ORIGINAL ARTICLE

Metabolically Unhealthy Phenotype and Its Determinants: A Population-based Study in Southern Iran

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Abstract

Background: The overall prevalence of metabolically unhealthy (MU) phenotype in Iranian adults is a matter of debate. This study aimed to estimate the prevalence and determinants of metabolically unhealthystate in people over 30 years old in the general population in Southern Iran.

Methods: In this cross-sectional population-based study, 891 participants aged ≥30 were selected using a multi-stage cluster sampling method. The study examined age, sex, education, marital status, smoking behavior, weight, height, blood pressure, fasting blood sugar, and lipid profiles. MU was defined as the existence of at least two of four constituents of metabolic abnormalities based on ATP III criteria. Data analysis was carried out in Stata version 14. Finally, a logistic regression was performed to identify the risk factors for MU prevalence.

Results: The overall prevalence of MU was 49.4%, corresponding to 37.5%, 55.6%, and 60.2% of normal weight, overweight, and obese participants, respectively. MU prevalence significantly increased from 30.6% in participants aged 30-39 years to 69.7% in participants aged 60 years or older. The results of multivariate logistic regression showed that dyslipidemia (OR=2.98, CI95%:2.13-4.16), high LDL (OR=2.73, CI95%:1.77-4.20), obesity (OR=2.83, CI95%:1.84-4.36), overweight (OR=2.13, CI95%:1.53-2.98), and higher age (OR=1.04, CI95%:1.03-1.05) was positively associated with the MU state.

Conclusion: Metabolically unhealthy state is a public health problem in the study area. In terms of public health, screening for obesity and other metabolic disorders should be regularly performed in clinical practice to take appropriate preventive measures.

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Introduction

One of the greatest global health problems is metabolic abnormalities. Metabolic disorders such as metabolic syndrome and dyslipidemia are corroborated to be pertinent to the development of diabetes mellitus. As used for defining metabolic syndrome, metabolic abnormalities are established on conditions to that of the National Cholesterol Education Program Expert Panel in Adults Adult Treatment Panel III.[1] These conditions are comprised of fasting triglyceride, high-density lipoprotein cholesterol (HDL-C), systolic and or diastolic blood pressure, and fasting blood sugar (FBS). Individuals with at least two of these disorders are defined as metabolically unhealthy (MU) people.

Results suggest that MU individuals have an increased risk of diabetes mellitus and heart disease events or death compared to participants with a metabolically healthy (MH) state.[2-4] The risk of cardiovascular disease events and all-cause mortality are significantly elevated in MU individuals in comparison to MH ones.[5]

In the study, 30291 Chinese individuals aged 20-99 years were surveyed, in which MU was detected in 33.5% of the participants.[6] Likewise, in another study on 7632 participants aged 18-85 years and found that 38.9% had MU.[7] In another study (CODING study) with 1907 participants aged 20-79 years, the prevalence of MU was 39.1%.[8] However, a study showed that among 2000 individuals,12.8% of had at least two components of metabolic syndrome.[9]

In a study carried out on 1000 adults in the Mazandaran province of Iran, the prevalence of MU was found to be 69.2%.[10] However, in another study in Jahrom, Fars Province in southern Iran, 28.8% of the participants aged 30 or older had metabolic syndrome.[11] In this area, the prevalence of hypertension and type 2 diabetes mellitus, as components of cardio-metabolic risk factors, were 35.4% and 11.9%, respectively and 20% of pre-diabetes participants were obese.[12-14] Other components, such as hypertriglyceridemia and low HDL, were 19.8% and 32.3% among men and 16.2% and 51.3% in women, respectively.[15] According to the prevalence of cardio-metabolic risk factors in previous studies in the study area and the importance of early detection of metabolic syndrome, this study was performed. Therefore, this study aimed to estimate the prevalence and associated factors of metabolically unhealthy individuals aged 30 years or older.

Methods

Source of Data/Participants

This cross-sectional study was conducted using data of a Jahrom heart study (JHS) among participants aged 30-85 years old of the urban adult population, in Jahrom, Fars province, southern Iran. In this survey, 1000 participants were selected using a multistage cluster random sampling approach.[16] Given the number of comprehensive urban health centers, Jahrom was divided into three clusters, and three health centers were randomly selected from each cluster. In each health center, individuals aged from 30 to 85 years old were selected based on their health records using simple random sampling. Demographic and biochemical measures data were completed for 891 participants. For the participants enrolled, anthropometric quantities were obtained by a trained physician. Height was determined to the nearest 0.1 cm with a stadiometer and weight was measured to the nearest 0.1 kg on a portable Seca 700 (Seca, Germany). Body mass index (BMI) was calculated as weight in kilograms divided by the squared height in meters. Blood pressure (BP) was measured on the right arm after five minutes of resting in a seating position using a mercury sphygmomanometer (Richter, Germany). We measured systolic and diastolic BP twice at five-minute intervals.

Participants were asked about their smoking status (smoker, smoking at least one cigarette per week or non-smoker). Levels of education were classified as illiterate, secondary school to a diploma and university graduates; meanwhile, marital status was categorized as married or others (unmarried, widow, divorced).

After 8-10 hours of overnight fasting, 10cc blood was taken from each subject by the trained healthcare staff in a central laboratory (Paymanieh Hospital). Meanwhile, fasting blood glucose (FBS), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein cholesterol (HDL), and triglyceride (TG) were measured. TC and triglyceride levels were determined by enzymatic techniques using a Selectra E bio-chromatic analyzer. HDL and LDL levels were measured after heparin-manganese chloride precipitation of the other lipoproteins. Plasma glucose levels were measured by the glucose oxidase method. Remnant cholesterol was calculated by total cholesterol – (HDL+LDL) and non-HDL cholesterol by total cholesterol – HDL.

Measures

Normal weight was specified as BMI less than 25 kg/m^2, overweight by 25 to <30 kg/m^2, and obese as ≥30kg/m^2 (21). In this study, we used the components of the metabolic syndrome defined by IDF (International Diabetes Federation) (23): BP≥130/85 mmHg or received anti-hypertensive drugs (high blood pressure); FBS≥100 mg/dl or taking anti-diabetic drugs (high FBS); TG≥150mg/dl (high TG); and HDL cholesterol<40mg/dl in men and <50 mg/dl in women or taking fat-lowering drugs (low HDL). Participants with 0–1 component of metabolic syndrome were defined as metabolically healthy (MH) and those with at least 2 components of metabolic syndrome were defined as metabolically unhealthy (MU). High blood pressure was defined as an SBP≥140 mm Hg or DBP≥90 mm Hg, and/or the consumption of antihypertensive medications. Diabetes was defined as having fasting serum glucose equal to or greater than 126 mg/dL through twice analysis or being treated for diabetes. Hypercholesterolemia and hypertriglyceridemia were considered as serum total cholesterol (TC) and triglyceride of 240 and 200 mg/dl or more or receiving lipid-lowering drugs as NCEEP, ATP III, respectively.[17] Also, an LDL level of 160 mg/dl or above was defined as high LDL. If at least one of the serum levels of TG, TC, and LDL was equal to or greater than 150, 200, and 130 mg/dl, respectively, and/or HDL was less than 40 mg/dl, or if lipid-lowering drugs were being used, it was defined as dyslipidemia.

Table 1: Demographic, anthropometric, and cardio-metabolic factors among metabolically healthy and unhealthy participants

Variable	MH (n=451)	MU (n=440)	P value
Prevalence, frequency (percent)	451 (50.6)	440 (49.4)	0.72*
Age, year, mean (SD)	46.6 (12.8)	53.5 (13.2)	<0.001**
Sex, frequency (percent)			0.312*
Men	212 (52.5)	192 (47.5)	
Women	239 (49.1)	248 (50.9)	
Education, frequency (percent)			<0.001*
Illiterate or primary school	170 (42.9)	226 (57.1)	
Secondary school or diploma	196 (55.2)	159 (44.8)	
University	85 (60.7)	55 (39.3)	
Marital status, frequency (percent)			0.037*
Married	413 (51.8)	384 (48.2)	
Single, widowed or divorced	38 (40.4)	56 (59.6)	
Smoking, frequency (percent)			0.211*
Yes	65 (56.0)	51 (44.0)	
No	386 (49.8)	389 (50.2)	
Body Mass Index group, frequency (percent)			<0.001*
Normal weight	217 (62.5)	130 (37.5)	
Overweight	170 (44.4)	213 (55.6)	
Obesity	64 (39.8)	97 (60.2)	
Hypertension, frequency (percent)			<0.001*
Yes	74 (23.5)	241 (76.5)	
No	377 (65.5)	199 (34.5)	
Type 2 Diabetes Mellitus, frequency (percent)			<0.001*
Yes	6 (5.8)	98 (94.2)	
No	445 (56.5)	342 (43.5)	
Hypertriglyceridemia, frequency (percent)			<0.001*
Yes	25 (10.5)	214 (89.5)	
No	426 (65.3)	226 (34.7)	
Hypercholesterolemia, frequency (percent)			<0.001*
Yes	46 (22.8)	156 (77.2)	
No	404 (58.8)	284 (41.2)	
High LDL, frequency (percent)			<0.001*
Yes	37 (20.8)	141 (79.2)	
No	414 (58.1)	299 (41.9)	
Dyslipidemia, frequency (percent)			<0.001*
Yes	221 (38.2)	357 (61.8)	
No	230 (73.5)	83 (26.5)	
Body Mass Index, kg/m^2, mean (SD)	25.6 (4.4)	27.2 (4.2)	<0.001**
Systolic BP, mmHg, mean (SD)	119.5 (16.5)	135.0 (19.5)	<0.001**
Diastolic BP, mmHg, mean (SD)	76.8 (10.9)	83.7 (10.8)	<0.001**
Fasting Blood Sugar, mg/dl, mean (SD)	84.8 (19.4)	111.9 (47.8)	<0.001**
Triglyceride, mg/dl, mean (SD)	104.4 (59.9)	182.6 (96.6)	<0.001**
Total Cholesterol, mg/dl, mean (SD)	186.0 (37.2)	197.1 (43.0)	<0.001**
Low Density Lipoprotein, mg/dl, mean (SD)	114.2 (29.9)	117.0 (33.8)	0.183**
High Density Lipoprotein, mg/dl, mean (SD)	50.8 (10.7)	44.9 (9.6)	<0.001**
Remnant Cholesterol, mg/dl, mean (SD)	21.0 (10.2)	35.2 (19.9)	<0.001**
Non HDL Cholesterol, mg/dl, mean (SD)	135.2 (33.1)	152.2 (40.2)	<0.001**
Triglyceride/HDL Ratio, mean (SD)	2.16 (1.38)	4.35 (2.73)	<0.001**
LDL/HDL Ratio, mean (SD)	2.31 (0.65)	2.68 (0.80)	<0.001**
Remnant Cholesterol/HDL Ratio, mean (SD)	0.43 (0.21)	0.84 (0.64)	<0.001**
Metabolic Component, frequency (percent)			
High Triglyceride	44 (9.8)	312 (70.9)	<0.001*
Low HDL	109 (24.2)	272 (61.8)	<0.001*
High Blood Pressure	117 (25.9)	328 (74.5)	<0.001*
High Fasting Blood Sugar	24 (5.3)	220 (50.0)	<0.001*

HDL: High Density Lipoprotein; MH: Metabolically Healthy; MU: Metabolically Unhealthy; BP: Blood pressure; HDL: high-density lipoprotein; LDL: low-density lipoprotein; SD: Standard Deviation; *Chi-squared test; **Independent t-test; Significance level<0.05

Statistical Analysis

Stata version 14 (Stata Corp LP, College Station, TX) was used to analyze the data. Qualitative data are presented as numbers and percentages; quantitative data are reported as mean and standard deviation. First, the Kolmogorov-Smirnov test was applied to evaluate whether data had normal distribution or not. Then, we compared the values of demographic, anthropometric, and metabolic factors between MH and MU participants according to the number of the presence of any of the components by chi-square, t-test- or one-way ANOVA tests. Binary logistic regression analysis was performed to determine the odds ratios at the 95% confidence interval for the association between MU and anthropometry and demographic features such as age, sex, marital status, education level, smoking, BMI, BMI groups, hypercholesterolemia, high LDL level, dyslipidemia, remnant cholesterol, and non-HDL cholesterol with cardio-metabolic risk factors (diabetes mellitus, hypertension, hypertriglyceridemia, low HDL, TG/HDL ratio, LDL/HDL ratio, and remnant-C/HDL ratio) in model 1 and all variables except cardio-metabolic factors in model 2. P-values less than 0.05 were considered statistically significant.

Results

In total, we selected 891 participants, of whom 45.3% were men and 89.5% were married; furthermore, 15.7%, 39.8%, and 44.5% had an academic degree, secondary school to diploma, and less than secondary school education, respectively. The mean age of the participants was 50.0±13.4 years.

MU obesity was determined in 49.4% of all participants. They were older than MH participants (Table 1). In individuals with lower education, MU prevalence was higher than those with MH, while in married individuals, MU prevalence was lower. However, the MU was not different proportionate to sex and smoking status. BMI, SBP, DBP, FBS, TG, total cholesterol, remnant-C, non-HDL-C, TG/HDL ratio, LDL/HDL ratio, and remnant-C/HDL ratio were significantly higher; on the other hand, HDL level was lower in the MU group. Nevertheless, there was no difference in the serum concentration of LDL between MU and MH individuals. The obese and overweight participants had a significantly higher prevalence of MU than individuals with BMI 25 mg/kg^2. It was 4.6% more obese than overweight participants (Table 1).

In participants with MU, the prevalence of hypertension, diabetes, hypertriglyceridemia, hypercholesterolemia, higher LDL, and dyslipidemia was higher compared to individuals with MH. The trend of age-specific prevalence in MU was seen, so that the incidence of MU was 30.6% and 69.7% in participants aged 30-39 and ≥60 years, respectively (P=0.001) (Figure 1). Most participants had one, followed by two abnormal metabolic components; however, simultaneous occurrence of four components had the lowest frequency. The imperative result related to frequency was the fact that only 17.7% of participants had no abnormal metabolic component. The mean age and BMI had a positive correlation with the number of abnormal metabolic components; that is, the more BMI and mean age, the more abnormal metabolic components. The metabolically unhealthy components (MUC) significantly increased with the number of MUC in participants (P<0.001). Among the participants with one and two MUC, high blood pressure and high FBS were the most and the least common components, respectively. However, for participants with three MUC, these were high TG and high FBS, respectively (Table 2).

Age, sex, marital status, education, hypercholesterolemia, high LDL level, dyslipidemia, BMI, overweight and obesity, hypertension, diabetes mellitus, hypertriglyceridemia, and low HDL level were associated with MU. However, sex and smoking were not associated with MU

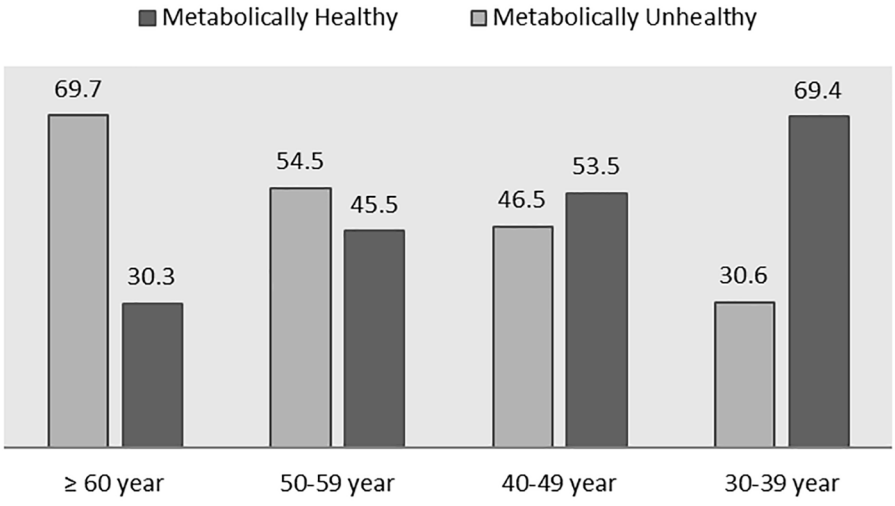

Figure 1: Prevalence (%) of metabolically healthy status by age.

Table 2: Comparison of the number of MH abnormality according to the demographic variable and cardio-metabolic risk factors among the participants

Number of abnormal Metabolic components	0 factor (n=158)	1 factor (n=293)	2 factor (n=231)	3 factor (n=165)	4 factor (n=44)	P value
Prevalence, frequency (percent)	158 (17.7)	293 (32.9)	231 (26.0)	165 (18.5)	44 (4.9)	-
Age, Year, mean (SD)	45.4 (11.4)	47.2 (13.4)	52.0 (13.4)	54.0 (12.6)	58.61 (13.4)	<0.001*
BMI, kg/m^2, mean (SD)	25.1 (4.3)	25.8 (4.5)	26.8 (4.2)	27.7 (4.1)	27.7 (4.9)	<0.001*
MU Components: frequency (percent)						
High blood pressure	-	117 (39.9)	151 (65.4)	133 (80.6)	44 (100.0)	<0.001**
High FBS	-	24 (8.2)	71 (30.7)	105 (63.6)	44 (100.0)	<0.001**
High TG	-	43 (14.7)	123 (53.2)	146 (88.5)	44 (100.0)	<0.001**
Low HDL	-	109 (37.2)	117 (50.6)	111 (67.3)	44 (100.0)	<0.001**

BMI: Body Mass Index; FBS: Fasting Blood Sugar; HDL: High Density Lipoprotein; MU: Metabolically Unhealthy; SD: Standard Deviation; TG: Triglyceride; MH: Metabolically Healthy; -: Not applicable; *One-way ANOVA, ** Chi-squared test, significance level<0.05

Table 3: Crude and Adjusted Odds Ratio of study variables for MU participants

Variables	Crude Odds Ratio (OR)		Adjusted OR			
			Model 1		Model 2	
	OR (CI95%)	P*	OR (CI95%)	P**	OR (CI95%)	P**
Age	1.04 (1.03-1.05)	<0.001	1.03 (1.02-1.05)	<0.001	1.04 (1.03-1.05)	<0.001
Sex, female	1.15 (0.88-1.49)	0.312	0.61 (0.39-0.95)	0.030	1.06 (0.77-1.45)	0.738
Marital status, married	0.63 (0.41-0.97)	0.038	0.99 (0.48-2.08)	0.996	0.71 (0.43-1.18)	0.185
Educate, primary and illiterate	Ref	-	Ref	-	Ref	-
Secondary to diploma	0.49 (0.33-0.72)	<0.001	0.95 (0.51-1.80)	0.880	0.91 (0.57-1.45)	0.691
University	0.61 (0.46-0.81)	0.001	1.07 (0.64-1.80)	0.794	1.05 (0.73-1.51)	0.793
Smoker	0.78 (0.53-1.15)	0.212	0.93 (0.48-1.81)	0.834	1.00 (0.63-1.60)	0.997
Hypercholesterolemia	4.84 (3.37-6.95)	<0.001	1.43 (0.73-2.78)	0.295	1.50 (0.77-2.94)	0.234
High LDL cholesterol	5.28 (3.57-7.80)	<0.001	1.13 (0.45-2.86)	0.797	2.73 (1.77-4.20)	<0.001
Dyslipidemia	4.48 (3.31-6.05)	<0.001	1.54 (0.99-2.42)	0.058	2.98 (2.13-4.16)	<0.001
BMI, Normal weight	Ref	-	Ref	-	Ref	-
Overweight	2.10 (1.56-2.81)	<0.001	2.25 (1.43-3.54)	<0.001	2.13 (1.53-2.98)	<0.001
Obese	2.53 (1.73-3.71)	<0.001	2.59 (1.43-4.70)	0.002	2.83 (1.84-4.36)	<0.001
Hypertension	4.75 (3.46-6.51)	<0.001	11.9 (6.9-20.6)	<0.001	-	-
Diabetes mellitus	21.3 (9.2-49.0)	<0.001	34.7 (12.1-99.5)	<0.001	-	-
Hypertriglyceridemia	16.1 (10.3-25.2)	<0.001	21.9 (11.4-42.3)	<0.001	-	-
Low HDL-cholesterol	5.08 (3.81-6.78)	<0.001	23.6 (13.5-41.3)	<0.001	-	-

BMI: Body Mass Index; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; Ref: Reference group; OR: Odds Ratio; MU: Metabolically Unhealthy, -: Not applicable; *Univariate logistic regression; **Multivariable logistic regressions; Significance level<0.05. Variables entered in Model 1: age, sex, marital status, education level, smoking, BMI, hypercholesterolemia, high LDL level, dyslipidemia, remnant cholesterol, and non-HDL cholesterol with cardio-metabolic risk factors (diabetes mellitus, Hypertension, hypertriglyceridemia, low HDL, TG/HDL ratio, LDL/HDL ratio, and remnant-C/HDL ratio). Variables entered in Model 2: age, sex, marital status, education level, smoking, BMI, hypercholesterolemia, high LDL level, dyslipidemia, remnant cholesterol, and non-HDL cholesterol.

obesity. Among them, diabetes mellitus (OR: 21.3, 95%CI: 9.2-49.0, P<0.001) and hypertriglyceridemia (OR: 16.1, 95%CI: 10.3-25.2, P<0.001) were the strongest predictor of MU, respectively. In model 1, we entered all the variables mentioned above. Adjusted OR was significantly different in age, sex, overweight and obesity, HTN, diabetes mellitus, hypertriglyceridemia, and low HDL. The estimated risk of MU status was the highest in participants with diabetes mellitus (OR: 34.7, P<0.001), low HDL (OR: 23.6, P<0.001), and hypertriglyceridemia (OR: 21.9, P<0.001), respectively. In model 2, that is, without MUC, the most imperative factor was dyslipidemia (OR: 2.98, P<0.001), obesity (OR: 2.83, P<0.001), and high LDL (OR: 2.73, P<0.001), respectively (Table 3).

Discussion

In this study, MU prevalence was 49.4%. This prevalence increased with increasing age. Consequently, 37.5%, 55.6%, and 60.2% of normal weight, overweight, and obese participants were metabolically unhealthy, respectively. The robust risk factors for the development of MU were dyslipidemia, obesity, high LDL level, overweight, and age.

Dyslipidemia, obesity, and high LDL level were the most significant risk factors associated with the metabolically unhealthy state. In a study performed on the Korean population, male sex, current smoker, higher age, and lower education were associated with the higher risk of metabolically unhealthy obesity in participants with BMI≥25.0 kg/m^2.[18] In another study,

higher age and dyslipidemia were determinants of metabolically unhealthy status in obese individuals.[16] In overweight/obese participants, the relationship between metabolically unhealthy status and different items, including older age, female sex, and abnormal waist circumference were found in another study.[10] It seems that lifestyles like low physical activity, inappropriate nutritional behaviors and consumption of high-fat foods are germane to creating this result, which has also been mentioned in comparative studies.

MU prevalence in this study was lower than the study conducted in Iranian adult population (49.4% vs. 69.2%).[10] From 10 cohort studies across Europe, the authors found a high prevalence of MU in obese participants in the Dilgom's study in Finland (71.6%) and the lowest in the Chris's study in Italy (40.0).[19] Meanwhile, in the Coding's study, the prevalence was 39.1%,[8] which was lower than our result. In another descriptive study, 25.0% of individuals over 20 years and 38.9% of those aged 18-85 years had metabolic syndrome and >2 abnormal metabolic components of metabolic syndrome, respectively.[7, 18] Prevalence of pre-metabolic syndrome (having two of five metabolic components) was 29.4% for U.S individuals.[20] However, in Nigeria, 12.9% of the participants aged 18-64 years had at least two metabolic components of metabolic syndrome.[9] These findings indicated a wide variation in the prevalence of MH and MU. This variation is more likely due to the variety in definitions of metabolic disorder and the use of different metabolic abnormality criteria (such as CDS, ATP III, Wildman, Karelis and Homa), revealing the fact that the results amongst studies were not comparable.

Our result showed that the prevalence of MU and MH in obese participants was 60.2% and 39.8%, respectively although it was 62.5% for MH in normal weight. In one study reported that 74.5% of obese participants were MU, while 36.0 of normal-weight participants were MH.[21] The China Hypertension Survey indicated that 46.6% of abnormal-weight individuals (overweight and obese) had the MU status.[22]

In an obese population with no metabolic abnormalities, better fitness with 30 to 50 percent lower mortality than obese peers with these risk factors was observed.[23] This risk difference suggests that there may be a heterogeneous risk profile among obese individuals. Thus, a subset of obesity is defined as healthy metabolic obesity (MHO), including obese individuals who appear to be protected against obesity-related metabolic complications and do not have a set of cardiac metabolic abnormalities. Conversely, obesity with metabolic risk factors is called unhealthy metabolic obesity (MUO). MHOs include people possessing large amounts of fat mass or body weight but displaying healthy metabolic characteristics. Therefore, it is referred to as a benign disease.[24]

The higher prevalence of metabolic unhealthiness (MU) was found to be associated with older age. Previous studies have also observed a significant variation in obesity prevalence across different age groups. A follow-up study conducted in England revealed that 44.5% of individuals initially classified as metabolically healthy (MH) were transitioned into MU within eight years, suggesting that MH is a temporary state. This observation supports the notion that the increasing susceptibility to MU with advancing age in our study can be explained by this phenomenon. In obese individuals, MU prevalence increased under 65 years of age and then declined.[1] However, a study suggested that the prevalence of having at least two components of the metabolic syndrome had no particular trend based on age group.[9] In normal-weight and overweight/obese individuals, the mean age of MU was significantly higher than the MH state.[10] All these results indicate the effect of aging on different body systems in the development of metabolic syndrome.

Individuals with MU, with and without anthropometric abnormality, had an increased risk of cardiovascular disease, liver disorder, and diabetes.[26-29] In a VMCUN study, diabetes mellitus incidence was higher in unhealthy participants (one or more risk factors) compared to healthy ones.[30] It showed that the risk of cardiovascular disease was 1.27 times higher in participants older than 55 years who had metabolic syndrome than individuals without metabolic syndrome.[31] In a 7.43-year follow-up study on participants aged more than 20 years, the risk of ischemic stroke was 1.4%. It significantly increased the MU in normal-weight and obese participants compared to the MH groups.[32]

Strengths and Limitations

The strengths of this study were a well-defined study with large sample size. Findings were compared between males, females and other groups. However, the study had several limitations as well. First, owing to differences in the definition of the MU state, it is difficult to compare our findings with other studies. Second, BMI was not considered in the analysis due to the lack of data. Also, we did not use lifestyle and food data that could affect cardio-metabolic risk factors. Third, due to the nature of the cross-sectional design of the study, causal relationships could not be determined clearly.

Conclusions

The results of this study showed that MU was a public health problem in the study area. Higher age, dyslipidemia, and high LDL were significantly associated with MU states. In terms of public health, it would be better to screen for obesity and other metabolic disorders

in clinical practice to establish suitable preventive strategies. Furthermore, in the scope of public health policies, the allocation of the national budget for planning eligible strategies in order to determine and identify suitable programs to prevent and treat these risk factors is proposed. These strategies can increase the general health condition of the community and reduce the costs of its complications.

Ethics Approval and Consent to Participate

The ethical considerations of the study entailing the required information regarding the research objectives, voluntary participation in the study, and data confidentiality were fully illustrated to the participants. After the accomplishment of the consent forms by the participants, they received the questionnaires and were subsequently examined. The study protocol was consistent with the ethical principles of the Helsinki Declaration and was approved by the Research Ethics Committee of Jahrom University of Medical Sciences with the Ethics ID JUMS.REC.1378.51.7.

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Authors' Contribution

KR, and MS conceived and designed the study. KR, and VR were responsible for literature search and screening. KR, and VR were responsible for data collection and analyses. KR, MS, contributed to data interpretation. KR and VR drafted the manuscript and MS, critically revised the manuscript.

Conflicts of Interest: None declared.

References

1 Liu C, Wang C, Guan S, Liu H, Wu X, Zhang Z, et al. The Prevalence of Metabolically Healthy and Unhealthy Obesity according to Different Criteria. Obes Facts 2019; 12(1): 78-90. doi: 10.1159/000495852. PMCID: PMC6465689. PMID: 30814477.

2 Song Z, Gao M, Lv J, Yu C, Guo Y, Bian Z, et al. Metabolically healthy obesity, transition to unhealthy phenotypes, and type 2 diabetes in 0.5 million Chinese adults: the China Kadoorie Biobank. Eur J Endocrinol. 2022; 186(2): 233-44. doi: 10.1530/EJE-21-0743. PMID: 34874895. PMCID: PMC8789025.

3 Wang W, He J, Hu Y, Song Y, Zhang X, Guo H, et al. Comparison of the Incidence of Cardiovascular Diseases in Weight Groups with Healthy and Unhealthy Metabolism. Diabetes Metab Syndr Obes 2021; 14: 4155. doi: 10.2147/DMSO.S330212. PMID: 34621129. PMCID: PMC8491784.

4 Dehghani A, Korozhdehi H, Hossein Khalilzadeh S, Fallahzadeh H, Rahmanian V. Prevalence of diabetes and its correlates among Iranian adults: Results of the first phase of Shahedieh cohort study. Health Sci Rep. 2023; 6(4): e1170. doi: 10.1002/hsr2.1170. PMID: 37021014. PMCID: PMC10069239.

5 Mongraw-Chaffin M, Foster MC, Anderson CAM, Burke GL, Haq N, Kalyani RR, et al. Metabolically Healthy Obesity, Transition to Metabolic Syndrome, and Cardiovascular Risk. J Am Coll Cardiol 2018; 71(17): 1857-65. doi: 10.1016/j.jacc.2018.02.055. PMID: 29699611. PMCID: PMC6002856.

6 Yu X, Wang L, Zhang W, Ming J, Jia A, Xu S, et al. Fasting triglycerides and glucose index is more suitable for the identification of metabolically unhealthy individuals in the Chinese adult population: A nationwide study. J Diabetes Investig 2019; 10(4): 1050-8. doi: 10.1111/jdi.12975. PMID: 30417578. PMCID: PMC6626942.

7 Tian S, Xu Y, Dong H. The effect of metabolic health and obesity phenotypes on risk of hypertension: A nationwide population-based study using 5 representative definitions of metabolic health. Medicine 2018; 97: 38. doi: 10.1097/MD.0000000000012425. PMID: 30235720. PMCID: PMC6160160.

8 Shea JL, Randell EW, Sun G. The Prevalence of Metabolically Healthy Obese Subjects Defined by BMI and Dual-Energy X-Ray Absorptiometry. Obesity 2011; 19(3): 624-30. doi: 10.1038/oby.2010.174. PMID: 20706202.

9 Oladapo OO, Salako L, Sodiq O, Shoyinka K, Adedapo K, Falase AO. A prevalence of cardiometabolic risk factors among a rural Yoruba south-western Nigerian population: a population-based survey. Cardiovasc J Afr. 2010; 21(1): 26-31. PMID: 20224842. PMCID: PMC3721297.

10 Hajian-Tilaki K, Heidari B. Metabolically healthy obese and unhealthy normal weight in Iranian adult population: Prevalence and the associated factors. Diabetes Metab Syndr. 2018; 12(2): 129-34. doi: 10.1016/j.dsx.2017.11.005. PMID: 29196231.

11 Rahmanian K, Shojaie M. Prevalence of Metabolic Syndrome in an Adult Urban Population in The South of Iran. Iranian Journal of Diabetes and Obesity 2011; 3(2): 77-82.

12 Rahmanian K, Shojaie M. The prevalence of pre-hypertension and its association to established cardiovascular risk factors in south of Iran. BMC Res Notes. 2012; 5: 386. doi: 10.1186/1756-0500-5-386. PMID: 22838639. PMCID: PMC3506467.

13 Rahmanian K, Shojaei M, Sotoodeh.Jahromi A. Relation of type 2 diabetes mellitus with gender, education, and marital status in an Iranian urban population. Rep Biochem Mol Biol. 2013; 1(2): 64-8. PMID: 26989710. PMCID: PMC4757057.

14 Rahmanian K, Shojaei M, Sotoodeh Jahromi A, Madani

A. The Association Between Pre-Diabetes With Body Mass Index and Marital Status in an Iranian Urban Population. Glob J Health Sci. 2016; 8(4): 95-101. doi: 10.5539/gjhs.v8n4p95. PMID: 26573038. PMCID: PMC4873576.

15 Shojaei M, Jahromi AS, Rahmanian K, et.al. Gender differences in the prevalence of cardiovascular risk factors in an iranian urban population. OnLine Journal of Biological Sciences 2015; 15(3): 178-84. doi: 10.3844/ojbsci.2015.178.184.

16 Rahmanian K, Shojaei M, Sotoodeh Jahromi A. Prevalence and clinical characteristics of metabolically unhealthy obesity in an Iranian adult population. Diabetes Metab Syndr Obes. 2019; 12: 1387-95. doi: 10.2147/DMSO.S197476. PMID: 31496776. PMCID: PMC6698163.

17 Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001; 285: 2486–97. doi: 10.1001/jama.285.19.2486. PMID: 11368702.

18 Lee K. Metabolically obese but normal weight (MONW) and metabolically healthy but obese (MHO) phenotypes in Koreans: characteristics and health behaviors. Asia Pac J Clin Nutr 2009; 18 (2): 280-4. PMID: 19713189.

19 van Vliet-Ostaptchouk JV, Nuotio ML, Slagter SN, Doiron D, Fischer K, Foco L, et al. The prevalence of metabolic syndrome and metabolically healthy obesity in Europe: a collaborative analysis of ten large cohort studies. BMC Endocrine Disorders 2014; 14: 9. doi: 10.1186/1472-6823-14-9. PMID: 24484869. PMCID: PMC3923238.

20 Okosun IS, Boltri JM, Davis-Smith M, Ndirangu M. Premetabolic syndrome and clustering of cardiometabolic risk factors in White, Black and Mexican American adults. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2009; 3(3): 143-8. doi: 10.1016/j.dsx.2009.07.006.

21 Izumida T, Nakamura Y, Ishikawa S. Impact of body mass index and metabolically unhealthy status on mortality in the Japanese general population: The JMS cohort study. PLoS ONE 2019; 14(11): e0224802. doi: 10.1371/journal.pone.0224802. PMID: 31697720. PMCID: PMC6837339.

22 Ren H, Zhang L, Liu Z, Zhou X, Yuan G. Sleep duration and apolipoprotein B in metabolically healthy and unhealthy overweight/obese phenotypes: a cross-sectional study in Chinese adults. BMJ Open 2019; 9: e023817. doi: 10.1136/bmjopen-2018-023817. PMID: 30755447. PMCID: PMC6377547.

23 Ortega FB, Lee DC, Katzmarzyk PT, Ruiz JR, Sui X, Church TS, et al. The intriguing metabolically healthy but obese phenotype: cardiovascular prognosis and role of fitness. Eur Heart J 2013; 34(5): 389-97. doi: 10.1093/eurheartj/ehs174. PMID: 22947612. PMCID: PMC3561613.

24 Tsatsoulis A, Paschou SA. Metabolically healthy obesity: criteria, epidemiology, controversies, and consequences. Curr Obes Rep 2020; 9(2): 109-20. doi: 10.1007/s13679-020-00375-0. PMID: 32301039.

25 Hamer M, Bell JA, Sabia S, Batty GD, Kivimäki M. Stability of metabolically healthy obesity over 8 years: the English Longitudinal Study of Ageing. Eur J Endocrinol 2015; 173(5): 703-8. doi: 10.1530/EJE-15-0449. PMID: 26286585.

26 Hinnouho GM, Czernichow S, Dugravot A, Nabi H, Brunner EJ, Kivimaki M, et al. Metabolically healthy obesity and the risk of cardiovascular disease and type 2 diabetes: the Whitehall II cohort study. European Heart Journal 2015; 36: 551–9. doi: 10.1093/eurheartj/ehu123. PMID: 24670711. PMCID: PMC4344958.

27 Chang Y, Jung HS, Yun KE, Cho J, Ahn J, Chung EC, et al. Metabolically Healthy Obesity is Associated with an Increased Risk of Diabetes Independently of Nonalcoholic Fatty Liver Disease. Obesity 2016; 24: 1996–2003. doi: 10.1002/oby.21580. PMID: 27474900.

28 Aung K, Lorenzo C, Hinojosa MA, Haffne SM. Risk of Developing Diabetes and Cardiovascular Disease in Metabolically Unhealthy Normal-Weight and Metabolically Healthy Obese Individuals. J Clin Endocrinol Metab 2014; 99: 462–8. doi: 10.1210/jc.2013-2832. PMID: 24257907. PMCID: PMC3913817.

29 Xie J, Zhang S, Yu X, Yang Y, Liu Z, Yuan G, et al. Association between Liver Enzymes with Metabolically Unhealthy Obese Phenotype. Lipids Health Dis. 2018; 17(1): 198. doi: 10.1186/s12944-018-0847-9. PMID: 30134916. PMCID: PMC6106819.

30 Navarro-Gonzalez D, Sanchez-Inigo L, Fernandez-Montero A, Pastrana-Delgado J, Martınez JA. Are All Metabolically Healthy Individuals with Obesity at the Same Risk of Diabetes Onset? Obesity 2016; 24: 2615-23. doi: 10.1002/oby.21667. PMID: 27804254.

31 Dhana K, Koolhaas CM, van Rossum EF, Ikram MA, Hofman A, Kavousi M, et al. Metabolically Healthy Obesity and the Risk of Cardiovascular Disease in the Elderly Population. PLoS ONE; 11(4): e0154273. doi: 10.1371/journal.pone.0154273. PMID: 27100779. PMCID: PMC4839559.

32 Lee H-J, Choi E-K, Lee S-H, Kim Y-J, Han K-D, Oh S. Risk of ischemic stroke in metabolically healthy obesity: A nationwide populationbased study. PLoS ONE 2018; 13(3): e0195210. doi: 10.1371/journal.pone.0195210. PMID: 29601602. PMCID: PMC5877885.