

"An Analytical Study of Insulin Resistance (HOMA-IR) And Obesity Indices in Obese Non-Diabetic Population at a Tertiary Care Hospital in Western Maharashtra"

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KEYWORDS

ABSTRACT

Blood pressure, HOMA-IR, Non-Diabetic, insulin **Introduction:** Obesity is a growing global concern, with a doubled number of children and adolescents with type 2 diabetes. Obesity is associated with insulin resistance, which causes T2DM and hypertension. The pandemic has increased obesity cases, and the homeostasis model of insulin resistance (HOMA-IR) can help stratify diabetes risk in Asian Indians beyond obesity. **Methodology:** This study surveyed 60 non-diabetic obese patients at Krishna Hospital & Medical Research Centre over 18 months. The study assessed insulin resistance using the HOMA-IR index. Data analysis included anthropometric measurements, blood pressure, and laboratory investigations. The study was approved by the institutional ethics committee. **Results:** A study of 60 non-diabetic patients found that 38.33% were over 60 years old, with a mean age of 53.88 ± 14.41 years. The study also evaluated blood sugar parameters, with 20 patients (33.33%) being insulin sensitive and 40 (66.67%) insulin resistant. The mean age of insulin-sensitive patients was 59.05 years, while those with insulin resistance were 54.18 years. The study found no significant difference in systolic blood pressure, diastolic blood pressure, or HbA1c levels between the insulin-sensitive and insulin-resistant groups. **Discussion:** The study reveals an older, male-dominated population in the Asian Indian population, with a higher prevalence of obesity and metabolic disorders. The majority (66.67%) exhibit insulin resistance, a marker for assessing insulin sensitivity and predicting diabetes risk. Differences in FBS levels, HbA1c levels, and fasting insulin levels between insulin-sensitive and resistant groups highlight the complex interplay between obesity, insulin resistance, and metabolic parameters. The study highlights the importance of BMI and waist circumference in assessing metabolic health. Conclusion: The study found that obesity, lipid profile, blood sugars, and metabolic syndrome are significant factors in insulin resistance, emphasizing the need for effective management.

Introduction:

Obesity is a growing concern worldwide. Obesity cases have doubled in the last two decades.¹ The epidemic status of obesity is seen with an increasing number of children and adolescents with type 2 diabetes.² Overweight and obesity are important risk factors of type 2 diabetes; they are associated with insulin resistance in persons with normal glucose level.³

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As well, some association between the body mass index (BMI) and age at diagnosis of type 2 diabetes has been reported, spurring interest as to whether abnormal glucose metabolism can be detected at an early age. ⁴ In previous studies more insulin resistance was noted for young individuals with prominent obesity. ^{5,6} Obesity associated with insulin resistance was also reported in various studies with hyperlipidemia and middle-aged Indian offspring of hypertensive parents. ^{7,8} Meanwhile, data on whether being overweight is associated with insulin resistance in healthy individuals are lacking.

Visceral adiposity is associated with the impairment in the insulin signaling. ⁹ Recent studies mention than more evidence is required to check this issue. ^{10,11} Insulin resistance causes type 2 diabetes mellitus (T2DM), and is also accompanies hypertension and Deranged lipids. T2DM is associated with obesity, and insulin resistance and weight mention that slim people with no history of obesity or DM became insulin resistant. That's why physiological basis of the insulin resistance in the obesity cases need to be studied. ^{12,13}

The increase cases of T2DM and is because of the pandemic of obesity. ¹⁴ Indian cases are also increasing. The trend of obesity in children and adolescent is the rising prevalence of IR. ¹⁵ Now however, there is no strong evidence the cut-off values of HOMA-IR for the Indian individuals. A south Indian part study observed a correlation of HOMA-IR and glucose intolerance.

Therefore, the present study was conducted determine whether insulin resistance (IR) measured by homeostasis model of insulin resistance (HOMA-IR) can further stratify diabetes risk in Asian Indians beyond obesity. In this study we investigated the association in various indices of the obesity with insulin resistance as measured by HOMA-IR in Obese non diabetic Indians.

Methodology:

This single-center, hospital-based cross-sectional observational study was conducted on 60 non-diabetic obese patients admitted to the General Medicine wards of Krishna Hospital & Medical Research Centre, Karad, over 18 months (2022-2023). The sample size was calculated based on a Z-value of 1.96, precision of 0.1, and an estimated proportion of raised HOMA-IR in non-diabetic obese patients at 16.5%, as reported by SM Lim et al., resulting in a minimum sample size of 53, with 60 patients enrolled to account for potential dropouts.

Inclusion criteria consisted of obese individuals without a known diagnosis of diabetes mellitus, while those with type I or type II diabetes or non-obese individuals were excluded. Anthropometric measurements, blood pressure, and a range of laboratory investigations, including fasting blood glucose, serum insulin, and lipid profile, were conducted. Insulin resistance was assessed using the HOMA-IR index, with a value greater than 2.0 indicating insulin resistance.

Data analysis was performed using SPSS version 21, with qualitative data represented as frequencies and percentages, and quantitative data as means and standard deviations. Statistical significance was assessed using chi-square tests for categorical variables and unpaired t-tests for quantitative variables, with significance set at p < 0.05. Correlation and ROC curve analyses were used to evaluate the relationship between HOMA-IR levels and obesity, defined by BMI.

Data was collected after obtaining a written informed consent from all the participants. This study was approved by institutional ethics committee



Observations and Results:

We evaluated 60 non-diabetic cases reported to our hospital. It was observed that maximum number of subjects 23 (38.33%) were in age group >60 years followed by 51-60 years (20%). The Mean age was 53.88 ± 14.41 years. We had 36 (60%) males and 24 females (40%). The mean weight was 79.52 kg (SD = 13.02), height was 1.61 m (SD = 0.08), BMI was 30.85 (SD = 4.89), waist circumference was 0.97 m (SD = 0.12), hip circumference was 1.05 m (SD = 0.08), WHR was 0.92 (SD = 0.11), and SFT was 27.95 mm (SD = 6.37).

We evaluated various blood sugar parameters of the study participants. The table 1 shows the following blood sugar levels and related indices: mean FBS is 102.58 mg/dL (SD = 14.71), HbA1c is 5.66% (SD = 0.44), fasting insulin was 19.16 μ IU/mL (SD = 25.81), and HOMA-IR index was 4.65 (SD = 3.71). [Table 1]

Table 1: Distribution according to mean fasting blood sugar levels, HbA1c, fasting insulin levels and HOMA IR index among patients

Blood sugar levels	Mean	SD	Median
FBS	102.58	14.71	103
HbA1c	5.66	0.44	5.8
F-Insulin	19.16	25.81	10.63
HOMA-IR Index	4.65	3.71	2.5

Mean hemoglobin was 12.91 g/dL (SD = 2.79) and serum creatinine is 0.9 mg/dL (SD = 0.21). Mean triglycerides were 140.82 mg/dL (SD = 54.11), HDL was 33.21 mg/dL (SD = 6.98), LDL was 88.24 mg/dL (SD = 29.37), and the HDL to LDL ratio was 0.41 (SD = 0.13).

We observed the patients according to the HOMA-IR Index. Among the 60 patients, 20 (33.33%) are insulin sensitive (HOMA-IR < 2), while 40 (66.67%) exhibit insulin resistance (HOMA-IR \geq 2). [Fig 1]

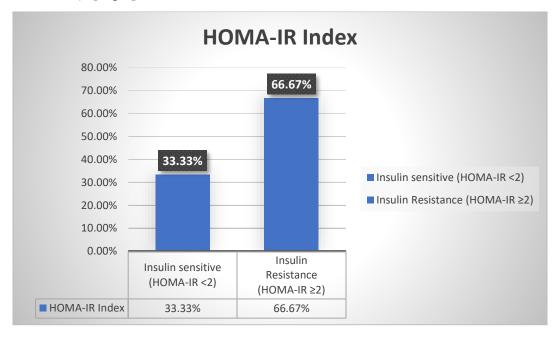


Fig 1: Distribution according to HOMA-IR Index among patients



The mean age of insulin-sensitive patients (HOMA-IR < 2) is 59.05 years (SD = 14.15), while for those with insulin resistance (HOMA-IR \geq 2), the mean age is 54.18 years (SD = 10.79), with a p-value of 0.14, indicating no significant difference. Among the insulin-sensitive group, 9 out of 20 patients (45%) are male, compared to 27 out of 40 patients (67.5%) in the insulin-resistant group. The difference in age and gender distribution indicates a trend, but it is not statistically significant (p-value > 0.05).

In the insulin-sensitive group (HOMA-IR < 2, n=20), the mean systolic blood pressure is 139.28 mm Hg (SD = 21.04), whereas in the insulin-resistant group (HOMA-IR \geq 2, n=40), it is 140.48 mm Hg (SD = 18.95). The p-value for systolic blood pressure is 0.324, indicating no significant difference between the groups. For diastolic blood pressure, the mean in the insulin-sensitive group is 82.78 mm Hg (SD = 11.42), and in the insulin-resistant group, it is 82.37 mm Hg (SD = 11.63), with a p-value of 0.712, also indicating no significant difference.

Table 2: Association of blood sugar indices and HOMA-IR Index among patients					
Blood Sugar Indices	Insulin Sensitive	Insulin Resistance	I		

Blood Sugar Indices	Insulin Sensitive (HOMA-IR <2)	Insulin Resistance (HOMA-IR ≥2)	P Value
Normal Fasting blood sugar (<100 mg/dl)	15	15	X ² =7.5 P=0.006 (S)
Impaired Fasting blood sugar (100-125 mg/dl)	05	25	
Normal HbA1c levels (<5.7%)	13	14	X ² = 4.85 P=0.03 (S)
Impaired HbA1c levels (5.7-6.4%)	07	26	
Normal Fasting insulin levels (<24.9)	20	31	X ² = 5.29 P=0.02 (S)
High Fasting insulin levels (≥24.9)	00	09	

In the insulin-sensitive group (HOMA-IR < 2, n=20), 15 patients (75%) have normal FBS levels (<100 mg/dL), and 5 patients (25%) have impaired glucose tolerance (100-125 mg/dL). In the insulin-resistant group (HOMA-IR \geq 2, n=40), 15 patients (37.5%) have normal FBS levels, and 25 patients (62.5%) have impaired glucose tolerance. We observed that in the insulin-sensitive group (HOMA-IR < 2, n=20), 13 patients (65%) have normal HbA1c levels (<5.7%), and 7 patients (35%) have impaired glucose tolerance (5.7-6.4%). In the insulin-resistant group (HOMA-IR \geq 2, n=40), 14 patients (35%) have normal HbA1c levels, and 26 patients (65%) have impaired glucose tolerance. In the insulin-sensitive group (HOMA-IR < 2, n=20), all 20 patients (100%) have normal fasting insulin levels (<24.9 μ IU/mL). In contrast, in the insulin-resistant group (HOMA-IR \geq 2, n=40), 31 patients (77.5%) have normal fasting insulin levels, while 9 patients (22.5%) had elevated levels (\geq 24.9 μ IU/mL). All these indices showed significant difference with the insulin resistance (p<0.05).



Table 3: Association of fasting lipid parameters and HOMA-IR Index among patients

Lipid profile	Insulin Sensitive (HOMA-IR <2)	Insulin Resistance (HOMA-IR ≥2)	P value
Triglycerides	126.45 ± 39.75	149.1 ± 60.37	0.031*
HDL	36.40 ± 7.65	31.62 ± 6.69	0.042*
LDL	84.29 ± 29.90	90.21 ± 29.28	0.251
HDL: LDL	0.41 ± 0.11	0.40 ± 0.15	0.372

(* p statistically significant <0.05)

Table 3 presents the association of fasting lipid profile parameters with the HOMA-IR Index among patients. In the insulin-sensitive group (HOMA-IR < 2), the mean triglyceride level is 126.45 mg/dL (SD = 39.75), while in the insulin-resistant group (HOMA-IR \geq 2), it is 149.1 mg/dL (SD = 60.37). The p-value for triglycerides is 0.031, indicating a statistically significant difference between the groups. For HDL cholesterol, the mean is 36.40 mg/dL (SD = 7.65) in the insulin-sensitive group and 31.62 mg/dL (SD = 6.69) in the insulin-resistant group, with a p-value of 0.042, indicating a significant difference. However, there is no significant difference in LDL cholesterol levels between the two groups (p = 0.251). Similarly, the HDL to LDL ratio shows no significant difference (p = 0.372). [Table 3]

In the insulin-sensitive group (HOMA-IR < 2, n=20), 14 patients (70%) fall under the Obese-I category (BMI 25-29.9), and 6 patients (30%) fall under the Obese-II category (BMI \geq 30). In contrast, in the insulin-resistant group (HOMA-IR \geq 2, n=40), 16 patients (40%) are categorized as Obese-I, and 24 patients (60%) are categorized as Obese-II. The chi-square test yields X2 = 4.8 with a p-value of 0.028, indicating a statistically significant association between BMI classification and the HOMA-IR Index.

Table 4: Association of waist hip ratio and HOMA-IR Index among patients

Waist hip ratio (WHR)		Insulin	Insulin	P value
		Sensitive (HOMA-IR <2)	Resistance (HOMA-IR ≥2)	
Males	>0.9	04	21	X2=6.4 P=0.09 (NS)
	≤0.9	05	06	1 0.05 (115)
Females	>0.85	06	09	
	≤0.85	05	04	

Table 4 describes the association between waist-hip ratio (WHR) and the HOMA-IR Index among patients, categorized by gender. Among males, 4 individuals (16.67%) in the insulin-sensitive group (HOMA-IR < 2) have a WHR > 0.9, while 21 individuals (84.00%) in the insulin-resistant group (HOMA-IR \geq 2) have a WHR > 0.9 (X2 = 6.4, p = 0.09, not significant). Conversely, in males with a WHR \leq 0.9, there are 5 individuals (20.83%) in the insulin-sensitive group and 6 individuals (24.00%) in the insulin-resistant group. Among females, 6 individuals (33.33%) in the insulin-sensitive group have a WHR > 0.85 compared to 9 individuals (50.00%) in the insulin-resistant group, while 5 individuals (27.78%) in both groups have a WHR \leq 0.85. These findings suggest that while there are trends towards higher



WHR values in the insulin-resistant groups, the differences observed do not reach statistical significance, particularly among males.

Table 5: Association of anthropometry profile and HOMA-IR Index among patients

Anthropometry	Insulin Sensitive (HOMA-IR <2)	Insulin Resistance (HOMA-IR ≥2)	P value
Weight	73.25 ±11.35	82.65 ±12.77	0.007*
Height	1.59 ±0.09	1.61 ±0.08	0.543
BMI	29.69 ±4.77	31.43 ±4.89	0.19
Waist circumference	0.92 ±0.10	1.04 ±0.13	0.456
Hip circumference	1.05 ±0.08	1.05 ±0.09	<0.001*
WHR	0.86 ±0.08	0.94 ±0.09	<0.001*
SFT	26.7 ±3.68	28.58 ±7.31	0.28

^{*(}P<0.05 statistically significant)

Table 5 presents the association between anthropometric measurements and the HOMA-IR Index among patients, distinguishing between those classified as insulin-sensitive (HOMA-IR < 2) and insulin-resistant (HOMA-IR ≥ 2). The findings reveal significant differences in several parameters. Insulin-resistant individuals demonstrate higher mean weights (82.65 kg) compared to insulin-sensitive counterparts (73.25 kg), a statistically significant difference (p = 0.007). Hip circumference (1.05 m) and waist-hip ratio (WHR) (0.94) are notably higher in the insulin-resistant group compared to the insulin-sensitive group (hip circumference: 1.05 m, p < 0.001; WHR: 0.94, p < 0.001). Conversely, other measures like height, BMI, waist circumference, and skinfold thickness show no significant differences between the groups. These results underscore the importance of hip circumference and WHR as potential markers of insulin resistance, suggesting their utility in assessing metabolic health and related risks in clinical settings. [Table 5]

Table 6: Association of metabolic syndrome with HOMA IR Index

Metabolic Syndrome	Insulin Sensitive (HOMA-IR <2)	Insulin Resistance (HOMA-IR≥2)	P Value
Not Satisfying Metabolic Syndrome Criteria	10	12	0.129, NS
Satisfying Metabolic Syndrome Criteria	10	28	
Total	20	40	

The association of metabolic syndrome with insulin resistance, as measured by HOMA-IR, reveals notable trends. Among the participants who were insulin Sensitive (HOMA-IR <2), 10 each were satisfying the criteria for metabolic syndrome and not satisfying the criteria for metabolic syndrome (50%). Among the participants who were insulin resistance (HOMA-IR \ge 2), 12 were satisfying the criteria for metabolic syndrome (30%) and 28 were not satisfying the criteria for metabolic syndrome (70%). Despite these differences, the p-value of 0.129



indicates that the observed association between metabolic syndrome and insulin resistance is not statistically significant.

Discussion:

The study's age distribution reveals a predominantly older population, with a mean age of 53.88 years similarly observed by Singh et al., 2022 [18]. This demographic profile is typical in studies involving insulin resistance and obesity, where advancing age correlates with increased risk factors such as decreased insulin sensitivity and higher BMI (Gupta et al., 2020) [6].

The gender distribution in this study leans towards males (60%) also reported by Verma et al., 2019 [162], reflecting a higher prevalence of obesity and associated metabolic disorders in men within the Asian Indian population. Studies suggest that male gender may predispose individuals to higher levels of central adiposity and insulin resistance (Singh et al., 2022) [16].

The majority of the study population (66.67%) exhibits insulin resistance (HOMA-IR \geq 2) which was reported similarly by Singh et al., 2022 of 65% cases with raised values of HOMA-IR \geq 2 [15], highlighting the prevalence of this condition among obese non-diabetic Asian Indians. HOMA-IR serves as a reliable marker for assessing insulin sensitivity and predicting diabetes risk in such populations (Gupta et al., 2020) [14].

Significant differences in FBS levels between insulin-sensitive and resistant groups similarly quoted by Singh et al., 2022) [13] who underscore the role of HOMA-IR in predicting glucose intolerance. These findings are consistent with previous studies linking elevated HOMA-IR with impaired fasting glucose (Gupta et al., 2020) [12].

The association between elevated HbA1c levels and insulin resistance was also observed by Verma et al., 2019 [12] highlights the utility of HOMA-IR in identifying individuals at risk of diabetes. These results support the use of HbA1c as a marker for long-term glycemic control and diabetes risk assessment (Singh et al., 2022) [11].

Elevated fasting insulin levels in insulin-resistant individuals, Gupta et al., 2020 also observed higher insulin levels similar to our study [9] which underscore the compensatory hyperinsulinemia characteristic of early insulin resistance. This finding emphasizes the role of HOMA-IR as a practical tool in clinical settings for assessing insulin sensitivity (Verma et al., 2019) [10].

Differences in triglycerides and HDL cholesterol levels between insulin-sensitive and resistant groups highlight the role of dyslipidemia in insulin resistance. Elevated triglycerides and low HDL levels are associated with increased cardiovascular risk as reported by Gupta et al., 2020 [20].

These findings collectively underscore the complex interplay between obesity, insulin resistance, and associated metabolic parameters in the Asian Indian population, providing insights into potential avenues for targeted interventions and management strategies.

The various anthropometric measures including weight, hip circumference, and WHR show statistically significant differences between insulin-sensitive and insulin-resistant groups. Higher weight (p = 0.007), hip circumference (p < 0.001), and WHR (p < 0.001) are noted in the insulin-resistant group, emphasizing their potential as indicators of metabolic dysfunction and insulin resistance, as supported by studies by Tan et al. (2020) [19].

Overall, this study underscores the complex interplay between obesity indices and insulin resistance, highlighting BMI and WC as prominent markers in assessing metabolic health



among this patient cohort. Further research is warranted to elucidate additional factors influencing insulin sensitivity and resistance in diverse clinical populations.

Conclusion:

The study population consisted of patients predominantly from an older age group, with a higher percentage of males. The mean BMI indicated a high prevalence of obesity, and both waist circumference and waist-hip ratio were closely linked to insulin resistance. Elevated fasting blood sugar, HbA1c, and fasting insulin levels were significantly associated with insulin resistance, as were higher triglyceride levels and lower HDL cholesterol in the lipid profile. Components of metabolic syndrome, including abdominal obesity, low HDL, and high triglycerides, further underscored the association with insulin resistance. These findings highlight the importance of obesity indices, lipid profile, blood sugars, and metabolic syndrome in understanding and managing insulin resistance within this patient group.

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References:

- 1. Chinn S, Rona RJ. Prevalence and trends in overweight and obesity in three cross sectional studies of British children, 1974–94. BMJ. 2001; 322(7277):24–6.
- 2. Pinhas-Hamiel O, Dolan LM, Daniels SR, Standiford D, Khoury PR, Zeitler P. Increased incidence of non-insulin-dependent diabetes mellitus among adolescents. The Journal of pediatrics. 1996; 128 (5):608–15.
- 3. Bonadonna RC, Leif G, Kraemer N, Ferrannini E, Prato SD, DeFronzo RA. Obesity and insulin resistance in humans: a dose-response study. Metabolism. 1990; 39(5):452–9.
- 4. Hillier TA, Pedula KL. Characteristics of an Adult Population With Newly Diagnosed Type 2 Diabetes The relation of obesity and age of onset. Diabetes care. 2001; 24(9):1522–7.
- 5. Sinha R, Fisch G, Teague B, Tamborlane WV, Banyas B, Allen K, et al. Prevalence of impaired glucose tolerance among children and adolescents with marked obesity. New England Journal of Medicine. 2002; 346(11):802–10.
- 6. GøGel RJ, Jensen SM, Freague B, Tamborlane WV, Banyas B, Allen K, et al. Prevalence of impaired glucose tolerance among children and adolescents with



marked obesity. New England journal of medicine. 2002 Mar 14;346(11):802-10.

- 7. Lee HJ, Shin G, Park SH, Cho HK. Insulin Resistance and Visceral Fat Obesity in Hyperlipidemia. Korean Circulation Journal. 1999; 29(7):673–9.
- 8. Cho H, Shin G, Koo B, Kim SS, Huh KB, Kim H, et al. Insulin resistance in middle aged normotensive offspring of the hypertensive parents in Korea. Korean Circulation Journal. 1997; 27(11):1087–95.
- 9. Matthews D, Hosker J, Rudenski A, Naylor B, Treacher D, Turner R. Homeostasis model assessment: insulin resistance and d tensive parents in Korea. Korean Circulation Journal. 1997;27(11ions in man. Diabetologia. 1985; 28(7):412–9.
- 10. Keskin M, Kurtoglu S, Kendirci M, Atabek ME, Yazici C. Homeostasis model assessment is more reliable than the fasting glucose/insulin ratio and quantitative insulin sensitivity check index for assessing insulin resistance among obese children and adolescents. Pediatrics. 2005; 115(4):e500–e3. PMID: 15741351
- 11. Moon JS, Lee SY, Nam CM, Choi J-M, Choe B-K, Seo J-W, et al. 2007 Korean National Growth Charts: review of developmental process and an outlook. Korean Journal of Pediatrics. 2008; 51(1):1–25.
- 12. Lee SY, Kim YN, Kang YJ, Jang M-J, Kim J, Moon JS, et al. The methodology for developing the 2007 Korean growth charts and blood pressure nomogram in Korean children and adolescents. Korean Journal of Pediatrics. 2008; 51(1):26–32.
- 13. Nguyen QM, Srinivasan SR, Xu J-H, Chen W, Berenson GS. Changes in risk variables of metabolic syndrome since childhood in pre-diabetic and type 2 diabetic subjects the Bogalusa Heart Study. Diabetes Care. 2008; 31(10):2044–9.
- 14. Franks PW, Hanson RL, Knowler WC, Moffett C, Enos G, Infante AM, et al. Childhood predictors of young-onset type 2 diabetes. Diabetes. 2007; 56(12):2964–72.
- 15. Shalitin S, Abrahami M, Lilos P, Phillip M. Insulin resistance and impaired glucose tolerance in obese children and adolescents referred to a tertiary-care



center in Israel. International Journal of Obesity. 2005; 29(6):571–8.

- 16. World Health Organization (WHO). 10 Facts on obesity. 2016. Retrieved from https://www.who.int/features/factfiles/obesity/facts/en/
- 17. Capodaglio, P., & Desity: A disabling disease or a condition favoring disability? European Journal of Physical and Rehabilitation Medicine. 2013; 49(3), 395–398.
- 18. Cefalu, W. T., Bray, G. A., Home, P. D., Garvey, W. T., Klein, S., Pi-Sunyer, F. X. Ryan, D. H., et al. Advances in the science, treatment, and prevention of the disease of obesity: Reflections from a diabetes care editors' expert forum. Diabetes Care. 2015; 38(8), 1567–1582.
- 19. World Health Organization. Nutrition, overweight and obesity: factsheet on Sustainable Development Goals (SDGs): health targets. World Health Organization. Regional Office for Europe; 2024.
- 20. Chaudhary M, Sharma P. Abdominal obesity in India: analysis of the National Family Health Survey-5 (2019–2021) data. The Lancet Regional Health-Southeast Asia. 2023 Jul 1;14-21.