table represents the distribution and prevalence of different obesity phenotypes in the study population, stratified by overall population (N=403), male participants (n=184), and female participants (n=219). Phenotypes include: MHNW: metabolically healthy normal weight, MUNW: metabolically unhealthy normal weight, MUO: metabolically unhealthy obese, MHO: metabolically healthy obese.

Figure 2 compares the mean values of cardio-metabolic risk components between males and females across four

obesity phenotypes: MHNW, MUNW, MUO, and MHO. Error bars represent the variability (standard error) within each group.

Table: 3 Anthropometric and cardio-metabolic risk profile across different obesity phenotypes in young adults.

Parameters		Mean	SD	Q-1	Q-2	Q-3	IQR	95% CI of mean
Height (cm)	MHNW	162.73	8.25	156.5	164	169	12.5	161.83-163.63
	MUO	163.79	2.86	162	163	166	4	162.8-164.79
	MHO	166.38	3.85	162.75	167	169	6.25	164.75-168
	MUNW	166.21	5.28	165.25	166.5	168.75	3.5	163.17-169.26
Weight (kg)	MHNW	56.38	9.17	49	56	64.5	15.5	55.39-57.38
	MUO	73.53	7.22	70	70	77	7	71.01-76.05
	MHO	71.38	4.53	70	70.5	73	3	69.46-73.29
	MUNW	62.79	5.98	60.5	65	67	6.5	59.34-66.24
BMI (kg/m ²)	MHNW	21.19	2.33	19.72	21.16	23.31	3.59	20.94-21.44
	MUO	27.36	1.94	26.67	26.67	27.79	1.12	26.69-28.04
	MHO	25.76	0.82	25.15	25.45	26.28	1.13	25.42-26.11
	MUNW	22.72	1.89	21.82	22.76	24.37	2.54	21.63-23.81
WC (cm)	MHNW	79.42	5.94	75	78	84	9	78.77-80.06
	MUO	97.32	10.07	91	92	101.5	10.5	93.81-100.84
	MHO	90.08	5.19	86.75	89	94	7.25	87.89-92.28
	MUNW	86.64	5.21	84.25	89	91	6.75	83.63-89.65
SBP (mmHg)	MHNW	122.22	8.08	120	124	126	6	121.34-123.1
	MUO	132.29	4.46	130	131	136	6	130.74-133.85
	MHO	126.5	5.79	120	127	130	10	124.06-128.94
	MUNW	129.43	5.35	130	132	132	2	126.34-132.51
DBP (mmHg)	MHNW	79.58	6.04	80	80	82	2	78.92-80.24
	MUO	88.71	3.02	90	90	90	0	87.65-89.76
	MHO	84.79	3.72	81.5	84.5	88	6.5	83.22-86.36
	MUNW	86.71	4.05	86	88	90	4	84.38-89.05
FBG (mg/dl)	MHNW	89.86	6.53	85	91	95.8	10.8	89.15-90.57
	MUO	100.5	4.83	97.25	101	103.6	6.35	98.81-102.19
	MHO	93.65	5.95	92	96	98	6	91.14-96.16
	MUNW	95.19	7.93	91.05	97.5	100.25	9.2	90.61-99.76
TG (mg/dl)	MHNW	147.76	5.3	146	148	149	3	147.18-148.33
	MUO	159.76	8	156	158	162.75	6.75	156.97-162.56
	MHO	150.42	6.7	147	148	149.75	2.75	147.59-153.25
	MUNW	155	3.59	152.25	154.5	157	4.75	152.92-157.08
HDL (mg/dl)	MHNW	50.11	7.88	43	49	57	14	49.26-50.97
	MUO	38.38	5.37	36	37	38.75	2.75	36.51-40.26
	MHO	44.46	7.3	39.5	42.5	48	8.5	41.37-47.54
	MUNW	42.07	6.74	37.25	39	47.5	10.25	38.17-45.96

This table represents descriptive statistics for various health parameters stratified by obesity phenotypes: metabolically healthy normal weight (MHNW), metabolically unhealthy obesity (MUO), metabolically healthy obesity (MHO), and metabolically unhealthy normal weight (MUNW). The parameters include height (cm), weight (kg), BMI (kg/m²), waist circumference (WC, cm), systolic blood pressure (SBP, mmHg), diastolic blood pressure (DBP, mmHg), fasting blood glucose (FBG, mg/dl), triglycerides (TG, mg/dl), and high-density lipoprotein (HDL, mg/dl). For each parameter, the table includes the mean, standard deviation (SD), quartiles (Q1, Q2, Q3), interquartile range (IQR), and the 95% confidence interval (CI) of the mean.

Table 4: Repeated measures ANOVA results for the impact of phenotypic variation on cardio-metabolic parameters.

	Sum of squares	df	Mean squares	F	p	η ²	η ² p
WC (cm), SBP (mmHg), DBP (mmHg), FBG (mg/dl), TG (mg/dl), HDL (mg/dl)	2537397.71	5	507479.54	12342.53	<0.001	0.95	0.97
Phenotype	13826.79	3	4608.93	81.74	<0.001	0.01	0.38
RM factor x phenotype	19790.85	15	1319.39	32.09	<0.001	0.01	0.19
Residuals (between subjects)	22498.32	399	56.39				
Residuals (within subjects)	82027.11	1995	41.12				

Sum of squares: the total variation explained by each factor; df: degrees of freedom associated with the effect; mean squares: the average variation per degree of freedom; F: The F-statistic value for the ANOVA test; p: the p value indicating the significance of the results; η² (eta-squared): the proportion of the total variance explained by the factor; η²p (partial eta-squared): the proportion of the effect size attributed to the factor, excluding other sources of variation.

Table 3 represents the mean, standard deviation (SD), mean of parameter in three quartile (Q-1, Q-2, Q-3), inter-

quartile range (IQR), and 95% confidence intervals (CI) for various anthropometric measurements and cardio-metabolic risk factor across four distinct phenotypes.

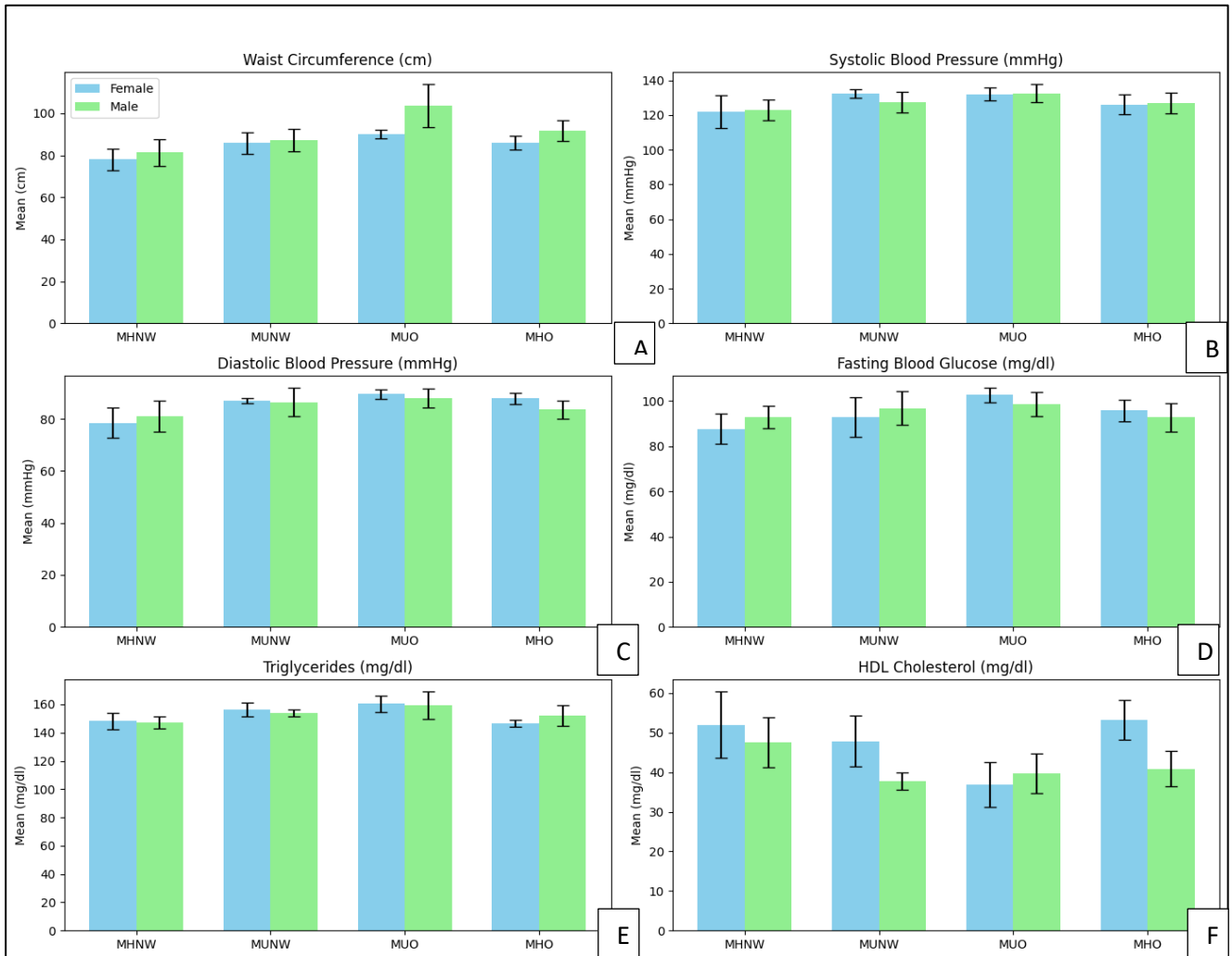


Figure 2 (A-F): Gender-specific mean comparisons of cardio -metabolic parameters across obesity phenotypes.

Table 4 represents the results of repeated measures ANOVA examining the effect of phenotypic variation on six key metabolic parameters: waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood glucose (FBG), triglycerides (TG), and high-density lipoprotein (HDL).

Table 5 represents the mean differences, standard errors, t-values, and p-values for each pair-wise comparison. Significant differences ($p < 0.001$) were observed between MHNW and MUNW, MHNW and MUO, MHNW and MHO, MUNW and MUO, and MUO and MHO, indicating distinct metabolic profiles across these phenotypes. The comparison between MUNW and MHO did not show a significant difference ($p=1$).

Table 5: Bonferroni post-hoc test results for pair wise comparisons of cardio-metabolic parameters across different obesity phenotypes (MHNW, MUNW, MUO, MHO) among young adult.

	Mean diff.	Std. error	t-value	P value
MHNW-MUNW	-4.35	0.84	-5.2	<0.001
MHNW-MUO	-8	0.55	-14.5	<0.001
MHNW-MHO	-3.49	0.65	-5.39	<0.001
MUNW-MUO	-3.66	0.97	-3.75	0.001
MUNW-MHO	0.86	1.03	0.83	1
MUO-MHO	4.51	0.82	5.52	<0.001

This table represents pairwise comparisons between obesity phenotypes (MHNW, MUNW, MUO, and MHO). The mean differences, standard errors, t-values, and p values collectively provide a comprehensive view of these statistical relationships.

DISCUSSION

Prevalence of obesity phenotypes

In our study overall, the data indicates that both male and female young adults having distinct cardio-metabolic risk profiles, with a higher prevalence of MUO and MHO phenotypes among males than female. The low prevalence of MUNW corroborates previous findings that suggest this phenotype is rare in the general population.⁶ This distribution is also consistent with existing literature that indicates MHO is relatively uncommon and that most obese individuals exhibit metabolic abnormalities.^{10,11}

Cardio-metabolic risk profiles across phenotypes

Our study shows notable differences of cardio-metabolic risk among the four obesity phenotypes. MUO individuals exhibited the utmost metabolic risk, with the highest BMI (27.36 ± 1.94 kg/m²), waist circumference (97.32 ± 10.07 cm), systolic blood pressure (132.29 ± 4.46 mmHg), fasting blood glucose (100.5 ± 4.83 mg/dl), and triglycerides (159.76 ± 8 mg/dl), along with the lowest HDL levels (38.38 ± 5.37 mg/dl). Our findings are consistent with earlier results indicating that MUO individuals face an elevated risk of metabolic syndrome and cardiovascular diseases.¹²⁻¹⁴ This result is also in line with Després et al, who identified visceral obesity as strongly associated with metabolic syndrome components.¹⁵ In contrast, MHO individuals, despite having a higher BMI (25.76 ± 0.82 kg/m²) and waist circumference (90.08 ± 5.19 cm), showed a comparatively better metabolic profile than MUO, with lower FBG (93.65 ± 5.95 mg/dl) and higher HDL (44.46 ± 7.3 mg/dl). An extremely attention-grabbing finding is that MHO phenotype in spite of illustrating better cardio-metabolic health profile compared to MUO but not significantly different from MUNW in most parameters. This outcome aligns with Wildman et al, which suggested that metabolically healthy obese individuals still face some metabolic risks despite a relatively better profile.⁶ MUNW displayed moderate cardio-metabolic risk, with elevated systolic blood pressure (129.43 ± 5.35 mmHg) and triglycerides (155 ± 3.59 mg/dl). The transitional values for MUNW emphasize the unpredictability in metabolic health among individuals with normal weight.¹⁸ Previous studies have highlighted that individuals with normal weight can still exhibit metabolic abnormalities, often referred to as “normal weight obesity” or “metabolically unhealthy normal weight”.^{7,18} MHNW consistently presented the most favourable health indicators, with the lowest BMI (21.19 ± 2.33 kg/m²) and the narrowest waist circumference (79.42 ± 5.94 cm). The 95% confidence intervals (CIs) for the means show precise estimates, with narrower CIs reflecting more reliable data for anthropometric parameters (e.g., MHNW height: 161.83-163.63 cm) and wider CIs for some metabolic measures, indicating greater variability and potential subgroup differences. The cardio-metabolic profiles across the different obesity phenotypes indicate that MUO individuals have the most adverse

outcomes in terms of waist circumference (WC), systolic and diastolic blood pressure (SBP and DBP), fasting blood glucose (FBG), triglycerides (TG), and high-density lipoprotein cholesterol (HDL). In contrast, MHO individuals illustrated a quite good metabolic health profiles, similar with prior research outcome that shows metabolically healthy individuals, despite being obese, generally have better metabolic health compared to those with metabolic abnormalities.^{16,17} This underscores the importance of not exclusively relying on body weight or BMI as indicators of metabolic health and highlights the need for comprehensive metabolic assessments.

Effects of different phenotypes on various cardio-metabolic parameters

The overall model explains a large proportion of the variability in these parameters, with phenotypic differences and their interactions playing substantial roles. The ANOVA results show significant differences across obesity phenotypes for all metabolic parameters ($F=12342.53$, $p<0.001$), with a high effect size ($\eta^2=0.95$), representing a vital impact of phenotype categorization linked with cardio-metabolic health. These findings reveal that cardio-metabolic parameters are significantly influenced by phenotypic differences and their interactions with repeated measures factors. The significant interaction effects ($F=32.09$, $p<0.001$) suggest complex relationships between metabolic parameters and obesity phenotypes, supporting findings from Lee et al and Xiong et al, who observed considerable variability in metabolic risk across different phenotypes.^{19,20} Despite the significant findings, residuals indicate that further research is needed to explore additional factors contributing to cardio-metabolic variability. This comprehensive analysis underscores the importance of considering both phenotypic and temporal factors in understanding cardio-metabolic health.

Pair wise comparisons of cardio-metabolic parameters among different obesity phenotypes

Post-hoc analyses using Bonferroni correction reveal significant differences between phenotypes. MUO individuals showed significantly worse metabolic outcomes compared to MHNW, MUNW, and MHO individuals. These results are consistent with literature that highlights severe metabolic disturbances in MUO individuals.¹⁵ This observation is consistent with previous research indicating that MHO individuals, despite having better metabolic health than MUO individuals, are not entirely free from metabolic risks.⁶ In our finding MHNW individuals showing significantly lower values compared to MUNW (mean difference: -4.35 , $p<0.001$) and MUO (mean difference: -8 , $p<0.001$), consistent with Kumanyika et al study report highlighting the metabolic health associated with obesity and metabolic health risk, regardless of weight status.²¹ Amusingly, the non-significant difference between MUNW and MHO (mean difference: 0.86 , $p=1$) aligns with Kahn et al, result which, suggesting that metabolic health can be compromised in

normal-weight individuals, similar to or worse than in obese but metabolically healthy individuals.¹¹ The observed differences between MUO and MHO (mean difference: 4.51, $p < 0.001$) further reinforce the heterogeneity within obese populations, as reported in prior studies.²² The comparison between MHO and MHNW did not show significant differences for most parameters, suggesting that while MHO individuals have a better metabolic profile compared to MUO, they still face some degree of metabolic risk compared to MHNW.²³ This finding is in line with Wildman et al, who noted that metabolically healthy obese individuals are not entirely free from metabolic risks.¹⁷ This study is the first to explore obesity phenotypes among young adults in middle India, highlighting the variations in metabolic health across different phenotypes, including MHNW, MUNW, MUO, and MHO. The research provides novel insights into cardio-metabolic risk factors in this demographic, emphasizing the complexity of obesity beyond body weight, and underscores the need for region-specific health strategies.

This research report estimated the prevalence and cardio-metabolic risk profiles across various obesity phenotypes in young adult population at the inaugural moment in India. Our findings provide important insight about complex and distinct cardio-metabolic risk report among different obesity phenotypes. MHO phenotype, relatively having favorable metabolic profiles compared to MUO phenotype, but they are still are susceptible to some degree of metabolic risk. Though MHO individuals generally have better cardio-metabolic health, but metabolic risk components are more elevated compared to MHNW phenotype, which high a persistent metabolic risk. On the other side, the MUNW group represents an interesting profile, showed intermediate values for most metabolic parameters, reflecting variability in metabolic health among those with normal weight. This suggests that normal weight individuals are always not metabolically healthy. These results reaffirm the importance of identification of obesity phenotypes when assessing cardio-metabolic risk. MHO individuals, despite of having better metabolic profiles compared to MUO individuals, still face risks that need to be addressed. Conversely, MUNW individuals, with normal BMI, can exhibit significant metabolic abnormalities. These findings strongly reinforce the concept that metabolic health cannot be accurately assessed by BMI alone.

While this study provides valuable insights into the prevalence and cardio-metabolic risk profiles of different obesity phenotypes among young adults, several limitations must be acknowledged. First, the cross-sectional design of the study limits the ability to infer causal relationships between obesity phenotypes and metabolic health. Second, the sample was drawn from a specific geographic location (Rajnandgaon, Chhattisgarh), which may limit the generalizability of the findings to other regions or populations

CONCLUSION

This study is one of the first in middle India, and indeed in India, to explore the prevalence and cardio-metabolic risk profiles of different obesity phenotypes among young adults. It underscores the need to consider obesity phenotypes when evaluating cardio-metabolic risk, as BMI alone does not provide a complete picture of metabolic health. These findings contribute to the understanding of obesity's complex relationship with metabolic health and emphasize the importance of personalized interventions targeting specific obesity phenotypes. Future research should focus on elucidating the underlying mechanisms driving metabolic variability across these phenotypes and developing early-stage interventions to mitigate long-term cardio-metabolic risks in young adults.

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