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Prevalence of metabolically healthy obesity and healthy overweight and the associated factors in southern Iran: A population-based cross-sectional study

Erfan Taherifard[1] | Ehsan Taherifard[2] | Marjan Jeddi[3] | Alireza Ahmadkhani[2] | Roya Kelishadi[4] | Hossein Poustchi[5] | Abdullah Gandomkar[6] | Fatemeh Malekzadeh[6,7] | Zahra Mohammadi[5] | Hossein Molavi Vardanjani[1,8]

[1]MD-MPH Department, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Endocrinology and Metabolism Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

[4]Department of Pediatrics, Child Growth and Development Research Center, Research Institute for Primordial Prevention of Non-communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran

[5]Liver and Pancreatobiliary Diseases Research Center, Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran

[6]Non-communicable Disease Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

[7]Digestive Diseases Research Center, Digestive Diseases Research Institute, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

[8]Research Center for Traditional Medicine and History of Medicine, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Correspondence
Hossein Molavi Vardanjani, MD-MPH Department, Research Center for Traditional Medicine and History of Medicine, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.
Email: hosseinmolavi@ymail.com

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Abstract

Background and Aims: Obesity is considered a major growing threat to public health which could negatively affect the quality of life. The current cross-sectional study was conducted to investigate the population-based prevalence of metabolically healthy obesity (MHO) and healthy overweight (MHOW) and associated factors in southern Iran.

Methods: Baseline data from the Pars Cohort Study was analyzed. Metabolically healthy participants were identified based on the definition of the American Heart Association for the metabolic syndrome. The prevalence of MHOW and MHO and their 95% confidence intervals were estimated. Poisson regression was applied for the calculation of prevalence ratios (PRs).

Results: Gender- and age-standardized prevalences of MHOW and MHO were 6.3% (6.0%–6.6%) and 2.3% (2.1%–2.5%), respectively. The following factors were associated with being MHOW compared with those with normal weight: Being younger, female gender (1.31, 1.20–1.43), higher socioeconomic status, being noncurrent cigarette smoker (1.27, 1.11–1.45), low level of physical activity (1.14,

Erfan Taherifard and Ehsan Taherifard contributed equally to this study.

1.03–1.25), having normal overweight during adolescence, and overweight (1.35, 1.24–1.48) or obesity (1.68, 1.53–1.86) during young adulthood. We also found strong associations between MHO and younger age groups, female gender (2.87, 2.40–3.42), being married (1.57, 1.08–2.27), Fars ethnicity (1.25, 1.10–1.43), higher socioeconomic status, ever use of tobacco (1.14, 1.00–1.30), never use of opium (1.85, 1.19–2.86), lower physical activity (1.45, 1.20–1.72), being normal weight in 15-year body pictogram and being overweight (1.87, 1.59–2.20) or obese (3.20, 2.74–3.72) in 30-year body pictogram when considering those with normal weight or MHO.

Conclusion: Potentially modifiable factors including physical activity should be more emphasized. Furthermore, our study issued that it would be more reasonable that the prevention of unhealthy obesity be initiated before the development of MHO, where there are more protective factors and they could be more effective.

KEYWORDS

epidemiology, Iran, metabolic syndrome, obesity, overweight

1 | INTRODUCTION

Obesity is increasing and it is considered a major threat to public health in both developing and developed countries.[1] It has been estimated that the age-standardized prevalence of obesity is more than one-quarter of the population and as the prevalence of this major public health issue increases, its associated burdens including those physical and economic ones would increase.[2] Previous studies have reported that individuals with obesity are at higher risk of developing a wide range of comorbidities from cardiovascular diseases, gastrointestinal diseases, and other organ involvements to psychological disorders.[3] Besides, obesity and its associated comorbidities would pose a substantial economic burden on individuals and the healthcare system.[4] Therefore, obesity could negatively affect the quality of life and contribute to a higher rate of mortality.

However, all obese individuals do not share a single and homogenous phenotype.[5] In a part of these obese individuals, the morbidity and mortality rate is lower and there is a relatively more favorable cardiometabolic profile and lower levels of inflammation and endothelial dysfunction; this subset of obese individuals is referred to as metabolically healthy obesity (MHO) and it accounts for about 9.2% of obese men and 16.4% of obese women.[6] On the other hand, in the other subset of obesity, metabolically unhealthy obesity (MUO), obese individuals have developed metabolic syndrome.[7] In other words, body weight and body mass index (BMI), on their own, cannot accurately predict the metabolic risk and health status of all obese individuals; the definition of metabolic syndrome has, therefore, been used to better distinguish these two subsets of obese population.[8] However, as these two subsets, MHO and MUO, are not two distinct "biologically determined" groups of obese individuals, there is no general agreement upon the classification criteria.[9] In a systematic review by Rey-López et al., 30 definitions to determine the healthy status of obese individuals were found in the literature; however, most of them were quite similar, varying in cutoff values.[10] In a cohort study that included 4007 participants with obesity, the participants were followed for a mean of 18.7 years.[11] In this study, it was shown that the hazard ratios for the development of diabetes, coronary heart disease, and stroke were significantly higher among participants with unhealthy status. Besides, it was reported that they also had a higher hazard of mortality. MHO phenotype is believed to be a relatively dynamic or transient state and a large proportion of individuals with this phenotype will have transition to MUO.[12,13] In an 8-year follow-up study on participants with MHO, the metabolic health deteriorated in nearly half of the population, and more than 40% developed metabolic syndrome.[12] However, the exact physiopathology which underlies this transition is not completely understood.

We hypothesized that in the course in which the normal healthy individuals become MUO, there may be another state which is MHO in the majority of cases. Furthermore, MHO, even if not progress into MUO, is not a benign phenotype and is considered to be associated with intermediate cardiovascular risk and all-cause mortality between metabolically healthy normal weight and MUO.[5,14] Therefore, it is important to consider and manage sociodemographic and behavioral factors associated with MHO. Identification of these factors, particularly in the case that they are potentially modifiable, could be effective in the prevention or retardation of the comorbidities with obesity, especially cardiometabolic diseases.[14] Educational level, physical activity, lifestyle, and smoking are among those factors that have been reported to be associated with MHO prevalence.[15,16] However, the role of these factors and whether to have associations or not varies between different populations with different cultural, behavioral, and geographical backgrounds.

The current study was conducted to assess the population-based prevalence of MHO and factors that are associated with the prevalence in a rural southern area of Iran. Baseline data of the Pars Cohort Study (PCS) was used for interpretation and analysis in this cross-sectional study.

2 | METHODS

2.1 | Study design and setting

PCS is a prospective 10-year cohort study developed in 2012 by the collaboration of research teams from the Non-Communicable Disease Research Center of Shiraz University of Medical Sciences and the Digestive Diseases Research Institute of Tehran University of Medical Sciences. This study aimed to assess the prevalence and risk factors associated with non-communicable diseases in the Valashahr district. Valashahr district has over 40,000 residents mainly of Fars or Azari ethnicities. All residents of the district who were aged between 40 and 75 years old were eligible to be included in the study and therefore, all residents in this age group were contacted and invited to participate. Of a total number of 9721 residents, 9264 individuals decided to participate in the PCS and were referred to our center for the interview, physical examination, and biochemical tests. Further details about the design and protocol of PCS have been discussed elsewhere.[17] As PCS baseline data were used for this cross-sectional study, no further sample size calculation was done. We adhered to the recommendations outlined by Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) for cross-sectional studies in reporting our study.[18]

2.2 | Data collection

Data were gathered from all participants using a structured questionnaire in a face-to-face interview for self-reported data, performing physical examinations for measuring blood pressure (BP) and anthropometric indexes, and taking venous blood samples for biochemical data. The process of data collection was conducted by trained staff at the PCS center located in Valashahr and the details are described elsewhere.[17]

2.3 | Self-reported data

In the structured general questionnaire, the following self-reported data were collected from the participants: age with the date of birth (in full form), gender (male or female), marital status (single, married or being divorced or widowed), ethnicity (Fars or non-Fars), education (illiterate or literate), ever use of cigarette, current cigarette smoking and ever use of tobacco, opium, and alcohol. Participants were asked if they had any underlying diseases that had been diagnosed by a physician or healthcare provider. Furthermore, participants were asked to bring their current "medication bag" with them when referring for an interview and then the drugs each participant had were listed by a trained nurse. Besides, the participants were asked whether they are using each one of the listed drugs currently.

Socioeconomic status (SES) level and physical activity were also determined using the self-reported data. Accordingly, data on a series of assets including the housing conditions, living infrastructure, the householder's educational level, and ownership of a range of durable participants' individual and family assets were analyzed jointly and then, based on the composite measure, the participants were relatively ranked into four categories of SES level, low, low–middle, middle–high, and high SES.[19] The Iranian version of the international physical activity questionnaire was used for assessing physical activity data which then was converted to Metabolic Equivalent of Task (MET) score. Participants were categorized into three groups based on the MET scores including low (less than 600 MET-minutes/week), moderate (at least 600 MET-minutes/week), and high (at least 3000 MET-minutes/week).[20]

In addition, we instructed the participants to report their body size at the age of 15 and 30 years, as well as at the time of the interview, using a pictorial representation known as the body image pictogram, which ranges from very lean to obese.[21] The body image pictogram assigns scores between 1 and 7 for males and 1–9 for females. Its validity for estimating an individual's BMI in the Iranian population has been shown.[22] Furthermore, its validity has been specifically assessed within the PCS.[23,24] Based on the pictogram scores, participants are categorized into three groups: normal weight (scores 1, 2, and 3), overweight (score 4), and obesity (scores equal to or higher than 5).

2.4 | Physical measurements

After the interview, physical examinations were carried out for measurement of anthropometric indexes including height, weight, waist circumference (WC), hip circumference (HP), and measurement of BP. The measurements were conducted based on the standards of the World Health Organization's STEPwise approach to non-communicable risk factor surveillance.[25]

The participants were asked to wear light clothes when they referred to the PCS center for anthropometric measurements. Besides, before measurement of both height and weight, the participants were asked to take off their footwear and headgear. During the measurements, the height was measured to the nearest centimeter using a stadiometer (Seca Model 222), and the weight was measured to the nearest 0.1 kg using a digital scale (Seca Model 707). A constant tension tape (Seca) was used for the measurement of WC and HP. For WC measurement, the tension tape was positioned at the midpoint between the lowest palpable rib and the highest part of the iliac crest, and the measurement was done at the end of a normal expiration. Then, the tape was set on the widest part of the buttocks and HP was measured. For both WC and HP, the subjects were asked to relax their arms on both sides.

Afterward, the participants were asked to rest in a sitting position quietly for at least 5 min and then, BP was measured twice in each arm with an interval of a few minutes. Routine recommendations such as having an empty bladder, not using cigars or coffee, and so forth, for measurement of a correct BP were given to the patients before their attendance. The BP measurement was done by a Mercury Richter Sphygmomanometer (Diplomat 1002) and a Riester stethoscope (Duplex 4200) with appropriate-sized cuffs. The participants' arms were supported at the level of the heart at the time of measurement.

2.5 | Biochemical measurements

Sampling from the participants was performed in the morning and they were instructed to fast for 12 h before the sampling. A tube containing 15 mL of venous blood sample was obtained from each participant while was sitting. The sample was then centrifuged immediately. Fasting plasma glucose (FPG) and lipid profile including triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL), and low-density lipoprotein cholesterol (LDL) were measured using a chemical auto-analyzer (model BT1500; Biotecnica Instruments) with Pars Azmoon Company Kits.

2.6 | Variable definition

Variables were defined as below[26,27]:

1. BMI categories: BMI was calculated from the weight in kg divided by the square of the height in meters (m). Then, the score was categorized into four groups of underweight (<18.5 kg/m^2), normal weight (≥18.5 and <25 kg/m^2), overweight (≥25 and <30 kg/m^2), and obese (≥30 kg/m^2).[4]
2. Abnormal WC: WC of more than 102 and 88 cm were defined as abnormal WC for men and women, respectively.[27]
3. Abnormal waist-to-hip ratio (WHR): WHR more than 0.90 for males and more than 0.85 for females were considered as abnormal WHR.[3]
4. Abnormal waist-to-height ratio (WHtR): 0.55 and 0.62 were defined as cut-offs for abnormal WHtR in men and women, respectively.[28]
5. Abdominal obesity: abdominal obesity was considered for those who had an abnormal WC, abnormal WHR, or abnormal WHtR.
6. Raised BP: participants with systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg were considered as having raised BP.[29]
7. Raised FPG: raised FPG or fasting blood sugar (FBS) was defined as a blood sugar level of 110 mg/dL and above 110 mg/dL.[29]
8. Abnormal lipid profile: abnormal lipid profile was considered as either of the following: raised total cholesterol (≥200 mg/dL), high low-density lipoprotein (LDL, ≥200 mg/dL), low high-density lipoprotein (HDL, <40 mg/dL for men and <50 mg/dL for women), raised triglyceride (≥150 mg/dL).[26]
9. Polypharmacy: polypharmacy was defined as a concurrent use of five or more drugs.[30]
10. Multimorbidity: multimorbidity was defined as having two or more underlying diseases.[31]
11. Metabolic syndrome: metabolic syndrome was determined by the American Heart Association (AHA). Based on AHA criteria, individuals who fulfill at least three of the following criteria are labeled to have metabolic syndrome: WC of more than 89 and 79 cm in men and women respectively, raised TG (≥150 mg/dL), low HDL (<40 mg/dL for men and <50 mg/dL for women), SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg or those who are currently on medication for hypertension, plasma venous sugar >100 mg/dL or where the participant is currently on medication for diabetes mellitus. The Anatomical Therapeutic Chemical (ATC) classification system was used for the determination of whether the participants were on medication for metabolic syndrome components.[32]
12. Metabolically healthy overweight (MHOW) and MHO: MHOW and MHO were classified based on the definitions of BMI and metabolic syndrome.[33,34] Participants categorized as overweight were further divided into two groups: MHOW and metabolically unhealthy overweight, determined by the presence or absence of metabolic syndrome. Similarly, obesity groups, MHO and MUO, were identified based on the criteria for metabolic syndrome.

2.7 | Statistical analysis

Data management and analysis were performed using Stata software version 16 (developed by StataCorp). In our study, we followed the recommendations outlined by Assel et al. for reporting statistical details.[35] There was less than 5% missing across all the variables in this study and the observed pattern of missing data appeared to be completely at random. Therefore, we decided not to use any imputation techniques. Comorbidities with prevalence of less than 0.1% of the study population were removed from the quantitative analyses. The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test which indicated that data distribution was normal for all the continuous variables. Descriptive statistics were estimated. For categorical variables, their frequencies and relative frequencies were calculated and for continuous variables, means and standard deviations (SD) were calculated. The world standard population distribution in 2000–2025 was used for the estimation of age-standardized prevalence of MHO and MHOW and their confidence intervals (CIs). The χ^2 test assumptions were met and therefore, was employed to assess the univariate associations between various categorical variables and the outcome variables of MHO and MHOW. A 2-sided $p < 0.05$ was considered as statistically significant for the univariate analyses.

Furthermore, we applied the modified Poisson regression (Poisson regression with robust standard errors) modeling for the determination of the independent associative factors of MHOW and MHO. Four multivariable models were constructed in this study aiming to identify the following factors: (1) factors associated with being MHOW among normal weight individuals and those with MHOW, (2) factors associated with being MHOW among all overweight individuals, (3) factors associated with MHO among normal weight individuals and those with MHO, and (4) factors associated with MHO among all obese individuals. In our study, we adopted a comprehensive approach to select variables for the multivariable models. This approach involved two key criteria: clinical and evidential relevance and initial statistical associations. We carefully considered the clinical significance and established evidence in the literature to identify variables that were conceptually linked to our study's objectives. This ensured that the selected variables were not only statistically relevant but also clinically meaningful. Simultaneously, we examined the initial statistical associations of variables with the outcomes, MHOW and MHO, in our univariate analyses. Variables with a univariate p value of less than 0.3 were included in the selection process to avoid overlooking potentially relevant factors. Notably, it is essential to highlight that certain variables, despite having significant associations (p value of less than 0.05) with the outcomes in the univariate analyses, such as raised blood pressure, raised fasting blood sugar, abnormal waist-to-hip ratio, and abdominal obesity, were not included in the multivariable models. These variables were themselves components of the metabolic syndrome, which is integral to the definition of our outcomes. The final saturated model was fitted using a backward elimination technique. Then, the adjusted prevalence ratios (APRs) and their 95% CIs were estimated.

2.8 | Ethical considerations

This study was conducted in accordance with the principles outlined in the 1964 Helsinki Declaration and its later amendments and written informed consent was obtained from all the participants. The PCS, from which we derived the baseline data for this research, had previously obtained ethical approval from the ethical committees of both Shiraz University of Medical Sciences and Tehran University of Medical Sciences. However, it is important to note that for our present study utilizing only the baseline data, we acquired a separate and distinct ethical approval from the ethical committee of Shiraz University of Medical Sciences, under the ethical code IR.SUMS.MED.REC.1400.576. This additional approval specifically pertains to the use of the baseline data in our current study, ensuring compliance with all ethical standards and regulations.

3 | RESULTS

Data from 9264 participants including 4277 men (46.2%) and 4991 women (53.8%) were analyzed in the study. The mean age of the study participants was 52.6 ± 9.6 years. Crude prevalence of MHOW was 19.6% (95% CI, 18.7%–20.5%). Gender- and age-standardized prevalence was 6.3% (95% CI, 6.0%–6.6%). Age-standardized prevalence was 6.1% (95% CI, 5.7%–6.5%) and 6.4% (95% CI, 6.0%–6.7%) for men and women, respectively. Besides, the crude prevalence of MHO was 7.5% (95% CI, 6.6%–8.0%). Gender- and age-standardized prevalence was 2.3% (95% CI, 2.1%–2.5%). Age-standardized prevalence was 1.2% (95% CI, 1.0%–1.4%) and 3.3% (95% CI, 3.0%–3.6%) for men and women, respectively (Table 1).

Table 2 demonstrates the prevalence of MHOW and MHO and their associations with different diseases that the participants of our study had. The analyses showed that the prevalence of MHOW was significantly higher among patients with some diseases including participants with a recent history of anxiety or depressive disorder, sleep disorder, hypertension, diabetes mellitus, heart disease, and irritable bowel syndrome (all $p < 0.05$). Besides, there was a statistically significant association between MHOW and multimorbidity ($p < 0.001$). About half of those with MHOW (50.0%; 95% CI, 46.8%–53.4%) were shown to have multimorbidity. Furthermore, there were significant associations between having musculoskeletal disorders, insomnia, diabetes mellitus, hypertension, and cardiovascular disease and MHO (Table 2).

Based on the multivariate analysis, having an obese body image in a 30-year pictogram had the highest APR for association with being MHOW when only considering those with normal weight or MHOW participants (APR, 1.68; 95% CI, 1.53–1.86). Other factors with significant association with being MHOW were being in an SES other than low SES, having an overweight body image in a 30-year pictogram (APR, 1.35; 95% CI, 1.24–1.48), female gender (APR, 1.31; 95% CI, 1.20–1.43). The prevalence of having an obese or overweight body image in a 15-year pictogram, having a high level of physical activity, current use of cigarettes, and being elderly were significantly higher in the participants with normal weight (second column of Table 3). The second multivariable analysis was conducted only among the participants with overweight. Higher age groups (participants between 50 and 60 years and those above 60 years), female gender, being married, widowed, or divorced, Fars ethnicity, low level of physical activity, having normal weight in 15-year body image pictogram and being overweight or obese in 30-year body image pictogram were associated with an unhealthy metabolic status (third column of Table 3). The crude prevalence ratio of associated factors with the prevalence of MHOW and MHO is documented in Table S1.

A similar pattern was also observed when comparing obese individuals and those with normal weight. When only considering individuals with normal weight or MHO, there was a strong association between being MHO and younger age groups, female gender, being married, Fars ethnicity, higher SES, ever use of tobacco, never use of opium, lower level of physical activity, being overweight or obese in 15-year body image pictogram and being normal weight in 30-year body image pictogram (fourth column of Table 3). The female gender had the highest adjusted PR (APR, 2.87; 95% CI, 2.40–3.42). The last logistic analysis was on the participants with obesity. Among the obese population, only being elder (APR, 0.69;

TABLE 1 Characteristics of the participants enrolled in the Pars Cohort Study.

	Total *n* (%)	Overweight *n* (%: CI)	Metabolically healthy overweight *n* (%: CI)	*p* Value	Obese *n* (%: CI)	Metabolically healthy obese *n* (%: CI)	*p* Value
Total	9264 (100)	3442 (37)	1817 (19)		1675 (18)	692 (7)	
Age (years)				<0.001[a]			<0.001[a]
40–49	4217 (45)	1658 (39: 37, 41)	1013 (24: 22, 25)		826 (19: 18, 20)	418 (9: 8, 10)	
50–59	2810 (30)	1049 (37: 35, 39)	519 (18: 16, 20)		508 (18: 16, 19)	179 (6: 5, 7)	
60+	2242 (24)	735 (32: 30, 35)	285 (12: 11, 14)		341 (15: 13, 16)	95 (4: 3, 5)	
Gender				0.149[a]			<0.001[a]
Male	4277 (46)	1428 (33: 31, 35)	811 (18: 17, 20)		386 (9: 8, 9)	161 (3: 3, 4)	
Female	4991 (53)	2014 (40: 38, 42)	1006 (20: 18, 21)		1289 (25: 24, 27)	531 (10: 9, 11)	
Marital status				0.002[a]			0.151[a]
Single	297 (3)	107 (36: 29, 43)	69 (23: 18, 29)		44 (14: 10, 19)	21 (7: 4, 10)	
Married	8210 (88)	3030 (36: 35, 38)	1634 (19: 18, 20)		1477 (17: 17, 18)	628 (7: 7, 8)	
Being divorced or widowed	752 (8)	304 (40: 36, 45)	113 (15: 12, 18)		153 (20: 17, 23)	43 (5: 4, 7)	
Ethnicity				0.290[a]			<0.001[a]
Non-Fars	4047 (43)	2575 (63: 61, 66)	814 (20: 18, 21)		619 (15: 14, 16)	257 (6: 5, 7)	
Fars	5215 (56)	3245 (62: 60, 64)	1003 (19: 18, 20)		1056 (20: 19, 21)	435 (8: 7, 9)	
Socioeconomic status				<0.001[a]			<0.001[a]
Low	2408 (26)	762 (31: 29, 33)	385 (15: 14, 17)		338 (14: 12, 15)	145 (6: 5, 7)	
Low–middle	2490 (26)	913 (36: 34, 39)	497 (19: 18, 21)		372 (14: 13, 16)	127 (5: 4, 6)	
Middle–high	2043 (22)	763 (37: 34, 40)	407 (19: 18, 21)		425 (20: 18, 22)	185 (9: 7, 10)	
High	2291 (24)	1000 (43: 40, 46)	526 (22: 21, 25)		535 (23: 21, 25)	233 (10: 8, 11)	
Education				<0.001[a]			0.002[a]
Illiterate	4538 (48)	1610 (35: 33, 37)	760 (16: 15, 17)		845 (18: 17, 19)	300 (6: 5, 7)	
Literate	4732 (51)	1832 (38: 36, 40)	1057 (22: 21, 23)		830 (17: 16, 18)	392 (8: 7, 9)	
Ever cigarette use	1917 (20)	600 (31: 28, 33)	327 (17: 15, 19)	0.002[a]	151 (7: 6, 9)	60 (3: 2, 4)	<0.001[a]
Current use of cigarette	1296 (14)	385 (29: 26, 32)	215 (16: 14, 18)	0.003[a]	86 (6: 5, 8)	40 (3: 2, 4)	<0.001[a]
Ever tobacco use	3537 (38)	1353 (38: 36, 40)	679 (19: 17, 20)	0.409[a]	736 (20: 19, 22)	285 (8: 7, 9)	0.099[a]
Ever opium use	774 (8)	214 (27: 24, 31)	120 (15: 12, 18)	0.003[a]	56 (7: 5, 9)	19 (2: 1, 3)	<0.001[a]

TABLE 1 (Continued)

	Total *n* (%)	Overweight *n* (%: CI)	Metabolically healthy overweight *n* (%: CI)	*p* Value	Obese *n* (%: CI)	Metabolically healthy obese *n* (%: CI)	*p* Value
Ever alcohol use	196 (2)	81 (41: 32, 51)	42 (21: 15, 28)	0.519[a]	21 (10: 6, 16)	7 (3: 1, 7)	0.036[a]
Physical activity				0.028[a]			<0.001[a]
Mild	3060 (33)	1211 (39: 37, 41)	570 (18: 17, 20)		713 (23: 21, 25)	279 (9: 8, 10)	
Moderate	3056 (33)	1201 (39: 37, 41)	647 (21: 19, 22)		597 (19: 17, 21)	252 (8: 7, 9)	
High	3146 (33)	1030 (32: 30, 34)	600 (19: 17, 20)		365 (11: 10, 12)	161 (5: 4, 5)	
Raised triglyceride	3649 (39)	1619 (44: 42, 47)	423 (11: 10, 12)	<0.001[a]	909 (25: 23, 27)	172 (4: 4, 5)	<0.001[a]
Raised total cholesterol	3942 (42)	1585 (40: 38, 42)	755 (19: 17, 20)	0.350[a]	856 (22: 20, 23)	319 (8: 7, 9)	0.048[a]
High low-density lipoprotein	593 (6)	233 (39: 34, 45)	101 (17: 13, 20)	0.103[a]	146 (25: 21, 29)	45 (7: 5, 10)	0.906[a]
Low high-density lipoprotein	1373 (14)	597 (43: 40, 47)	84 (6: 4, 7)	<0.001[a]	352 (26: 23, 28)	39 (2: 2, 3)	<0.001[a]
Raised blood pressure	1446 (15)	567 (39: 36, 43)	126 (8: 7, 11)	<0.001[a]	384 (27: 24, 29)	46 (3: 2, 4)	<0.001[a]
Raised fasting blood sugar	1638 (17)	710 (43: 40, 47)	154 (9: 7, 11)	<0.001[a]	446 (27: 25, 30)	56 (3: 2, 4)	<0.001[a]
Polypharmacy	964 (10)	386 (40: 36, 44)	88 (9: 7, 11)	<0.001[a]	284 (29: 26, 33)	58 (6: 4, 7)	<0.071[a]
Abnormal waist-to-hip ratio	7426 (80)	3281 (44: 43, 46)	1695 (22: 21, 23)	<0.001[a]	1644 (22: 21, 23)	673 (9: 8, 9)	<0.001[a]
Abnormal waist-to-height ratio	3623 (39)	1824 (50: 48, 53)	878 (24: 23, 26)	<0.001[a]	1557 (43: 41, 45)	631 (7: 16, 19)	<0.001[a]
Abnormal waist circumference	3829 (41)	1872 (49: 47, 51)	871 (22: 21, 24)	<0.001[a]	1583 (41: 39, 43)	650 (16: 15, 18)	<0.001[a]
Abdominal obesity	7484 (81)	3310 (44: 43, 46)	1710 (23: 22, 24)	<0.001[a]	1670 (22: 21, 23)	688 (9: 9, 10)	<0.001[a]
15-year-old pictogram				0.532[a]			0.664[a]
Normal weight	7329 (79)	2765 (38: 36, 39)	1440 (19: 18, 20)		1340 (18: 17, 19)	557 (7: 6, 8)	
Overweight	912 (9)	290 (32: 28, 36)	170 (18: 15, 21)		159 (17: 15, 20)	64 (7: 5, 8)	
Obese	991 (10)	383 (39: 35, 43)	205 (20: 17,23)		171 (17: 15, 20)	69 (6: 5, 8)	
30-year-old pictogram				0.143[a]			<0.001[a]
Normal weight	5141 (55)	1749 (34: 32, 36)	979 (19: 17, 20)		622 (12: 11, 13)	274 (5: 4, 5)	
Overweight	2294 (24)	939 (41: 38, 44)	482 (21: 19, 22)		464 (20: 18, 22)	186 (8: 6, 9)	
Obese	1797 (19)	750 (42: 39, 45)	354 (19: 17, 21)		584 (32: 30, 35)	230 (12: 11, 14)	

[a]Calculated with χ^2 test.

TABLE 2 Prevalence of metabolically healthy overweight and metabolically healthy obesity among participants with chronic underlying diseases in the Pars Cohort Study.

	Total *n* (%)	Overweight *n* (%: CI)	Metabolically healthy overweight *n* (%: CI)	*p* Value	Obese *n* (%: CI)	Metabolically healthy obese *n* (%: CI)	*p* Value
Total	9264 (100)	3442 (37)	1817 (19)		1675 (18)	692 (7)	
Decayed teeth	6397 (69)	2416 (38: 36, 39)	1293 (20: 19, 21)	0.027[a]	1213 (19: 18, 20)	515 (8: 7, 8)	0.001[a]
Joint pain disease	5028 (54)	1930 (38: 37, 40)	969 (19: 18, 20)	0.361[a]	1062 (21: 20, 22)	410 (8: 7, 8)	0.006[a]
Back pain disease	4604 (49)	1776 (39: 37, 40)	922 (20: 18, 21)	0.325[a]	948 (20: 19, 22)	388 (8: 7, 9)	<0.001[a]
Anxiety	2744 (29)	1065 (39: 37, 41)	487 (17: 16, 19)	0.003[a]	552 (20: 18, 22)	202 (7: 6, 8)	0.794[a]
Gastrointestinal reflux disease	2325 (25)	909 (39: 37, 42)	438 (18: 17, 20)	0.274[a]	449 (19: 18, 21)	177 (7: 6, 8)	0.764[a]
Depression	1795 (19)	661 (37: 34, 40)	293 (16: 14, 18)	<0.001[a]	337 (19: 17, 21)	118 (6: 5, 7)	0.107[a]
Insomnia	1795 (19)	657 (37: 34, 40)	308 (17: 15, 19)	0.003[a]	302 (17: 15, 19)	104 (5: 4, 7)	0.003[a]
Hypertension	1513 (16)	624 (41: 38, 45)	105 (6: 5, 8)	<0.001[a]	411 (27: 25, 30)	47 (3: 2, 4)	<0.001[a]
Irritable bowel syndrome	1067 (11)	387 (36: 33, 40)	183 (17: 14, 19)	0.025[a]	184 (17: 15, 20)	79 (7: 5, 9)	0.903[a]
Heart disease	961 (10)	378 (39: 35, 44)	111 (11: 9, 13)	<0.001[a]	214 (22: 19, 25)	43 (4: 3, 6)	<0.001[a]
Diabetes mellitus	874 (9)	403 (46: 42, 51)	56 (6: 4, 8)	<0.001[a]	216 (25: 22, 28)	28 (3: 2, 4)	<0.001[a]
Functional constipation	752 (8)	269 (36: 32, 40)	139 (18: 15, 21)	0.414[a]	159 (21: 18, 25)	59 (7: 5, 10)	0.684[a]
Obstructive lung disease	353 (3)	147 (42: 35, 49)	68 (19: 14, 24)	0.864[a]	73 (20: 16, 26)	28 (7: 5, 11)	0.737[a]
Renal failure	103 (1)	40 (39: 28, 53)	15 (14: 8, 24)	0.194[a]	28 (27: 18, 39)	13 (12: 6, 21)	0.046[a]
Stroke	166 (1)	53 (32: 24, 42)	24 (14: 9, 21)	0.091[a]	38 (23: 16, 31)	8 (4: 2, 9)	0.190[a]
Cancer	107 (1)	39 (36: 26, 50)	20 (18: 11, 28)	0.808[a]	22 (21: 13, 31)	7 (6: 2, 13)	0.713[a]
Liver disease	25 (0.2)	11 (44: 22, 79)	3 (12: 2, 35)	0.337[a]	3 (12: 2, 35)	0 (0: 0, 14)	0.155[a]
Rheumatic heart disease	17 (0.1)	4 (24: 6, 60)	1 (5: 0.1, 32)	0.153[a]	7 (41: 17, 85)	3 (17: 3, 51)	0.110[a]
Multimorbidity	5247 (57)	2030 (39: 37, 40)	909 (17: 16, 18)	<0.001[a]	1063 (20: 19, 22)	372 (7: 6, 8)	0.117[a]

[a]Calculated with χ^2 test.

TABLE 3 Adjusted prevalence ratio of associated factors of metabolically healthy overweight and metabolically healthy obesity in participants enrolled in the Pars Cohort Study.

Outcome	Healthy overweight		Healthy obesity	
Compared group	Normal weight	Unhealthy overweight	Normal weight	Unhealthy obese
Age (years) (Ref.[36–45])				
50–59	0.80 (0.74–0.87)	0.80 (0.75–0.86)	0.69 (0.59–0.81)	0.69 (0.60–0.79)
60+	0.54 (0.48–0.61)	0.67 (0.60–0.74)	0.42 (0.34–0.52)	0.55 (0.45–0.66)
Gender (ref. male)				
Female	1.31 (1.20–1.43)	0.90 (0.84–0.96)	2.87 (2.40–3.42)	
Marital status (ref. single)				
Married		0.84 (0.72–0.97)	1.57 (1.08–2.27)	
Being divorced or widowed		0.70 (0.57–0.87)	1.20 (0.76–1.91)	
Ethnicity (ref. non-Fars)				
Fars		0.91 (0.86–0.97)	1.25 (1.10–1.43)	
Socioeconomic status (ref. Low)				
Low–middle	1.24 (1.11–1.38)		0.91 (0.74–1.12)	0.79 (0.66–0.95)
Middle–High	1.33 (1.19–1.49)		1.61 (1.33–1.94)	0.96 (0.82–1.13)
High	1.60 (1.44–1.79)		1.85 (1.54–2.23)	0.92 (0.78–1.07)
Current use of cigarette	0.79 (0.69–0.90)			
Ever tobacco use			1.14 (1.00–1.30)	
Ever opium use			0.54 (0.35–0.84)	
Physical activity (ref. mild)				
Moderate	1.03 (0.95–1.13)	1.09 (1.01–1.18)	0.89 (0.77–1.02)	
High	0.88 (0.80–0.97)	1.13 (1.04–1.22)	0.69 (0.58–0.83)	
15-year-old pictogram (ref. normal weight)				
Overweight	0.81 (0.71–0.92)	1.21 (1.09–1.34)	0.66 (0.54–0.82)	
Obese	0.82 (0.72–0.92)	1.20 (1.08–1.33)	0.50 (0.40–0.62)	
30-year-old pictogram (ref. normal weight)				
Overweight	1.35 (1.24–1.48)	0.90 (0.84–0.97)	1.87 (1.59–2.20)	
Obese	1.68 (1.53–1.86)	0.83 (0.76–0.91)	3.20 (2.74–3.72)	

95% CI, 0.60–0.79 and APR, 0.55; 95% CI, 0.45–0.66 for age between 50 and 60 years and age above 60 years, respectively) and having low–middle SES (APR, 0.79; 95% CI, 0.66–0.95) were associated, though negatively, with being healthy (fifth column of Table 3).

4 | DISCUSSION

Literature suggests that a cascade of events exists for the development of both obesity and metabolic syndrome.[46] When excess weight is gained by an individual, subclinical cardiometabolic and vascular dysfunction has already been formed and there is an increased risk of incidence of cardiovascular events and mortality. Obesity, insulin resistance, and sympathetic overactivity, which could also result from obesity, are the principal causative factors in the development of metabolic syndrome.[47,48] Therefore, progression toward unhealthy metabolic status is more probable in overweight or obese individuals; however, metabolic syndrome could even develop in the absence of excess weight but it is believed that this is not the dominant sequence.[48] Studies have shown that at the overweight or obesity stage, even in the absence of clinical criterion of the metabolic syndrome, there is no "pure healthy" metabolic status[5] and therefore, the associated factors which could protect against the cardiometabolic abnormalities may not preserve their association when an individual gets fat. A similar pattern of associated factors was seen in our study; many factors that were associated with MHO when compared with participants with normal weight, were not associated with a lower prevalence of MUO among the obese population. This issue emphasizes the importance of the identification of risk factors associated with MHO and the introduction of preventive measurements even before the development of MHO.

The study showed that the female gender is more prevalent among those with overweight or obesity than the population with normal weight. Besides, the female gender was associated with a higher rate of metabolically unhealthy overweight in the overweight population. In our study, women had a significantly higher prevalence of metabolic syndrome. Gender differences in the prevalence of abnormal weight and metabolic syndrome have been found in previous studies. However, the gender-specific effect is not consistent across studies.[36,37,49] These different reports may be mainly due to the different lifestyles of females in different communities. In our target study population, women are less likely to be involved in occupations requiring high-intensity physical activity and therefore, they may be more prone to have excess weight. Besides, there is a higher prevalence of abdominal obesity and lower HDL cholesterol levels in women than in men which could contribute to this gender difference.[36,38]

In this study, Fars ethnicity was associated with higher prevalence of MHO when compared to the population with normal weight. Furthermore, this ethnicity was associated with having an unhealthy metabolic status among the overweight population. It seems that this finding is in line with the role of SES in our population. Fars ethnicity constitutes more than half of the population and our data showed that there is a statistically significant relationship between Fars ethnic group and higher levels of SES. Adults with high levels of income have higher access to energy-dense foods.[39,40] Besides, these individuals have a higher risk of living a sedentary lifestyle.[40] Similar results were also found in other studies and they reported a higher risk of excess weight among families with high levels of SES. Furthermore, individuals from ethnic minorities are more steadfast in their cultural nutritional preferences whereas those from wealthier families and also those from ethnic majorities, for both participants with Fars ethnicity in our study, are known to be more susceptible to adopting a Western dietary pattern.[41,42]

Furthermore, the current study showed that current cigarette smoking and ever use of opium were associated with lower body weight when comparing those with MHOW and MHO and individuals with normal weight. These findings are in line with reports from previous studies.[43] Adult smokers are less likely to gain weight and it is reported that their body weight is usually about 5 kg less than nonsmokers.[43,44] This issue could be explained by the cigarette smoker's less desire for food which in turn results from nicotine introduction and its associated early satiety and fullness.[45] Besides, it has been reported that nicotine increases the body's basal metabolic rate and decreases the metabolic efficiency.[50] Similarly, opium use is previously observed to be associated with poor nutrition and lower body mass.[51] Contrary to current cigarette use, a positive relationship between ever use of tobacco and weight gain was seen in our study. The finding could be rooted in the fact that tobacco ever use also covers those who quit the use of tobacco products. Tobacco cessation is found to be associated with weight gain.[52] However, this contrary finding could also be due to the residual confounding effect of age on tobacco ever use. In the study, there was a statistically significant association between tobacco ever use and age group; nearly half of those above 60 years old reported ever use of tobacco. Unlike our expectations, neither the use of cigarettes or tobacco nor the use of opium was associated with the development of unhealthy cardiometabolic status among overweight and obese individuals. It has been reported in the literature that both tobacco use and opium use increase the risk of development of metabolic syndrome by alteration in the BP and the metabolism of glucose and lipids.[53,54] Further studies are required to assess the relationship between the use of these substances and unhealthy cardiometabolic status.

Our study showed that a higher level of physical activity was associated with lower body weight. Furthermore, the results showed that when assessing the individuals with overweight, higher levels of physical activity were more prevalent among those with MHOW. The positive effect of physical activity on weight reduction is one of those well-studied relationships. Regular physical activity has been reported to result in a healthier cardiometabolic profile including BP, blood sugar, and lipid profile which are the components in the definition of metabolic syndrome.[43,55] Besides, physical inactivity and sedentary are considered important risk factors for the development of cardiovascular and alimentary tract system diseases.[56] Contrary to most factors assessed in the current study, physical activity could be modifiable, and therefore, physical activity should be part of any plan for weight loss and prevention of cardiometabolic diseases.

The study also demonstrated that having abnormal weight in young adulthood was associated with the current BMI status of the participants. In the current study, we used a validated body image pictogram to assess body fatness at the age of 15 and 30 years which relies on the visual rather than numeric memory of body size; this method is believed to decrease bias of recalling.[22] This method is particularly more useful in cross-sectional study designs in which there is no record of body weights and the target population has a low level of education. Besides, the use of pictogram for the age of 15 years would account for variations in the stages of maturation of the adolescents, especially for males. Although the body image pictogram at the age of 30 years was strongly correlated with adulthood BMI status and the status of metabolic health there was an inverse association between a higher body image pictogram score at the age of 15 years and adulthood overweight or obesity. For those individuals who are overweight or obese in young adulthood, it is considered that they may have adopted an unhealthy lifestyle. In other words, many components of lifestyles that are formed before adulthood or at the earliest stage of adulthood would remain fixed for lifelong[57,58]; however, this issue seems not to be accurate for these participants. Although studies have reported that overweight/obesity during adolescence is associated with higher BMI in adulthood, these studies are mainly conducted among populations where the majority are from urban areas.[59] Our study was conducted in a rural southern area of Iran in which the abnormal weight in adolescence may be associated with negative perspectives and the individuals are mainly occupied with jobs requiring more physical activity and energy expenditure[60]; therefore the change in weight between adolescence and young adulthood and the life habit formed within this timespan seems to have more predicting value for adulthood weight status. However, further studies, particularly with longitudinal design, are required to shed light on this issue.

This study had several limitations. The primary and most significant limitation is that our study solely compared different related variables between individuals with different body weights and metabolic statuses and did not assess the dynamic process. Consequently, the findings should be approached with caution when considering their applicability to management and prevention strategies. However, this limitation comes from the cross-sectional nature of the study's methodology. The second limitation stems from the reliance of a portion of our data set on self-reported data from the study participants, particularly regarding their underlying health conditions as diagnosed by a physician. This reliance on self-reporting introduces the possibility of undiagnosed or underreported health conditions, which could potentially introduce confounding factors into the associations under investigation. Furthermore, it is important to acknowledge that this study, while population-based, focused on a specific district primarily comprised of individuals of Fars or Azari ethnicities. This homogeneity within the population may constrain the applicability of the findings to populations with diverse ethnic backgrounds or residing in different geographical regions.

5 | CONCLUSION

Our findings showed factors that could be associated with weight excess and unhealthy metabolic status. Among these factors, potentially modifiable factors including physical activity should be more emphasized by healthcare providers. Furthermore, our findings propose that the prevention of MUO should be initiated before the development of MHO, where the protective factors could be more effective and there is a need for more in-depth strategies. Besides, studies are still required, particularly those longitudinal ones, to assess factors associated with the transition toward weight excess and unhealthy metabolic status.

AUTHOR CONTRIBUTIONS

Erfan Taherifard: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; writing—original draft; writing—review and editing. **Ehsan Taherifard**: Conceptualization; data curation; investigation; methodology; project administration; writing—original draft; writing—review and editing. **Marjan Jeddi**: Conceptualization; investigation; methodology; supervision; writing—review and editing. **Alireza Ahmadkhani**: Data curation; formal analysis; methodology; validation; writing—original draft; writing—review and editing. **Roya Kelishadi**: Conceptualization; methodology; supervision; writing—review and editing. **Hossein Poustchi**: Conceptualization; data curation; funding acquisition; investigation; writing—review and editing. **Abdullah Gandomkar**: Conceptualization; data curation; methodology; resources; writing—review and editing. **Fatemeh Malekzadeh**: Conceptualization; data curation; methodology; resources; writing—review and editing. **Zahra Mohammadi**: Data curation; investigation; methodology; validation; writing—review and editing. **Hossein Molavi Vardanjani**: Conceptualization; formal analysis; funding acquisition; investigation; methodology; software; supervision; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The datasets used for statistical analyses in this study are not publicly available due to potential ethical issues and the Iran Cohort Consortium's regulations. However, it could be accessible upon a reasonable request to the corresponding author or request through the website of Iran Cohort Consortium at "https://irancohorts.ir/collaborations/join-projects/".

TRANSPARENCY STATEMENT

The lead author Hossein Molavi Vardanjani affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

ORCID

Erfan Taherifard http://orcid.org/0000-0002-9101-0321
Ehsan Taherifard https://orcid.org/0000-0002-8438-4990
Alireza Ahmadkhani https://orcid.org/0000-0001-8301-0455
Hossein Molavi Vardanjani https://orcid.org/0000-0001-7024-8894

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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