Original Article
http://mjiri.iums.ac.ir

Medical Journal of the Islamic Republic of Iran (MJIRI)
Iran University of Medical Sciences

Clustering and combining pattern of metabolic syndrome components among Iranian population with latent class analysis

Abbas Abbasi-Ghahramanloo[1], Sepideh Soltani[2], Ali Gholami[3]
Mohammadreza Erfani[4], Somayeh Yosaee*[5]

Received: 23 January 2016 Accepted: 21 August 2016 Published: 22 November 2016

Abstract

Background: Metabolic syndrome (MetS), a combination of coronary heart disease and diabetes mellitus risk factor, refer to one of the most challenging public health issues in worldwide. The aim of this study was to identify the subgroups of participants in a study on the basis of MetS components.

Methods: The cross-sectional study took place in the districts related to Tehran University of Medical Sciences. The randomly selected sample consists of 415 subjects. All participants provided written informed consent. Latent class analysis was performed to achieve the study's objectives. Analyses were conducted by using proc LCA in SAS 9.2 software.

Results: Except systolic and diastolic blood pressure, the prevalence of all MetS components is common in female than male. Four latent classes were identified: (a) non MetS, (b) low risk, (c) high risk, and (d) MetS. Notably, 24.2% and 1.3% of the subjects were in the high risk and MetS classes respectively.

Conclusion: Most of the study participants were identified as high risk and MetS. Design and implementation of preventive interventions for this segment of the population are necessary.

Keywords: Latent class analysis, Metabolic syndrome, MetS component subgrouping, Iran.

Cite this article as: Abbasi-Ghahramanloo A, Soltani S, Gholami A, Erfani M, Yosaee S. Clustering and combining pattern of metabolic syndrome components among Iranian population with latent class analysis l. *Med J Islam Repub Iran* 2016 (22 November). Vol. 30:445.

Introduction

Metabolic syndrome (MetS) is defined as the co-occurrence of three or more of the following features: increased waist circumference (WC), hypertension, dyslipidemia, and hyperglycemia (1). These cluster of risk factors was first described as syndrome X by Reaven in the 1988 Banting lecture. MetS lead to an enhanced risk of cardiovascular diseases and type 2 diabetes mellitus, cancers, and increased risk of morbidity and mortality (2-4). MetS is a serious health problem worldwide(5). The prevalence of MetS is expanding in worldwide. MetS prevalence in USA and Korea adult is estimated to be >25%, in another word currently one in five ad ults in these countries meet criteria for MetS (6,7). In northern Iran, the prevalence of MS is very high (36.5% in men and 47.1% in women) (8).

Clinical guidelines consider the MetS as a categorical state that is either present or absent, but it is not clear whether this approach is valid either (9,10). Prior methods to identify underlying features of the MetS may not be usable to address the question of whether a condition that is present or absent explains the observed manifestations of the metabolic syndrome as defined using

[1]. PhD Student in Epidemiology, School of Public Health, Department of Epidemiology, Iran University of Medical Sciences, Tehran, Iran, & Iran Virtual Research Core, Iran University of Medical Sciences, Tehran, Iran. abbasi.abbas49@yahoo.com
[2]. PhD student, Department of Nutritional Sciences, School of Public Health, Iran University of Medical Sciences, Tehran, Iran. s.soltani1979@yahoo.com
[3]. PhD Student, Department of Public Health, Neyshabur University of Medical Sciences, Neyshabur, Iran, & School of Public Health, Department of Epidemiology, Iran University of Medical Sciences, Tehran, Iran, & Iran Virtual Research Core, Iran University of Medical Sciences, Tehran, Iran. aagholami80@yahoo.com
[4]. PhD Student, Ewaz School of Health, Larestan School of Medical Sciences, Larestan, Iran. erfanimr@sums.ac.ir
[5]. (**Corresponding author**) PhD Student, Department of Nutritional Sciences, School of Public Health, Iran University of Medical Sciences, Tehran, Iran, & Ewaz School of Health, Larestan School of Medical Sciences, Larestan, Iran. s_yousai2006@yahoo.com

current criteria based on dichotomization of levels o blood pressure, lipid, glycemia, and central obesity (11).

The latent class analysis aims to classify similar individuals into groups, in which each latent class is viewed as consisting of homogeneous individuals with regards to the observed variables being studied (in our study, components of MetS), and the different. Latent classes are viewed as representing the unobserved heterogeneity among individuals in these observed variables (12). Considering the possibility that relationships among MetS components may meaningfully differ in subgroups of individuals, this person-centered analytic approach strives to identify quantitatively and qualitatively distinct profiles of individuals based on their presentation of MetS components.

Latent class analysis has been little used in medical research other than in the area of mental health. Based on the above-mentioned background, the aim of this study was to (a) identify the subgroups of participants in a study on the basis of components of MetS and (b) document the prevalence of the subgroups.

Methods

Data

The present cross-sectional study was conducted from fall 2012 to winter 2013. The study was restricted to Iranian adults>20 years of age who referred to the Endocrinology Center of Tehran University of Medical Sciences. We used the following sampling method in this study: From each week we randomly selected three days and in these days all patients who had the inclusion criteria was entered into the study. The sample size was calculated according to the study conducted in Iran by Zabetian et al. (13). In this study, the prevalence of MetS among Iranian above 20 years old, was reported as 33.2% by the ATPIII definition. All participants provided written informed consent.

Coronary artery disease, uncontrolled thyroid disorder, renal and hepatic failure, acute infection within the previous seven days, presence of any autoimmune disease, and any known malignancy, use of medications for dyslipidemia, hyperglycemia or hypertension, pregnancy, breast feeding, post-menopause, smoking, professional athlete, hypnotics, or having a special diet were considered as exclusion criteria (14). The age ranged 20-55 years and provided written consent informed were as inclusion criteria.

Height and weight were measured, with the participants wearing light clothing and no shoes. WC measurements were performed between the lower rib margin and the iliac crest by a flexible tape measure after normal expiration. Body mass index (BMI) of each subject was calculated as body weight in kilograms divided by the square of the height in meters (kg/m2). Blood pressure measurement was taken twice separately over a 3-min interval. The average of two consecutive readings considered as blood pressure value.

Fasting blood samples were drawn after an overnight fasting for measurements of HDL-C, FBS, and TG. FBS was assayed by an automated glucose oxidase method. TG, HDL-C were measured by enzymatic methods using an auto analyzer.

Statistical Analysis

The LCA was used in data analysis. The LCA is a latent categorical variable's model, and it classifies homogeneous individuals. It assumes that besides the measurement error, whether the correlation between observed variables could be justified by latent variable categories. By various iterations for the number of identified classes of the latent variable and comparing the frequencies of the observed response patterns with the expected ones, the LCA determines the best model and calculates a statistics similar to $\chi 2$ called G2. Based on G2 statistic, Akaike information criterion (AIC) and Bayesian information criterion (BIC) can be calculated for model selection(15). For all information criteria, a smaller value represents a more optimal

balance of model fit and parsimony; thus, a model with the minimum AIC or BIC might be selected. When the degrees of freedom are large, the reference distribution for the G2 statistic is not known, so we do not report p-values for tests of model fit. For performing LCA, seven dichotomous observable variables (i.e., indicators) were used for subgrouping of MetS as a latent variable. These indicators were WC, HDL, Triglyceride, SBP, DBP and FBS.

Analyses were conducted by using proc LCA in SAS 9.2 software (SAS Institute Inc. Cary, NC, USA).

Results

The mean±SD age of the subjects was 44.9±11.81yrs (range: 22-76yrs). The prevalence of waist circumference (WC)>102 for men and 88 for women, high-density lipoprotein-C (HDL-c)< 45 for men and 55 for women, Triglyceride>150, systole blood pressure (SBP)>130, diastole blood pressure (DBP)>85, BMI>25 as well as the prevalence of fasting blood sugar (FBS)>100 by sex is shown in Table 1. The data in Table 1 show that some of the MetS components are more normative than others. For example, it is not uncommon for subjects to having high WC. Also, the results show that except SBP and DBP, the prevalence of all MetS components is common in female than male.

With the seven dichotomous variables, 128 possible response patterns can exist. For selecting the best model the authors fit LCA models with classes ranging from 1 to 10 (Table 2). The statistical indices like G2, AIC and BIC were computed for each class. Because of the relatively large number of observed variables measuring the latent variable and the number of response categories per variable, the degrees of freedom are fairly large in our study. When the degrees of freedom are large, the reference distribution for the G2 statistic is not known, so we do not report p-values for tests of model fit. Because of the large degrees of freedom, the AIC and BIC were relied on more heavily for model selection.

As can be seen in Table 2 and based on model selection indices and interpretability of the results of the model, we concluded that the four-class latent model was appropriate for this subjects.

Table 3 presents a description of latent classes. The probabilities of membership in each latent class appear in the first section

Table 1. Frequency distribution of subjects' characteristics about components of syndrome metabolic

	Male(n=204)		Female(n=211)		Total(n=415)	
Items	N(%)	95% CI	N(%)	95% CI	N(%)	95% CI
Waist circumference	93(45.6)	40.5-55.1	181(86.2)	82.4-91.6	274(66.0)	64.0-73.2
High density lipoprotein	7(3.5)	0.3-5.1	52(25.0)	19.1-30.9	59(14.2)	11.0-18.1
Triglyceride	83(41.5)	32.5-46.8	88(42.3)	35.5-49.1	171(41.2)	36.2-46.0
Systolic blood pressure	92(45.1)	37.8-52.4	63(29.9)	24.0-36.6	155(37.3)	32.4-42.1
Diastolic blood pressure	83(40.9)	35.2-49.6	31(14.8)	10.0-19.8	114(27.5)	23.4-32.3
Body mass index (BMI>25)	55(28.9)	23.2-36.6	93(44.1)	37.9-51.5	148(35.7)	32.9-42.6
Fasting blood glucose	70(35.4)	29.4-43.4	113(54.3)	47.5-61.2	183(44.1)	41.0-50.9

Table 2. Comparison of LCA models with different latent classes based on model selection statistics

Number of latent class	Number of parameters estimated	G^2	df	AIC	BIC	Maximum log-likelihood
1	7	449.10	120	463.10	491.30	-1771.50
2	15	251.85	112	281.85	342.28	-1672.87
3	23	142.89	104	188.89	281.54	-1618.39
4	31	110.98	96	172.98	297.85	-1602.44
5	39	80.84	88	158.84	315.94	-1587.37
6	47	65.16	80	159.16	348.49	-1579.53
7	55	55.81	72	165.81	387.36	-1574.85
8	63	47.58	64	173.58	427.36	-1570.74
9	71	40.70	56	182.70	468.71	-1567.30
10	79	32.39	48	190.39	508.62	-1563.14

Note. LCA = latent class analysis; AIC = Akaike information criterion; BIC = Bayesian information criterion.

Table 3. The Four Latent Classes Model of components of metabolic syndrome

	Latent class			
	C1 (non MetS)	C2 (low risk)	C3 (high risk)	C4 (MetS)
Latent class prevalence	0.384	0.186	0.242	0.187
Item-response probabilities		Probability of a "Yes"*		
Waist circumference	0.261	**0.992**	**0.801**	**0.970**
High density lipoprotein	0.038	0.002	0.071	**0.589**
Triglyceride	0.250	0.418	0.424	**0.743**
Systolic blood pressure	0.127	0.149	**0.992**	0.305
Diastolic blood pressure	0.088	0.090	**0.860**	0.091
Body mass index	0.005	**0.957**	0.450	0.398
Fasting blood glucose	0.339	0.434	0.409	**0.740**

Note. The probability of a "No" response can be calculated by subtracting the item-response probabilities shown above from 1.
*Item-response probabilities >.5 in bold to facilitate interpretation.

of Table 3. The second section of Table 3, contain the conditional probabilities of a "Yes" response to MetS components. The probability of a "No" response can be calculated by subtracting the item-response probabilities from 1.These probabilities form the basis for interpretation and labeling of the latent classes. The larger conditional probabilities appear in bold font, to highlight the overall pattern. The first class, named "Non-MetS," described 38.4% of subjects, and was characterized by individuals exhibiting healthy MetS component status. The second class, named "low risk," described 18.6% of the individual, and was characterized by individuals exhibiting relatively healthy MetS components status with the exception of WC and BMI. The third class described 24.2% of the individual, and was characterized by individuals exhibiting clinically elevated levels of WC and BP. The fourth class described 18.7% of individual and was characterized by individuals exhibiting clinically elevated levels across most MetS components (With the exception of BP).

Discussion

The results of the study reported the prevalence of each component of MetS, namely, WC, HDL-c, Triglyceride, SBP, DBP, BMI and FBS. WC was a common component with the rate of prevalence of 66.0%, and HDL-c was uncommon with the prevalence rate of 14.2%. The results indicate that the prevalence of the components of MetS- except SBP and DBP- were more common among females, compared to males. This finding in our study is similar to other studies from Iran and other countries (16,17).

This is to author's knowledge the first attempt to using LCA to identifying the MetS components subgroups in Iran. Our results showed that one class (latent class four) was consistently associated with many MetS features. This class may represent a specific clinical state producing the observed features of the MetS.

Considering clustering of MetS components can be an effective approach in prevention programs. Some studies emphasized on the clustering and combining pattern of metabolic syndrome components (18). We examined this pattern differently by LCA and identified four latent classes. The four latent classes are the following: (a) non MetS, (b) low risk, (c) high risk, and (d) MetS. Clinicians believe that cardiovascular disease determinants tend to accumulate, and therefore the risk of developing these disease rises along with increases in their clustering abilities (19-21).

Our results showed that Individuals in latent class four-MetS- were likely to engage in most MetS components. In contrast, those in Latent Class 1, non MetS, were likely not engaged in any of the MetS components. Latent class two indicates persons who have low risk of having MetS components. This group had a high probability of having two components of MetS, namely, WC and BMI. It seems this type of people is obese and has no other components of MetS. With consideration of this features, we named this group "Low risk." Latent class 3 indicates another pattern of MetS

components. In this group, as can be in table 3, the probability of having high WC, high SBP, and high DPB is high. Probably these persons have a high risk of cardiovascular disease, but in this study, we could not assess this risk. In this group the probability of triglyceride, BMI and FBG are high also but for naming classes we used the larger conditional probabilities (>0.50) to highlight the overall pattern.

Prior studies recognized that cardiovascular disease risk factors and determinants tend to cluster (19-21). Thus the chance of this disease rises in line with increases in the mentioned determinants clustering ability. Our results show this clustering of MetS components in different patterns. This clustering of MetS components can be helpful in reinforcing the hypothesis that underlying pathophysiological mechanisms are involved in this process (18).

Moreover longitudinal studies have been showed that there are variations in the risk of mortality according to the different combination patterns of metabolic syndrome components (22,23). Our results indicated different combination pattern of MetS components. For example, we observed that in a combination of MetS components among individuals of latent class four, the blood pressure have no role. According to these patterns, probably the individuals of latent class three and four has a different chance of engaging in complications of metabolic syndrome.

Some studies declared that obesity has a fundamental role in the pathophysiological mechanism of metabolic syndrome (4,24). In our study, it could be seen that abdominal obesity has an important role in three latent classes of MetS. It should be noted that we couldn't assess pathophysiological mechanism of metabolic syndrome, but the co-occurrence of this components with other components shows the importance of abdominal obesity in combination patterns of MetS. These findings could be guided healthcare professionals.

The present work also has this limitation that due to the cross-sectional design of the study, causality could not be assessed. Also, we restricted the study to the patients who referred to the Endocrinology Center of Tehran University of Medical Sciences.

Conclusion

Our study represents the co-occurrence of MetS components by subgrouping a sample of Iranian population who referred to the Endocrinology Center of Tehran University of Medical Sciences into four classes. Results showed that notable percentages of subjects are in the high risk and MetS classes, which stresses the necessity of implementing preventive interventions for this stratum of the population.

Acknowledgments

We would wish to thank all the study participants for their valuable collaboration with the research team.

Conflicts of Interest

The authors report no conflicts of interest and are responsible for the content and writing of the article.

References

1. Alberti K, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; American heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. Circulation 2009;120(16):1640-5.

2. Potenza MV, Mechanick JI. The Metabolic Syndrome Definition, Global Impact, and Pathophysiology. Nutrition in Clinical Practice 2009;24(5):560-77.

3. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Rafaniello C, et al. Colorectal cancer association with metabolic syndrome and its components: a systematic review with meta-analysis. Endocrine 2013;44(3):634-47.

4. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. The Lancet 2005; 365(9468):1415-28.

5. Maury E, Brichard S. Adipokine dysregulation, adipose tissue inflammation and metabolic

syndrome. Molecular and cellular endocrinology 2010;314(1):1-16.
6. Mccullough AJ. Epidemiology of the metabolic syndrome in the USA. Journal of digestive diseases 2011;12(5):333-40.
7. Lim S, Shin H, Song JH, Kwak SH, Kang SM, Yoon JW, et al. Increasing prevalence of metabolic syndrome in Korea the Korean national health and nutrition examination survey for 1998–2007. Diabetes care 2011;34(6):1323-8.
8. Hajian-Tilaki K, Heidari B, Firouzjahi A, Bagherzadeh M, Hajian-Tilaki A, Halalkhor S. Prevalence of metabolic syndrome and the association with socio-demographic characteristics and physical activity in urban population of Iranian adults: a population-based study. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2014;8(3):170-6.
9. Alberti KGMM, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A consensus statement from the international diabetes federation. Diabetic medicine 2006;23(5):469-80.
10. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation 2005;112(17):2735-52.
11. Boyko EJ, Doheny RA, McNeely MJ, Kahn SE, Leonetti DL, Fujimoto WY. Latent class analysis of the metabolic syndrome. Diabetes research and clinical practice 2010;89(1):88-93.
12. Vermunt JK, Magidson J. Latent class cluster analysis. Applied latent class analysis 2002;11:89-106.
13. Zabetian A, Hadaegh F, Azizi F. Prevalence of metabolic syndrome in Iranian adult population, concordance between the IDF with the ATPIII and the WHO definitions. Diabetes research and clinical practice 2007;77(2):251-7.
14. Sharma SK, Agrawal S, Damodaran D, Sreenivas V, Kadhiravan T, Lakshmy R, et al. CPAP for the metabolic syndrome in patients with obstructive sleep apnea. New England Journal of Medicine 2011;365(24):2277-86.
15. Mohammadpoorasl A, Ghahramanloo AA, Allahverdipour H. Risk-Taking Behaviors and Subgrouping of College Students A Latent Class Analysis. American journal of men's health. 2013:1557988313483540.
16. Metelskaya VA, Shkolnikova MA, Shalnova SA, Andreev EM, Deev AD, Jdanov DA, et al. Prevalence, components, and correlates of metabolic syndrome (MetS) among elderly Muscovites. Archives of gerontology and geriatrics 2012; 55(2):231-7.
17. Karimi F, Jahandideh D, Dabbaghmanesh M, Fattahi M, Omrani GR. The prevalence of metabolic syndrome and its components among adults in a rural community, Fars, Iran. International Cardivascular Research Journal 2015;9(2):94-9.
18. Pimenta AM, Felisbino-Mendes MS, Velasquez-Melendez G. Clustering and combining pattern of metabolic syndrome components in a rural Brazilian adult population. Sao Paulo Medical Journal 2013;131(4):213-9.
19. Genest J, Cohn JS. Clustering of cardiovascular risk factors: targeting high-risk individuals. The American journal of cardiology 1995;76(1):8A-20A.
20. Yusuf HR, Giles WH, Croft JB, Anda RF, Casper ML. Impact of multiple risk factor profiles on determining cardiovascular disease risk. Preventive medicine 1998;27(1):1-9.
21. Katakami N, Kaneto H, Matsuhisa M, Umayahara Y, Kosugi K, Yamasaki Y. Clustering of several cardiovascular risk factors affects tissue characteristics of the carotid artery. Atherosclerosis 2008;198(1):208-13.
22. Guize L, Thomas F, Pannier B, Bean K, Jego B, Benetos A. All-cause mortality associated with specific combinations of the metabolic syndrome according to recent definitions. Diabetes care 2007;30(9):2381-7.
23. Hong Y, Jin X, Mo J, Lin HM, Duan Y, Pu M, et al. Metabolic syndrome, its preeminent clusters, incident coronary heart disease and all-cause mortality–results of prospective analysis for the Atherosclerosis Risk in Communities study. Journal of internal medicine 2007;262(1):113-22.
24. Cornier M-A, Dabelea D, Hernandez TL, Lindstrom RC, Steig AJ, Stob NR, et al. The metabolic syndrome. Endocrine reviews 2008; 29(7):777-822.