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Prevalence and impact of metabolic syndrome on outcomes of acute coronary syndrome patients in two different countries

Viola Keczeli[1], Led Al-Sadoon[1], Orsolya Máté[2], Sára Jeges[1], Éva Polyák[3], Annamária Karamánné Pakai[4], Mercédesz Ahmann[1], Andrea Gubicskóné Kisbenedek[3]*, Zsófia Verzár[1]*

[1]Doctoral School of Health Sciences, Faculty of Health Sciences, University of Pécs, Pécs, Hungary

[2] Institute of Nursing Sciences, Basic Health Sciences and Health Visiting, Faculty of Health Sciences, University of Pécs, Pécs, Hungary

[3] Institute of Human Nutrition and Dietetics, Faculty of Health Sciences, University of Pécs, Pécs, Hungary

[4] Institute of Nursing Sciences, Basic Health Sciences and Health Visiting, Faculty of Health Sciences, University of Pécs, Szombathely, Hungary

*equally contributed

Abstract

Introduction: This study aimed to ascertain the prevalence of metabolic syndrome (MetS) in patients from Hungary and Iraq, suffering from acute coronary syndrome (ACS) and investigate the effects of MetS on hospital outcomes, in particular mortality and its relation to differences in patients' baseline characteristics.

Material and methods: A prospective cohort study was conducted in two cardiac centers between May 2018 and May 2019. It included 164 consecutive ACS patients: 64 patients from the Cardiac Clinic in Pécs, Hungary and 100 patients from Al Nassiryah Heart Center, Iraq. Baseline characteristics, clinical management, and in-hospital and 30-day post-discharge outcomes were recorded.

Results: Prevalence of metabolic syndrome among ACS patients in Iraq? was not significantly higher than in Hungary (25.0% vs 34.1%; $P = 0.306$). There were no significant differences in age between those with and without MetS (64.2 vs 63.3 years; $P = 0.394$). MetS was associated with a higher median BMI (28.0 vs 23.7 kg/m^2; $P < 0.001$), hyperlipidemia (37.8% vs 12.8%; $P < 0.001$), hypertension (48.8% vs 27.4%; $P = 0.024$), high cholesterol (5.4 vs 4.1 mmol/L; $P < 0.001$), high LDL-C (3.5 vs 2.6 mmol/L; $P < 0.001$), and high triglycerides (1.4 vs 1.1 mmol/L; $P < 0.001$). MetS was associated with a higher risk of out hospital re-infarction (12.8% vs 3.7%; $P = 0.031$) and MACE (17.7% and 6.1%; $P = 0.027$).

Conclusions: Current study did not show any significant difference in the incidence of MetS between ACS patients in the two countries. But patients with MetS were significantly more likely to be associated with MACE ($P = 0.027$).

Key words: metabolic syndrome, outcomes, acute coronary syndrome, prevalence, major adverse cardiovascular events

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Address for correspondence: Viola Keczeli, University of Pécs, Faculty of Health Sciences, Doctoral School of Health Sciences, Vörösmarty street 4., 7621 Pécs, Hungary, e-mail: viola.keczeli@etk.pte.hu

Introduction

Metabolic Syndrome (MetS) is a cluster of risk factors that includes abdominal obesity, high triglyceride, low high-density lipoprotein cholesterol (HDL-C), raised blood pressure (BP), and raised fasting blood glucose [1–3]. The incidence of metabolic syndrome often parallels obesity and Type 2 diabetes [4]. Metabolic syndrome is a complex pathophysiological state associated with an imbalance of calorie intake and energy expenditure but is also affected by individual genetic/epigenetic makeup, predominance of a sedentary lifestyle, and other factors like quality and composition of food and composition of gut microbes [4]. The incidence can not be reduced by taking any drugs [5], but dietary intervention and regular exercise are essential as the first-line treatment for obese patients with MetS, and the principal rule of every dietary modification is caloric restriction and consequent weight loss. Adherence to the Mediterranean diet has also been shown to decrease the risk of MetS [6, 7].

Studies based on populations at high risk for cardiovascular diseases have shown a very high prevalence of metabolic syndrome. Obesity can be called comorbidity of MetS, but obesity alone is also a risk factor for the incidence of cardiovascular diseases. Obesity induces several cytokines and inflammatory markers which might contribute to adverse cardiovascular outcomes in overweight and obese people [6–11]. The prevalence of MetS among patients with acute coronary syndrome (ACS) varies between 29% and 46%, with a poor in-hospital prognosis. Symptomatic vascular diseases (e.g. coronary artery disease, stroke, or peripheral arterial disease) show that the prevalence of metabolic syndrome is correlated with the extent of vascular damage [12–13]. However, previous research has shown that the presence of metabolic syndrome as a risk factor plays a role in the progression and outcomes, for example, of deep sternal wound infections (DSWI) after CABG operations [14, 15].

Besides MetS the relationship between smoking and cardiovascular risk factors has long been investigated, and a wealth of data was published. Smoking is considered to cause an acutely and chronically accelerated heart rate due to sympathetic stimulation confirmed by numerous research data [16–19]. It is important that other forms of tobacco exposure (chewing, inhalation through water, and secondhand smoke) have also been documented to be important causes of coronary disease worldwide [20].

This study aimed to compare the prevalence of metabolic syndrome in patients from Hungary and Iraq, suffering from acute coronary syndrome diseases and to examine the effects of metabolic syndrome on hospital outcomes, in particular, death.

Material and methods

Study design and population

A prospective cohort study was conducted at two cardiac centers from May 2018 to May 2019. The study included 164 ACS patients: 64 patients from Cardiac Clinic in Pécs, Hungary, and 100 patients from Al-Nasiriyah Heart Center in Iraq. From known conditions of ACS, Troponin T-positive patients with ST-segment elevation and non-ST-segment elevation acute myocardial infarction were studied. ACS diagnosis was based on the guidelines of the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (AHA/ACC) [21, 22]. The study complied with the Declaration of Helsinki of 2003 and was approved by the local ethics committee of the Doctoral School of Health Sciences of the University of Pécs, Hungary. The study was approved by the Regional and Institutional Research Ethics Committee (4511/2016) of the University of Pécs, and all participants gave their informed consent in The study was approved by the Regional and Institutional Research Ethics Committee (4511/2016) of the University of Pécs, and Dhi-Qar health director /Al-Nasiriyah Heart Center. Written consent was obtained from each patient after they were informed clearly about the details of the study. (in the original text before the Dhi-Qar is a "and" conjunction not "in" preposition).

Data collection

Demographic and other baseline clinical characteristics of the patients along with in-hospital outcomes were evaluated. Outcome parameters evaluated during the hospital stay included in-hospital mortality, recurrent ischemia/re-infarction, heart failure (HF), cardiogenic shock, stroke, and major adverse cardiovascular events (MACEs). MACEs were defined as the composite of total death, re-infarction, and stroke. The patients with ACS were stratified into those with and without metabolic syndrome. Metabolic syndrome was defined according to the NCEP ATP III criteria [21, 23–26]. Patients received a diagnosis of metabolic syndrome if they had any 3 of the following 5 criteria: abdominal obesity (waist circumference > 102 cm [> 40 inches] for men and >88 cm [> 35 inches] for women), high triglyceride levels ≥ 150 mg/dL (1.7 mmol/ L), reduced or low HDL cholesterol levels < 40 mg/dL (1.04 mmol/L) in men and

< 50 mg/dL (1.30 mmol/L) in women, hyperglycemia (history of diagnosed diabetes mellitus or fasting blood glucose level ≥ 110 mg/dL (6.10 mmol/L), and elevated blood pressure (treated hypertension, systolic blood pressure ≥ 130 mm Hg, or diastolic blood pressure ≥ 85 mm Hg). If patients had only 2 of the following 5 criteria, they were classified as a group without MetS. Patients with acute coronary syndrome have a life-threatening condition, every minute can count on the patient's survival. Because of this, it was not possible to assess abdominal obesity in all cases, instead, we used BMI data to divide patients into 2 groups — patients with MetS and patients without MetS.

Statistical analysis

Continuous variables are expressed as the mean ± SD or median and interquartile range (IQR). Categorical variables are expressed as percentages and frequencies. Differences between groups (metabolic syndrome status, negative/positive) and between the two countries (Iraq and Hungary) were analyzed using the chi-square for the categorical variables and Student's t-test, Fisher's exact test, or the Mann-Whitney U test of continuous variables, based on the normal distribution. Values of $P < 0.05$ were considered significant. Statistical analyses were conducted using SPSS, version 22.0 (IBM Corporation, USA).

Results

Patient demographic and clinical characteristics

The demographic and clinical characteristics of the patients stratified by metabolic syndrome status are summarized in Table I. The overall prevalence of metabolic syndrome for this population with ACS in Iraq was 34.1% (56 patients) while in Hungary was 25% (41 patients). The mean age of the cohort was 63.8 + 11.9 years. There was no difference in age between patients with and without metabolic syndrome (64.2 +11.5 y vs 63.3+ 12.6 y respectively; P= 0.394). Most of the admitted patients were males (111; 67.7%). The metabolic syndrome cohort was more likely to be associated with a higher average BMI (28.0 vs 23.7 kg/m2; $P < 0.001$) and a previous history of hypertension (48.8% vs 27.4%; $P = 0.024$). Hyperlipidemia (37.8% vs 12.8%; $P < 0.001$), excluding the current smoking condition, was low (12.8% vs 16.5%; $P < 0.01$).

Metabolic syndrome was also associated with higher median total cholesterol (5.4 vs 4.1 mmol/L; $P < 0.001$), low-density lipoprotein cholesterol (LDL-C; 3.5 vs 2.6 mmol/L; $P < 0.001$), and triglycerides (1.4 vs 1.1 mmol/L; $P < 0.001$), except for HDL-C levels were low (0.9 vs 1.2 mmol/L; $P < 0.001$). Ninety-five percent of the participants had at least one criterion for metabolic syndrome. The table also indicates that even though there were no significant differences in the prevalence of metabolic syndrome between Hungarian and Iraqi patients (25.0% vs 34.1%; $P = 0.306$), patients with metabolic syndrome had a higher risk of developing STEMI (29.3% vs 20.1%) and NSTEMI (22.6% vs 12.8%), prior CABG (6.1% vs 3.0%), prior PCI (32.9% vs 17.1%), and renal failure (4.3% vs 3%) (Table 1).

Table 2 shows the prevalence of different types of metabolic syndrome abnormalities in the study cohort stratified by sex and nationality. High blood pressure (83.5%) was the most prevalent abnormality associated with metabolic syndrome; this was followed by high fasting blood glucose (75.3%). Approximately 62.9% of the cohort had increased abdominal obesity while low HDL cholesterol and hypertriglyceridemia were present in 58.8% and 30.9% of the ACS population, respectively. Table 2 also demonstrates that males were associated with a higher percentage of all the metabolic syndrome abnormalities, except high fasting blood glucose and low HDL cholesterol. Moreover, the table shows that Hungarian patients were more likely to be associated with increased abdominal obesity (35.1% vs 27.8%). In contrast, Iraqi patients were more likely to be associated with hypertriglyceridemia (18.6% vs 12.4%), high blood pressure (44.3% vs 39.2%), and high fasting glucose (45.4% vs 29.9%).

Table 3 shows in-hospital and 30-day post-hospital discharge outcomes for ACS patients stratified by metabolic syndrome. The table shows that there were no statistically significant differences between patients with or without metabolic syndrome regarding in-hospital outcomes. However, patients with metabolic syndrome had a higher rate of in-hospital mortality (3.0% vs 1.2%; $P = 0.499$), re-infarction (4.9% vs 3.0%; $P = 0.855$), cardiogenic shock (4.3% vs 1.8%; $P = 0.471$), stroke (1.2% vs 0.0%; $P = 0.237$) and major adverse cardiovascular events (7.9% vs 3.0%; $P = 0.232$). Moreover, the outcomes of hospital discharge after 30 days showed that patients with metabolic syndrome were significantly more likely to be associated with re-infarction (12.8% vs 3.7%; $P = 0.031$) and MACE (17.7% and 6.1%; $P = 0.027$).

Table 4 demonstrates metabolic syndrome and various in-hospital and 30 days post-discharge outcomes in the cohorts in Hungary and Iraq. There were no statistically significant differences between in-hospital and out-

Table 1. Demographic, clinical, and lipid characteristics of the acute coronary syndrome cohort stratified by metabolic syndrome

Variables	All patients (n = 164, 100%)	Metabolic syndrome (n = 97, 59.1%)	Without metabolic syndrome (n = 67, 40.9%)	P value
Nationality, n (%)				
Hungary	64 (39.0%)	41 (25.0%)	23 (14.0)	0.306
Iraq	100 (61.0%)	56 (34.1%)	44 (26.8%)	
Age, mean + SD, years	63.8 + 11.9	64.2 + 11.5	63.3 + 12.6	0.394
Male sex, n (%)	111 (67.7%)	60 (36.6%)	51 (31.1%)	0.055
Family history of CAD, n (%)	30 (18.3%)	22 (13.4%)	8 (4.9%)	0.080
BMI, median (IQR), kg/m^2	26.8 (23.0–31.9)	28.0 (25.8–32.3)	23.7 (22.0–29.0)	0.000
Current smoking, n (%)	48 (29.3%)	21 (12.8%)	27 (16.5%)	0.010
Hypertension, n (%)	125 (76.2%)	80 (48.8%)	45 (27.4%)	0.024
Diabetes mellitus, n (%)	71 (43.3%)	48 (29.3%)	23 (14.0%)	0.054
Hyperlipidemia, n (%)	83 (50.6%)	62 (37.8%)	21 (12.8%)	0.000
Prior MI, n (%)	87 (53.0%)	56 (34.1%)	31 (18.9%)	0.148
Prior PCI, n (%)	82 (50.0%)	54 (32.9%)	28 (17.1%)	0.081
Prior CABG, n (%)	15 (9.1%)	10 (6.1%)	5 (3.0%)	0.534
Renal failure, n (%)	12 (7.3%)	7 (4.3%)	5 (3.0%)	0.953
Ejection Fraction ≤ 30%, n (%)	7 (4.3%)	5 (3.0%)	2 (1.2%)	0.499
Diagnosis, n (%)				
ST-ACS	81 (49.4%)	48 (29.3%)	33 (20.1%)	0.977
NST-ACS	83 (50.6%)	49 (29.9%)	34 (20.7%)	
Cholesterol, median (IQR), mmol/L	4.7 (3.9–5.8)	5.4 (4.4–6.0)	4.1 (3.4–4.7)	0.000
Triglyceride, median (IQR), mmol/L	1.2 (1.0–1.6)	1.4 (1.1–1.7)	1.1 (0.9–1.5)	0.000
LDL-C, median (IQR), mmol/L	3.0 (2.3–4.0)	3.5 (2.6–4.5)	2.6 (2.1–3.1)	0.000
HDL-C, median (IQR), mmol/L	1.0 (0.9–1.3)	0.9 (0.8–1.0)	1.2 (1.0–1.5)	0.000

BMI: body mass index; CAD: coronary artery disease; MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; LDL: low-density lipoprotein; HDL: high-density lipoprotein; STE-ACS: ST-segment elevation acute coronary syndrome; NSTE-ACS: non-ST-segment elevation acute coronary syndrome

Data are expressed as mean ± SD or median (IQR) for the continuous variables. Data are expressed as n (%) percentages and frequencies for the categorical variables. Analyses were conducted using Pearson's chi-square test, Fisher exact test, Student's t-test, or Wilcoxon-Mann-Whitney test, whenever appropriate

Table 2. Prevalence of different types of metabolic syndrome abnormalities of the study cohort stratified by nationality and sex

Type of metabolic syndrome abnormalities, F (%)					
Parameter	**Abdominal obesity**	**Hypertriglyceridemia**	**Low HDL-C**	**High blood pressure**	**High fasting glucose**
Total	61 (62.9%)	30 (30.9%)	57 (58.8%)	81 (83.5%)	73 (75.3%)
Nationality					
Hungary	34 (35.1%)	12 (12.4%)	27 (27.8%)	38 (39.2%)	29 (29.9%)
Iraq	27 (27.8%)	18 (18.6%)	30 (30.0%)	43 (44.3%)	44 (45.4%)
Sex					
Male	38 (39.2%)	23 (23.7%)	25 (25.8%)	50 (51.5%)	28 (28.9%)
Female	23 (23.7%)	7 (7.2%)	32 (33.0%)	31 (32.0%)	45 (46.4%)

Note: The 5 metabolic syndrome abnormalities include increased BMI (higher 25 kg/m^2), high triglyceride levels (of > 150 mg/dL [1.7 mmol/L] or drug treatment), low HDL-cholesterol levels (of < 40 mg/dL [1.0 mmol/L]) for men and < 50 mg/dL [1.3 mmol/L] in women or drug treatment), blood pressure (> 130 mm Hg for systolic and/or > 85 mm Hg for diastolic or drug treatment), and blood sugar (> 100 mg/dL [> 5.6 mmol/L] or drug treatment)

Table 3. In-hospital and 30-day post-discharge outcomes of the acute coronary syndrome cohort stratified by metabolic syndrome

In-hospital outcomes	Metabolic syndrome (n = 97)	Without metabolic syndrome (n = 67)	P-value
Death	5 (3.0%)	2 (1.2%)	0.499
Re-infraction	8 (4.9%)	5 (3.0%)	0.855
Cardiogenic shock	7 (4.3%)	3 (1.8%)	0.471
Stroke	2 (1.2%)	0 (0.0%)	0.237
MACE (death, re-infraction, and stroke)	13 (7.9%)	5 (3.0%)	0.232
30-day post-discharge outcomes	**Metabolic syndrome**	**Without metabolic syndrome**	**P-value**
Death	7 (4.3%)	4 (2.4%)	0.754
Re-infraction	21 (12.8%)	6 (3.7%)	0.031
Cardiogenic shock	8 (4.9%)	4 (2.4%)	0.582
Stroke	5 (3.1%)	1 (0.6%)	0.215
MACE (death, re-infraction, and stroke)	29 (17.7%)	10 (6.1%)	0.027

Note: Data are expressed as n (%) percentages and frequencies

MACE: major adverse cardiovascular events

Table 4. Metabolic syndrome and various in-hospital and 30-day post-discharge outcomes in Iraq and Hungary

In-hospital outcomes	Metabolic syndrome patients		P-value
	Hungary	Iraq	
Death	2 (2.1%)	3 (3.1%)	0.916
Re-infraction	5 (5.2%)	3 (3.1%)	0.227
Cardiogenic shock	3 (3.1%)	4 (4.1%)	0.974
Stroke	0 (0.0%)	2 (2.1%)	0.221
MACE (death, re-infraction, and stroke)	5 (5.2%)	8 (8.2%)	0.765
30-day post-discharge outcomes	**Metabolic syndrome patients**		**P-value**
	Hungary	**Iraq**	
Death	3 (3.1%)	4 (4.1%)	0.974
Re-infraction	7 (7.2%)	14 (14.4%)	0.349
Cardiogenic shock	3 (3.1%)	5 (5.2%)	0.776
Stroke	3 (3.1%)	2 (2.1%)	0.422
MACE (death, re-infraction and stroke)	10 (10.3%)	19 (19.6%)	0.311

Note: Data are expressed as n (%) percentages and frequencies

MACE: major adverse cardiovascular events

hospital events for metabolic syndrome in Hungary and Iraq. However, Hungarian patients had a higher rate of in-hospital re-infarction (5.2% vs 3.1% P = 0.227) than Iraqi patients. In contrast, Iraqi patients had a higher rate of in-hospital mortality (3.1% vs 2.1%), cardiogenic shock (4.1% vs 3.1%), stroke (2.1% vs 0.0%), and MACE (8.2% vs 5.2%). Furthermore, Iraqi patients had a higher rate of out-hospital mortality (4.1% vs 3.1%), cardiogenic shock (5.2% vs 3.1%), re-infarction (5.2% vs 3.1%), and MACE (19.6% vs 10.3%) than Hungarian patients. In contrast, Hungarian patients had a higher rate of out-hospital stroke (3.1% vs 2.1%).

Discussion

This study is the first to examine the incidence of metabolic syndrome among patients with ACS in Iraq and Hungary by comparing the patient groups in the two countries separately.

Baseline characters in both countries

Remarkable demographic and clinical differences were found. The patients in Iraq suffered from physical inactivity, a higher prevalence of diabetes, the genetic factor of family history of CAD, and stress. These data are consistent with results proving ACS in Arab/Middle East patients may start when they are about a decade younger than patients in developed countries and Iraq has a higher prevalence of diabetes [27–29].

Ahamad [30] showed that oleuropein is an effective substant molecule in the treatment of metabolic syndrome. It can be found in fruits and oil which are essential components of Mediterranean diets. Oleuropein is reported to have a number of biological activities including antidyslipidemic, antiobesity, antidiabetic, antioxidant, antiatherogenic, antihypertensive, anti-inflammatory, and hepatoprotective properties. The scientific evidence supports the role of oleuropein as a potential agent against metabolic syndrome [30, 31]. Unhealthy lifestyles, like consuming small amounts of extra virgin olive oil instead of more saturated fatty acid, a sedentary lifestyle, too much stress, etc. may cause a higher prevalence of hypertension, dyslipidemia, previous myocardial infarction, and higher BMI in Hungary. Previous research in Hungary has shown that healthy eating and regular exercise are rarely practiced [32, 33]. More than half of overweight and obese patients consider their physical activity and nutrition to be average [34]. According to the 2014 Hungarian Diet and Nutritional Status Survey, the average BMI of men aged 34 to 65 age was 28.9 kg/m^2 (28.1–29.6) and over 65 years of age was 28.9 kg/m2 (27.9–29.9). The average BMI in women aged 34 to 65 was 28.2 kg/m2 and in women over 65 years of age was 29.5 kg/m2 [35]. In contrast with the previous Hungarian survey, the current study shows that the average BMI (26.8 kg/m2) of the patients with ACS was lower.

Comparison of the incidence of MetS

According to a former Iraqi study, the waist circumferences are 99 cm for men, and 97 cm for women [36]. According to the Hungarian Diet and Nutritional Status Survey 2014, the average waist circumference in Hungary was 101 cm for men aged 35–64, 104 cm for over 65 years, 92.1 cm for women aged 35–64, and 97.4 cm for women over 65 years [35]. These average numbers are significantly higher than the metrics identified in the 2007 Iraq study. Despite this, there is no significant difference in the incidence of metabolic syndrome between the two countries in patients with ACS.

Comparing the data of the current study with Farmanfarma (2019) (where the nutritional and lifestyle habits are quite similar to Iraq) it can be found that Iraqi patients with ACS have metabolic syndrome in 56% of cases while in Iran this is 50%, so the results are quite similar also in the general population [37].

Comparison of outcomes in both countries in patients with or without MetS

Regarding mortality in both countries in hospital and after 30-day follow-up, data show similar results although the complications during hospital admission were higher in Hungary. This difference could have resulted from a higher prevalence of risk factors such as higher age, dyslipidemia, previous MI, hypertension, and a higher average BMI in Hungary than in Iraq. The outcomes 30 days after hospital discharge show that patients with metabolic syndrome were significantly more likely to be associated with re-infarction and MACE. Zeller came in 2005 to similar conclusions to the current research stating that metabolic syndrome worsened the outcome of patients with ACS. Furthermore, the current study indicates that among metabolic syndrome comorbidities, hyperglycemia has the strongest relation to an increased incidence of congestive heart failure in patients with metabolic syndrome and MI [38].

Conclusions

There was no significant difference in the incidence of metabolic syndrome between ACS patients in the two countries, but there was a higher rate in Iraq. Iraqi patients were more likely to be associated with high fasting glucose (45.4% vs 29.9%). A significant difference was found in the presence of MetS. Patients with metabolic syndrome in our study had a higher BMI rate, a higher LDL cholesterol rate, and a higher rate of fatal outcomes during the hospital stay. A significant majority of the participants met at least one criterion of metabolic syndrome, so it is important to draw further attention to metabolic syndrome not only among ACS patients but also in primary prevention. Studies provided evidence supporting the beneficial role of the traditional Mediterranean diet in preventing diabetes and MetS [6, 7, 31].

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Conflict of interest

None.

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