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OPEN Cardiometabolic risk factor clusters in older adults using latent class analysis on the Bushehr elderly health program

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Metabolic syndrome (MetS), comprising obesity, insulin resistance, hypertension, and dyslipidemia, increases the risk of type II diabetes mellitus and cardiovascular disease. This study aimed to identify the prevalence and determinants of specific clusters of the MetS components and tobacco consumption among older adults in Iran. The current study was conducted in the second stage of the Bushehr Elderly Health (BEH) program in southern Iran—a population-based cohort including 2424 subjects aged \geq 60 years. Latent class analysis (LCA) was used to identify MetS and tobacco consumption patterns. Multinomial logistic regression was conducted to investigate factors associated with each MetS class, including sociodemographic and behavioral variables. Out of 2424 individuals, the overall percentage of people with one or more components of MetS or current tobacco use was 57.8% and 20.8%, respectively. The mean (SD) age of all participants was 69.3(6.4) years. LCA ascertained the presence of four latent classes: class 1 ("low risk"; with a prevalence of 35.3%), class 2 ("MetS with medication-controlled diabetes"; 11.1%), class 3 ("high risk of MetS and associated medication use"; 27.1%), and class 4 ("central obesity and treated hypertension"; 26.4%). Compared to participants with a body mass index (BMI) < 30, participants with BMI > 30 were more likely to belong to class 3 (OR 1.91, 95% CI 1.31-2.79) and class 4 (OR 1.49, 95% CI 1.06-2.08). Polypharmacy was associated with membership in class 2 (OR 2.07, 95% CI 1.12–3.81), class 3 (OR 9.77, 95% CI 6.12– 15.59), and class 4 (OR 1.76, 95% CI 1.07–2.91). The elevated triglyceride-glucose index was associated with membership in class 2 (OR 12.33, 95% CI 7.75–19.61) and class 3 (OR 12.04, 95% CI 8.31–17.45). Individuals with poor self-related health were more likely to belong to class 3 (OR 1.43; 95% CI 1.08-1.93). Four classes were identified among older adults in Iran with distinct patterns of cardiometabolic risk factors. Segmenting elderly individuals into these cardiometabolic categories has the potential to enhance the monitoring and management of cardiometabolic risk factors. This strategy may help reduce the severe outcomes of metabolic syndrome in this susceptible population.

Keywords Latent class analysis, Metabolic syndrome, Cardiometabolic, Older adults

Metabolic syndrome (MetS) is a major risk factor for the development of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM)¹. Mets, as defined by the International Diabetes Federation (IDF), comprises an increased waist circumference plus two or more of (i) hypertriglyceridemia, (ii) low high-density lipoprotein (HDL) cholesterol levels, (iii) high blood pressure, and (iv) elevated fasting blood glucose². The risk of

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developing MetS increases with age, with the highest incidence in men during their sixth decade of life and women during their seventh decade³. MetS has been associated with a 1.5-fold increase in the risk of all-cause mortality⁴. A recent meta-analysis of 69 surveys in 2019 conducted in Iran has revealed a concerning prevalence rate of 51.7% for MetS over among older adults. The deleterious effects of MetS may be effectively mitigated by improved identification and management of the component risk factors⁵. It has been observed that there could be a possible association between the presence of nonalcoholic fatty liver disease (NAFLD), polycystic ovary syndrome (PCOS), or sleep apnea in an individual's medical history and an increased likelihood of developing metabolic syndrome^{6–8}. Excess deep fat accumulation in the abdominal area, also known as visceral adiposity, can potentially disrupt the balance of adipokines in the body, leading to insulin resistance, impaired functioning of the endothelium, and a heightened risk of developing atherosclerosis⁹.

Smoking cessation is beneficial in preventing MetS and reducing the risk of cardiovascular disease in individuals with established MetS¹⁰. Active smokers have a 26% higher risk of developing metabolic syndrome compared to individuals who do not smoke. Cigarette smoking can contribute to the development of various components of metabolic syndrome, which can lead to the onset and progression of the disease through multiple synergistic mechanisms¹¹.

Latent class analysis (LCA) is a statistical technique used to identify groups of individuals with similar patterns of attributes or characteristics that may not be directly observed. To date, LCA has offered valuable insights into the underlying mechanisms and can identify different risk profiles in the context of metabolic syndrome¹²⁻¹⁴. Based on the available evidence, the sedentary lifestyle, technological advancements, shifts in behavioral and dietary habits, and rapid urbanization in Iran have contributed to the emergence of metabolic syndrome as a significant health concern. This is particularly critical as cardio-metabolic risk factors play a pivotal role in the development of cardiovascular diseases^{5,15}.

Extensive research efforts have been dedicated to understanding MetS and its associated risk factors. However, significant gaps in knowledge persist, particularly regarding the heterogeneous nature of MetS. Traditional analyses often oversimplify MetS as a uniform condition, failing to capture its complex mechanisms. By contrast, LCA offers a more nuanced approach by identifying distinct subgroups within the MetS population, each characterized by unique patterns of risk factors. LCA methodology allows for a deeper understanding of the underlying mechanisms of MetS and facilitates the development of more personalized and effective interventions¹⁶. This is particularly crucial for older adults, among whom MetS prevalence is high. Our aim was to use LCA to derive subtypes of MetS and tobacco consumption behavior among community-dwelling older adults in Iran and to identify the key determinants of each MetS subtype. This may help us better comprehend the intricate physiological and behavioral factors that contribute to metabolic syndrome in this population and may lead to personalized interventions and healthcare strategies for older adults, improving their well-being and promoting healthier aging.

Methods

Study design and participants

The present study utilized cross-sectional data obtained from the second stage of the Bushehr Elderly Health (BEH) program, a prospective demographic cohort study conducted in Bushehr, Southern Iran. The study design and methodology for the BEH program have been previously detailed^{7,17}. The first phase of BEH was initiated in March 2013 to examine the occurrence of cardiovascular risk factors and their association with adverse cardiovascular events in older persons. Using a stratified random sampling method, a total of 3000 individuals aged 60 and over were enlisted to participate in this study. Eligibility criteria for inclusion included (i) residing in Bushehr for a minimum of one year prior to recruitment, (ii) having no intention of leaving during the next two years, (iii) being capable of completing the study instruments, and (iv) providing written, informed consent. In 2018, the second stage of the initial study phase concluded, with an overall participation rate of 81%.

Questionnaires were utilized to gather data regarding demographic status, physical and mental health, functional status, lifestyle factors, and history of medication use by professional nurses through an interview. The study protocol was approved by the Ethics Research Committee of Bushehr University of Medical Sciences (IR.BPUMS.REC.1402.138) and the Endocrinology and Metabolism Research Institute of Tehran University of Medical Sciences.

Definition of metabolic syndrome

Metabolic syndrome was diagnosed in line with International Diabetes Federation (IDF) guidelines. MetS was diagnosed when an individual had central obesity in addition to at least two of the following criteria: (i)elevated blood triglyceride levels (\geq 150 mg/dl [1.7 mmol/L] or use of medication), (ii) reduced levels of high-density lipoprotein (<40 mg/dl [1.03 mmol/L] in men and <50 mg/dl [1.29 mmol/L] in women), (iii) elevated blood pressure (\geq 130 mmHg for systolic blood pressure and/or \geq 85 mmHg for diastolic blood pressure or use of antihypertensive medication), and (iv) impaired fasting glucose (\geq 100 mg/dl [5.6 mmol/L] or use of drug therapy). In line with the IDF guidelines, waist circumference cut-off points appropriate for the BEH context were used: \geq 80 cm for women and \geq 94 cm for men¹⁸.

Blood pressure

Systolic and diastolic blood pressures were measured twice using a standard mercury sphygmomanometer. The measurements were taken in the right arm after 15 min of rest in a sitting position, with a 10-min time interval between each measurement. The average of the two measurements was used^{7,17}.

Laboratory evaluations

Following a period of 8–10 h of fasting, trained nursing personnel collected venous blood samples amounting to 25 ml. Measurement of fasting blood glucose and the blood lipid profile (total cholesterol, HDL-c, LDL-c, and triglycerides) was performed by experienced and accredited clinical pathology professionals. The fasting blood glucose and lipid profile tests were measured using an enzymatic colorimetric method (Pars Azmun, Karaj, Iran).

Anthropometric and clinical assessments

Height and weight were measured using a fixed stadiometer and digital scale. Neck, waist, and hip circumferences were measured using a flexible, constant tension tape at the level of the umbilicus and the widest part over the buttocks. Body mass index (BMI) was calculated by dividing weight (in kilograms) by height squared (in meters).

Other covariates

Interviews were conducted to gather sociodemographic information, including age, gender, marital status, physical activity, income levels, education, occupation, smoking history (never used, past history of use, current user), medical history, and drug use. In order to assess the average physical activity level, the International Physical Activity Questionnaire (IPAQ) was employed to evaluate the metabolic equivalent of tasks within a 24-h timeframe. This self-report tool is commonly used to assess an individual's physical activity levels in the Iranian population. It has been validated and classified into three categories: no activity and sedentary (≤ 1.39), low active (1.4–1.59), and active ($\geq 1.6 \text{ MET}/24 \text{ h}$)^{17,19}. Polypharmacy was defined as the administration of more than five medications within a 24-h period. Triglyceride-glucose index (TyG) was calculated using the formula Ln [fasting triglycerides (mg/dl) × fasting glucose (mg/dl)/2]²⁰.

Individuals reported their perception of their overall health using a five-point scale, ranging from excellent to poor. For the purposes of this study, this was dichotomized into good self-rated health (excellent, very good, and good) vs. poor self-rated health (fair and poor)^{21,22}.

Statistical analysis

The LCA model was used to identify subgroups of metabolic syndrome components and tobacco consumption. In order to select the most appropriate number of latent classes, the likelihood-ratio statistic, G² statistic, Akaike information criterion (AIC), Bayesian information criterion (BIC), entropy, and the log-likelihood value were calculated for models ranging from one to seven classes. When selecting the best model, lower log-likelihood values, AIC, BIC, G2, and higher entropy values were considered. Finally, the four-class model was chosen due to clinical interpretability and model parsimony. We used nine variables to evaluate the latent classes: waist circumference (high, normal), fasting blood glucose (high, normal), triglycerides (high, normal), high-density lipoprotein (high, normal), blood pressure (high, normal), diabetes drugs (yes, no), antihypertensive drugs (yes, no), lipid-lowering drugs (yes, no), and tobacco (no, past, current). Each study participant was allocated to a single class with the greatest probability of membership. Multinomial logistic regression was performed to identify determinants of class membership, including age, gender, education, socioeconomic status, marital status, occupation, physical activity, self-related health, polypharmacy, and triglyceride-glucose index. LCA was performed using R version 4.1.1. In all analyses, a significance level of 0.05 was considered statistically significant.

Results

The current study included a total of 2424 individuals (Fig. 1), of which 52.1% were women. The mean (standard deviation, SD) age of all participants was 69.3 ± 6.4 years (69.5 ± 6.4 for men and 69.2 ± 6.4 for women). Overall, 77% of participants reported being sedentary or not engaging in regular physical activity. Additionally, 23.4% of men and 18.4% of women were current smokers. The prevalence of metabolic syndrome in women and men was 45.3 (95% confidence intervals, CI 42.4–48.2) and 69.4 (95% CI 66.7–71.9), respectively (P < 0.001). The prevalence of central obesity, low HDL, and hypertriglyceridemia were more common in women than men (P < 0.001; Table 1).

Latent class analysis

A four-class LCA model achieved the best compromise between model fit, parsimony, and clinical interpretability (Table 2). Although a five-class solution resulted in a slightly better model fit, this did not further improve clinical interpretability, so the four-class solution was used. These classes were labeled: "low risk" (class 1; 35.3%), "MetS with medication-controlled diabetes" (class 2; 11.1%), "high risk of MetS and related medication use" (class 3; 27.1%), and "central obesity and treated hypertension" (class 4; 26.4%).

Table 3 shows the prevalence of MetS components, medication use, and tobacco smoking among each latent class. Participants identified as Class 1, the "low risk" group, did not meet the criteria for a metabolic syndrome diagnosis. They were determined to be relatively metabolically healthy, except for elevated WC and BP measurements. The second class, classified as "MetS with administrating diabetes control medication," demonstrated the lowest prevalence at 11.1%. Individuals within this group exhibited a high probability of elevated FBS, high WC, and low HDL levels, as well as using glucose-lowering medications. The third group (high risk of MetS using associated medications), which accounted for 27.1% of the individuals, was identified by a high prevalence of MetS components, except for high triglycerides. This group of people was taking medications for diabetes, hypertension, and high cholesterol. The fourth category, comprising 26.4% of the study population, consisted of individuals with a high likelihood of hypertension, elevated WC, and using antihypertensive medications.



Fig. 1. Flow chart of enrolment in the Bushehr Elderly Health (BEH) program.

Factors associated with latent class membership

Multinomial logistic regression was performed to identify associations between sociodemographic and lifestyle factors and membership of each class (Table 4). Older age increased the odds of membership in class 4 (OR 1.61, CI 1.09–2.38, P=0.016) compared to latent class 1. Those who were unemployed and retired were less likely to be a member of class 2 than those who were in employment (OR 0.38, 95% CI 0.18–0.77, P=0.007 and OR 0.41, 95% CI 0.20–0.84, P=0.16, respectively). In addition, those with low physical activity levels were less likely to be a member of class 3 than those with no activity (OR 0.66, 95% CI 0.44–0.93, P=0.020). Individuals with obesity were most likely to be included in class 3 (OR 1.91, 95% CI 1.31–2.79, P=0.001), and class 4 (OR 1.49, 95% CI 1.06–2.08, P=0.019). Polypharmacy was associated with membership in class 2 (OR 2.07, 95% CI 1.12–3.81, P=0.020), class 3 (OR 9.77, 95% CI 6.12–15.59, P<0.001) and class 4 (OR 1.76, 95% CI 1.07–2.91, P=0.026) compared to class 1. A triglyceride-glucose index in tertile 3 (8.9–11.9) was associated with membership in class 2 (OR 12.33, 95% CI 7.75–19.61, P<0.001) and class 3 (OR 12.04, 95% CI 8.31–17.45, P<0.001).

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Characteristics	Categories	Men (n = 1161) Mean (SD) or proportion	Women (<i>n</i> = 1263) Mean (SD) or proportion	P-value	
	60–64 year	285(24.50)	313(24.80)		
A (0/)	65–69 year	422(36.30)	529(41.90)	0.016	
Age n (%)	70-74year	198(17.10)	180(14.30)	0.016	
Education (year)	> =75 year	256(22.00)	241(19.10)		
Education (year)		7.17±5.15	3.38 ± 4.15	< 0.001	
Manital status n (0/)	Married	1104(95.10)	758(60.00)	10.001	
Marital status n (%)	Single	57(4.90)	505(40.00)	< 0.001	
	Employed	112(9.60)	23(1.80)		
Occupation	Retired	952(82.00)	126(10.00)	< 0.001	
	Unemployed	97(8.40)	1114(88.20)		
	No active and sedentary	893(76.90)	976(77.30)		
Physical activity n (%)	Low active	180(15.50)	217(17.20)	0.086	
	Active	88(7.60)	70(5.50)		
	Low	168(14.50)	345(27.30)		
Household income n (%)	Moderate	641(55.20)	721(57.10)	< 0.001	
	High	352(30.30)	197(15.60)		
	No	321(27.60)	414(32.80)		
Tobacco n (%)	Past-cigarette or Hookah	568(48.90)	617(48.90)	< 0.001	
	current-cigarette or Hookah	272(23.40)	232(18.40)		
	Underweight and normal	434(37.4)	317(25.10)		
BMI n (%)	Overweight	539(46.40)	488(38.60)	< 0.001	
	Obesity	188(16.20)	458(36.30)	< 0.001	
	T1(6.96-8.41)	435(37.50)	373(29.50)		
Triglyceride-glucose index n (%)	T2(8.42-8.93)	371(32.00)	437(34.50)	< 0.001	
	T3(8.94-11.92)	355(30.60)	453(35.90)		
Dolumbormo cu n (%)	Yes	88(9.80)	251(22.80)	< 0.001	
Polyphannacy II (%)	No	806(90.20)	848(77.20)	< 0.001	
Solf rated boolth p (04)	Good	792(68.20)	602(47.70)	<0.001	
Sen-rated health if (70)	Poor	369(31.80)	661(52.30)	< 0.001	
Glucose (mmol/dl)	104.06±40.69 107.13±45.07		0.080		
Systolic blood pressure (mm Hg)		140.00 ± 19.45	139.34 ± 19.20	0.398	
Diastolic blood pressure (mm Hg)	1	82.39 ± 8.73	80.78 ± 8.54	< 0.001	
HDL cholesterol (mmol/dl)		42.80 ± 10.40	48.37 ± 12.14	< 0.001	
Triglycerides (mmol/dl)		129.85±67.66	140.73 ± 78.84	< 0.001	
Waist circumference (cm)		97.04±11.43	100.26±12.33	< 0.001	
Binary variables related to metabo	lic syndrome				
High glucose n (%)		440(37.90)	589(46.60)	< 0.001	
High triglyceride n (%)		339(29.20)	429(34.00)	0.013	
Low HDL n (%)		471(40.60)	711(56.30)	< 0.001	
High waist circumference n (%)		770(66.30)	1196(94.70)	< 0.001	
High blood pressure n (%)		953(82.10)	1059(83.80)	0.266	
Antihypertensive medication n (%	5)	523(45.00)	759(60.10)	< 0.001	
Lipid-lowering drugs n (%)		274(23.60)	495(39.20)	< 0.001	
Diabetes drugs n (%)		294(25.30)	419(33.20)	< 0.001	
Metabolic syndrome		526(45.30)	876(69.40)	< 0.001	

Table 1. Study characteristics, stratified by gender in the Bushehr Elderly Health (BEH) program. (N=2424). *BMI* Body mass index, *HDL* High-density lipoprotein.

Discussion

Having a comprehensive understanding of how the elements of metabolic syndrome come together is valuable in identifying and tackling common cardiometabolic risk factors, as well as in devising specific approaches to prevent the development of coronary artery disease and diabetes^{23,24}.

In this study, we used a person-centered analytical approach to identify latent classes based on the components of metabolic syndrome and smoking behavior. This analysis led to the discovery of four classes:¹ low-risk², metabolic syndrome with medication-controlled diabetes³, high-risk metabolic syndrome with associated

Number of latent classses	Number of parameters estimated	G ²	df	AIC	BIC	CAIC	ABIC	X ²	Entropy	Maximum log-likelihood
1	10	4282.6	757	28622.5	28680.4	28690.4	28648.6	6867.6	5.89	- 14301.2
2	21	1713.7	746	27118.0	26857.7	26878.7	26790.9	2162.9	5.50	- 13347.0
3	32	1193.3	735	26237.6	26423.0	26455.0	26321.3	1381.8	5.40	- 13086.8
4	43	790.7	724	25854.0	26106.1	26149.1	25969.5	796.3	5.31	- 12855.5
5	54	649.9	713	25738.1	26051.0	26105.0	25879.4	635.3	5.28	- 12815.0
6	65	566.9	702	25677.2	26053.8	26118.8	25847.2	560.4	5.27	- 12773.6
7	76	487.4	691	25619.7	26053.8	26136.0	25818.5	481.8	5.25	- 12733.8

Table 2. Comparison of latent class analysis models with different numbers of latent classes based on model selection statistics in the Bushehr Elderly Health (BEH) program (N=2424). *LCA* latent class analysis, *AIC* Akaike information criterion, *BIC* Bayesian information criterion, Consistent Akaike Information Criterion (CAIC), *df* degree of freedom, G^2 the likelihood-ratio statistic.

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	Latent class							
Items	Class 1 (low risk)	Class 2 (MetS with medication-controlled diabetes)	Class 3 (High Risk of MetS and associated medication use)	Class 4 (Central obesity and treated hypertension)				
Latent class prevalence	0.353	0.111	0.271	0.264				
Item-response probabilities								
High fasting blood glucose	0.101	0.989	0.996	0.054				
High waist circumference	0.694	0.813	0.924	0.828				
High triglycerides	0.219	0.399	0.427	0.289				
Low high-density lipoprotein	0.368	0.555	0.601	0.484				
High blood pressure	0.605	0.566	1.000	1.000				
Diabetes drugs	0.005	0.782	0.747	0.018				
Antihypertensive drugs	0.000	0.000	0.963	0.868				
Lipid-lowering drugs	0.118	0.296	0.552	0.319				
Tobacco								
No	0.291	0.253	0.340	0.298				
Past-cigarette or Hookah	0.434	0.461	0.543	0.505				
Current-cigarette or Hookah	0.274	0.283	0.115	0.195				

Table 3. The four latent class model of components of MetS, Tobacco in in the Bushehr Elderly Health (BEH) program. (N=2424) The probability of a "No" response can be calculated by subtracting the item-response probabilities shown above from 1. *Item-response probabilities > 0.5 in bold to facilitate interpretation. Item-response probabilities: Probability of reporting components of MetS and tobacco given membership in various classes. Latent class prevalence: probability of membership in various classes.

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medication use, and⁴ central obesity and treated hypertension. Individuals in class 1 had fewer than three of the MetS components, while members of classes 2, 3, and 4 typically had at least three or more MetS components.

Obesity, especially visceral obesity, can lead to insulin resistance, which increases the risk of developing type 2 diabetes, endothelial dysfunction, an abnormal lipid profile, high blood pressure, and vascular inflammation, all of which contribute to the development of cardiovascular disease²⁵. Previous studies have reported a relationship between obesity and MetS^{26,27}. The incidence of high WC was high among all study participants, but the link between abdominal obesity and being a member of class 3 and 4 was stronger than in other classes. Additionally, the prevalence of obesity and high waist circumference was significantly higher in women than in men. Some studies on MetS have also reported similar findings regarding obesity^{28,29} and high waist circumference²⁹ in women compared to men. This may be explained, in part, by the lower levels of physical activity observed in this study among women. Also, smoking acts as a risk factor for metabolic syndrome and cardiovascular disease through several mechanisms³⁰. For example, Weitzman et al. reported that tobacco smoking is associated with dyslipidemia, including increased LDL and decreased HDL, as well as endothelial dysfunction and dysregulated coagulation, all of which are observed in metabolic syndrome³¹. In the present study, tobacco use was more prevalent in men than in women. LCA suggested that individuals with a history of tobacco were more likely to be in the High Risk of MetS class (Class 3), which demonstrated correlation between tobacco use and low HDL.

We observed a greater prevalence of low HDL among men and a greater prevalence of high triglyceride among women. The prevalence of Low HDL—the most common metabolic abnormality in Iran—has decreased in recent years, particularly in women^{32,33}. Possible reasons for this include decreased carbohydrate consumption and increased unsaturated fat consumption³⁴. Low HDL and elevated triglycerides are two interrelated metabolic

Characteristics	Categories	Low risk	MetS with medication-controlled diabetes OR (95% CI)	High risk of MetS and associated medication use OR (95% CI)	Central obesity and treated hypertension OR (95% CI)
Age	60–64 year	1	REF	REF	REF
	65–69 year	1	0.84 (0.56 to 1.26)	1.30 (0.91 to 1.85)	1.14 (0.82 to 1.57)
	70–74year	1	0.77 (0.45 to 1.30)	1.29 (0.83 to 2.00)	1.28 (0.86 to 1.91)
	> =75 year	1	0.64 (0.37 to 1.11)	1.45 (0.93 to 2.26)	1.61 (1.09 to 2.38)
Sex	Male	1	REF	REF	REF
	Female	1	NA	NA	NA
	Married	1	REF REF		REF
Warital status	Single	1	NA NA		NA
Education (year)		1	0.97 (0.93 to 1.01)	0.99 (0.96 to 1.03)	0.99 (0.96 to 1.02)
Occupation	Employed	1	REF	REF	REF
	Retired	1	0.38 (0.18 to 0.77) 0.79 (0.38 to 1.62)		0.65 (0.36 to 1.17)
	Unemployed	1	0.41 (0.20 to 0.84)	1.23 (0.59 to 2.54)	0.97 (0.53 to 1.78)
Physical activity	No active and sedentary	1	REF	REF	REF
	Low active	1	0.85 (0.55 to 1.32)	0.64 (0.44 to 0.93)	0.74 (0.53 to 1.03)
	Active	1	0.95 (0.51 to 1.78)	0.69 (0.39 to 1.20)	0.75 (0.46 to 1.22)
Household income	Low	1	REF	REF	REF
	Moderate	1	1.23 (0.79 to 1.89)	1.52 (1.06 to 2.17)	1.27 (0.92 to 1.76)
	High	1	1.16 (0.66 to 2.03) 1.40 (0.88 to 2.24)		1.62 (1.07 to 2.46f)
ВМІ	Underweight and normal	1	REF	REF	REF
	Overweight	1	1.34 (0.90 to 1.98)	1.59 (1.13 to 2.22)	1.25 (0.94 to 1.66)
	Obesity	1	1.03 (0.64 to 1.64)	1.91 (1.31 to 2.79)	1.49 (1.06 to 2.08)
TyG index	Tertile 1 (6.96-8.41)	1	REF	REF	REF
	Tertile 2 (8.42-8.93)	1	2.71 (1.70 to 4.30)	2.49 (1.76 to 3.52)	1.18 (0.90 to 1.55)
	Tertile 3 (8.94–11.92)	1	12.33 (7.75 to 19.61)	12.04 (8.31 to 17.45)	1.40 (0.99 to 1.98)
Polypharmacy	No	1	REF	REF	REF
Polypnarmacy	Yes	1	2.07 (1.12 to 3.81)	9.77 (6.12 to 15.59)	1.76 (1.07 to 2.91)
Solf roted boolth	Good	1	REF	REF	REF
Sen-rated nearth	Poor	1	1.36 (0.97 to 1.92)	1.43 (1.08 to 1.89)	1.10 (0.85 to 1.41)

Table 4. Associations between latent class memberships with some of its risk factors in the Bushehr ElderlyHealth (BEH) program (N=2424). BMI body mass index, Triglyceride-glucose index (TyG), Multinomiallogistic regression, REF References group, NA Not applicable.

abnormalities that increase the risk of developing cardiovascular disease³⁵. Our study did not identify this association: membership of classes 3 and 4 was associated with low HDL levels, but elevated triglycerides were observed equally across all four classes.

High fasting blood glucose is one of the key components of metabolic syndrome but was not always observed to co-occur with abdominal obesity in this study (for example, in class 4). However, high fasting blood glucose, which is suggestive of insulin resistance and can lead to a diagnosis of type 2 diabetes, was seen to be associated with other components of metabolic syndrome, such as high blood pressure, abnormal cholesterol levels³⁶, and obesity³⁷.

Older participants were more likely to belong to class 4, although this relationship was not significant in other classes; however, as reported in some studies, the prevalence of components of metabolic syndrome increases with age^{38-41} . Therefore, when examining metabolic syndrome, it is possible to focus on the increase in age and older age of individuals.

In the present study, sedentary people were more likely to belong to the high-risk group for metabolic syndrome. Sedentary behavior is strongly associated with metabolic syndrome, as shown by Russ et al., and regular exercise can effectively reduce the risk of cardiovascular disease⁴². This study showed that people with poor self-related health are 42% more likely to be in the high-risk group for metabolic syndrome. In line with these results, Xiangfeng et al.'s study showed that people with poor self-related health face an increased risk of 68% and 47%, respectively, for stroke and ischemic stroke compared to people with good self-related health. The triglyceride-glucose index, associated with metabolic syndrome, can evaluate insulin resistance and forecast cardiovascular disease risk. Also, women exhibit a higher index than men, corresponding to their elevated fasting blood glucose and triglyceride levels⁴³⁻⁴⁶.

Strengths and limitations

The study's cross-sectional design prevents us from making any inferences regarding causality. Given the relatively large sample size, we expect that our findings are representative of older people in Iran. For future

studies, longitudinal and multi-region studies with a broader age distribution are required to determine and monitor the incidence rate of MetS in the older population and, more importantly, its impact on long-term outcomes.

Conclusion

Among older adults in Iran, the use of LCA identified four distinct subgroups of individuals with different patterns of cardiometabolic risk factors. Stratifying elderly individuals into these different cardiometabolic categories could lead to better monitoring and treatment of cardiometabolic risk factors, ultimately reducing the severe outcomes of metabolic syndrome in this susceptible group. Subsequent research should concentrate on developing targeted approaches for managing subgroups to customize therapeutic plans aimed at reducing risk.

Data availability

"The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request".

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References

- Wilson, P. W., D'Agostino, R. B., Parise, H., Sullivan, L. & Meigs, J. B. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. *Circulation*. 112 (20), 3066–3072 (2005).
- 2. Ramli, A. S. et al. JIS definition identified more Malaysian adults with metabolic syndrome compared to the NCEP-ATP III and IDF criteria. *Biomed. Res. Int.* 2013, 760963 (2013).
- 3. Razzouk, L. & Muntner, P. Ethnic, gender, and age-related differences in patients with the metabolic syndrome. *Curr. Hypertens. Rep.* **11** (2), 127–132 (2009).
- 4. Engin, A. The definition and prevalence of obesity and metabolic syndrome. In *Obesity and Lipotoxicity* (eds Engin, A. B. & Engin, A.) 1–17 (Springer International Publishing, 2017).
- Farmanfarma, K. K. et al. Prevalence of metabolic syndrome in Iran: A meta-analysis of 69 studies. Diabetes Metab. Syndr. Clin. Res. Rev. 13(1), 792–799 (2019).
- 6. Vanni, E. et al. From the metabolic syndrome to NAFLD or vice versa? Dig. Liver Dis. 42 (5), 320-330 (2010).
- 7. Afshin, O. et al. Bushehr Elderly Health (BEH) Programme, phase I (cardiovascular system). BMJ Open. 5 (12), e009597 (2015).
- Parish, J. M., Adam, T. & Facchiano, L. Relationship of metabolic syndrome and obstructive sleep apnea. J. Clin. Sleep Med. 3 (5), 467–472 (2007).
- 9. Ritchie, S. & Connell, J. The link between abdominal obesity, metabolic syndrome and cardiovascular disease. Nutr. Metab. Cardiovasc. Dis. 17 (4), 319-326 (2007).
- 10. Chen, C-C. et al. Association among cigarette smoking, metabolic syndrome, and its individual components: the metabolic syndrome study in Taiwan. *Metabolism.* **57** (4), 544–548 (2008).
- 11. Sun, K., Liu, J. & Ning, G. Active smoking and risk of metabolic syndrome: a meta-analysis of prospective studies. *PLoS One*. 7 (10), e47791 (2012).
- 12. Abbasi-Ghahramanloo, A. et al. Comorbidity of metabolic syndrome components in a population-based screening program: a latent class analysis. *Med. J. Islamic Repub. Iran.* 34, 69 (2020).
- 13. Boyko, E. J. et al. Latent class analysis of the metabolic syndrome. Diabetes Res. Clin. Pract. 89 (1), 88-93 (2010).
- 14. Lanza, S. T. & Rhoades, B. L. Latent class analysis: an alternative perspective on subgroup analysis in prevention and treatment. *Prev. Sci.* 14 (2), 157–168 (2013).
- 15. Hajian-Tilaki, K., Heidari, B. & Firouzjahi, A. Clustering of cardio metabolic risk factors in Iranian adult population: A growing problem in the north of Iran. *Diabetes Metab. Syndr. Clin. Res. Rev.* 11, S277–S81 (2017).
- Ahanchi, N. S. et al. Application of latent class analysis to identify metabolic syndrome components patterns in adults: Tehran lipid and glucose study. Sci. Rep. 9 (1), 1572 (2019).
- 17. Gita, S. et al. Bushehr Elderly Health (BEH) programme: study protocol and design of musculoskeletal system and cognitive function (stage II). *BMJ Open.* 7 (8), e013606 (2017).
- Ford, E. S. Prevalence of the metabolic syndrome defined by the International Diabetes Federation among adults in the US. Diabetes Care. 28 (11), 2745–2749 (2005).
- Moghaddam, M. B. et al. The Iranian version of International Physical Activity Questionnaire (IPAQ) in Iran: content and construct validity, factor structure, internal consistency and stability. World Appl. Sci. J. 18 (8), 1073–1080 (2012).
- 20. da Silva, A. et al. Triglyceride-glucose index is associated with symptomatic coronary artery disease in patients in secondary care. *Cardiovasc. Diabetol.* **18** (1), 89 (2019).
- Dong, W. et al. Determinants of self-rated health among Shanghai elders: a cross-sectional study. BMC Public. Health. 17 (1), 1–12 (2017).
- 22. Mofrad, Z. P., Jahantigh, M. & Arbabisarjou, A. Health promotion behaviors and chronic diseases of aging in the elderly people of Iranshahr*-IR Iran. *Glob. J. Health Sci.* 8 (3), 139 (2016).
- Riahi, S. M. et al. Patterns of clustering of the metabolic syndrome components and its association with coronary heart disease in the multi-ethnic study of atherosclerosis (MESA): a latent class analysis. *Int. J. Cardiol.* 271, 13–18 (2018).
- Esteghamati, A., Zandieh, A., Khalilzadeh, O., Meysamie, A. & Ashraf, H. Clustering of metabolic syndrome components in a middle eastern diabetic and non-diabetic population. *Diabetol. Metab. Syndr.* 2 (1), 1–8 (2010).
- da Ponte Neto, A. M. et al. Fecal microbiota transplantation in patients with metabolic syndrome and obesity: a randomized controlled trial. World J. Clin. Cases. 11 (19), 4612 (2023).
- Jialal, I., Adams-Huet, B. & Devaraj, S. Increased adipocyte hypertrophy in patients with nascent metabolic syndrome. J. Clin. Med. 12 (13), 4247 (2023).
- Mirrafiei, A. et al. Association of main meal quality index with the odds of metabolic syndrome in Iranian adults: a cross-sectional study. *BMC Nutr.* 9 (1), 1–11 (2023).
- García, G. Causes and components of the metabolic syndrome in renal transplant recipients from a gender perspective. *Nutr. Hosp.* 35 (5), 1079–1084 (2018).
- 29. Lekpa, F. K. et al. Gender difference in the association between gout at diagnosis and metabolic syndrome in African population: a retrospective cohort study. *Pan Afr. Med. J.* **43** (2022).
- 30. Balhara, Y. P. S. Tobacco and metabolic syndrome. Indian J. Endocrinol. Metabol. 16 (1), 81 (2012).
- 31. Weitzman, M. et al. Tobacco smoke exposure is associated with the metabolic syndrome in adolescents. *Circulation*. **112** (6), 862–869 (2005).

- 32. Ryu, S. Y. et al. Prevalence of metabolic syndrome and associations with lipid profiles in Iranian men: a population-based screening program. *World J. Men's Health.* **36** (1), 50–56 (2018).
- Karimi, F., Jahandideh, D., Dabbaghmanesh, M., Fattahi, M. & Ranjbar, O. G. The Prevalence of Metabolic Syndrome and its Components among Adults in a Rural Community (Fars, 2015).
- 34. Park, D. et al. 20-year trends in metabolic syndrome among Korean adults from 2001 to 2020. JACC: Asia. 3 (3_Part_2), 491-502 (2023).
- Hadaegh, F. et al. Triglyceride/HDL-cholesterol ratio is an independent predictor for coronary heart disease in a population of Iranian men. Nutr. Metab. Cardiovasc. Dis. 19 (6), 401–408 (2009).
- 36. Kurotani, K. et al. Metabolic syndrome components and diabetes incidence according to the presence or absence of impaired fasting glucose: the Japan Epidemiology Collaboration on Occupational Health Study. J. Epidemiol. 27 (9), 408–412 (2017).
- 37. Akter, R. et al. Effect of obesity on fasting blood sugar. Mymensingh Med. J. MMJ. 26 (1), 7-11 (2017).
- 38. Ahmed, A. E. et al. Metabolic syndrome and cardiometabolic risk factors in the mixed hypercholesterolemic populations with respect to gender, age, and obesity in Asir, Saudi Arabia. *Int. J. Environ. Res. Public Health.* **19** (22), 14985 (2022).
- 39. Ogbera, A. O. Prevalence and gender distribution of the metabolic syndrome. Diabetol. Metab. Syndr. 2, 1-5 (2010).
- Wang, B. et al. Prevalence of metabolically healthy obese and metabolically obese but normal weight in adults worldwide: a metaanalysis. *Horm. Metab. Res.* 47 (11), 839–845 (2015).
- 41. Fernández-Verdejo, R. & Galgani, J. E. Exploring the sequential accumulation of metabolic syndrome components in adults. *Sci. Rep.* **12** (1), 15925 (2022).
- 42. Rus, M. et al. Prevalence and risk factors of metabolic syndrome: a prospective study on Cardiovascular Health. *Medicina*. **59** (10), 1711 (2023).
- 43. Jiang, M. et al. Triglyceride-glucose index for the diagnosis of metabolic syndrome: a cross-sectional study of 298,652 individuals receiving a health check-up in China. *Int. J. Endocrinol.* **2022** (2022).
- 44. Zhang, X. et al. Association of metabolic syndrome with TyG index and TyG-related parameters in an urban Chinese population: a 15-year prospective study. *Diabetol. Metab. Syndr.* 14, 1 (2022).
- Tao, L-C., Xu, J., Wang, T., Hua, F. & Li, J-J. Triglyceride-glucose index as a marker in cardiovascular diseases: landscape and limitations. *Cardiovasc. Diabetol.* 21 (1), 1–17 (2022).
- 46. Son, D-H., Lee, H. S., Lee, Y-J., Lee, J-H. & Han, J-H. Comparison of triglyceride-glucose index and HOMA-IR for predicting prevalence and incidence of metabolic syndrome. *Nutr. Metab. Cardiovasc. Dis.* **32** (3), 596–604 (2022).

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Author contributions

S.A., A.F., and Z.J. conceived the study, performed data analysis and interpretation. N.D., A.J., and H.M. performed data analysis and interpretation and drafted the manuscript performed data analysis. J.B. and H.M. critically reviewed the manuscript. I.N. and B.L. revised the manuscript. All authors reviewed the manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

Ethics approval and consent to participate The Ethics Committee of Bushehr University of Medical Sciences granted ethical permission for this study (Ethical Code: IR.BPUMS.REC.1402.138) in compliance with the Helsinki Declaration and national guidelines for research ethics. Before research enrollment, all participants gave their informed consent after being informed about procedures involved in the study.

Consent for publication

The authors confirm that human research participants provided informed consent for publication of their data.

Informed consent

The participants provided their written informed consent to take part in this study. Participation was entirely optional, and any participant could withdraw consent at any moment with no repercussions.

Additional information

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