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Med Arh. 2015 Aug; 69(4): 226-228  
Received: June 19th 2015 | Accepted: July 24th 2015

Published online: 04/08/2015 Published print: 08/2015

# Hypoglycemia in Non-diabetics During Development of Acute Coronary Ischemia

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## ABSTRACT

**Introduction:** The occurrence of hyperglycemia in non-diabetics during development of acute coronary ischemia (ACI) indicates latent glucose metabolism disorder, or is a case of newly discovered diabetes mellitus (DM) as a result of stress. Acute coronary syndrome refers to a group of clinical syndromes caused by a sudden circulatory disorder in coronary arteries, resulting in the corresponding myocardial ischemia. It covers range from unstable angina and myocardial infarction (MI) without Q wave in the electrocardiogram finding (NSTEMI) up to myocardial infarction with Q wave in the electrocardiogram finding (STEMI). **Goal:** To determine the incidence of hyperglycemia in non-diabetics immediately after the occurrence of acute coronary ischemia and assess its risk factors. **Results:** The sample included 80 respondents. Men dominated with a total prevalence of 77.5%. The respondent was at mean age of 62.8±13.8 years. During the first measurement, immediately after hospital admission, 50% of respondents had increased blood glucose value and during the second measurement 62%. Hypertension as a risk factor has 54% and 56% smoking. The incidence of stress diabetes after ACI does not depend on the diagnosis of hypertension,  $\chi^2=0.050$ ;  $p=0.823$ . The differences of mean values (median) BMI between examined persons with/without stress DM are not statistically significant  $p=0.402$ . Independent t-test showed that there was no statistically significant difference in the average values of HDL and LDL in patients with stress diabetes than in patients without diabetes stress after ACI  $p>0.05$ . For each year of age odds ratio for "stress diabetes" increases by 7% and 95% CI is 2% -12%. **Conclusion:** The incidence of stress diabetes ACI is not dependent on the working diagnosis (MI or angina pectoris). As risk factors we set hypertension and current smoking. There were no statistically significant associations between active smoking and hypertension as a risk factor in relation to occurrence of stress diabetes.

**Key words:** acute coronary ischemia, non-diabetics, hyperglycemia.

## 1. INTRODUCTION

The occurrence of hyperglycemia in non-diabetics in development of acute coronary ischemia (ACI) indicates latent disorder of glucose metabolism or newly discovered diabetes mellitus (DM) as a result of stress, which leads to increased secretion of stress hormones (cortisol, catecholamines, glucagon, growth hormone and mediators of inflammation—interleukin and tumor necrosis factor TNF- $\alpha$ ), which weakens the effect of insulin in cells. Acute coronary syndrome refers to a group of clinical syndromes caused by a sudden circulatory disorder in coronary arteries, resulting in the corresponding portion of myocardial ischemia. It covers range from unstable angina and myocardial infarction (MI) without Q wave in the electrocardiogram (NSTEMI) myocardial infarction with Q wave in the electrocardiogram (STEMI) (1). Transiently elevated levels of plasma glucose or stress hyperglycemia in patients with acute MI are very frequent. The most commonly is detected by routine determination of plasma glucose when starting clinical treatment of pa-

tients, so the value of glycemia on admission is most often used as an indicator of the presence or absence, or level of stress hyperglycemia (2, 3, 4). A Blood glucose level on admission is an independent factor (independent on existence of DM) that has predictive value as far as the hospital mortality, but the long-term impact on mortality has not been proven (3, 5, 6).

## 2. GOAL

To determine the incidence of hypoglycemia in non-diabetics immediately after the occurrence of acute coronary ischemia and assess its risk factors.

## 3. MATERIAL AND METHODS

The study included 80 patients, treated in intensive coronary care unit of Clinical Hospital Mostar, in the period from January 1, 2013 to December 31, 2013. The participants were at age from 27 to 80 years, non-diabetics of both sexes, who developed ACI. We analyzed: demographic characteristics: age, sex, BMI; diagnosis (myo-

cardial infarction, angina pectoris); Clinical parameters: systolic and diastolic blood pressure; selected hematological-biochemical parameters: glucose, lipids, HbA1c, erythrocyte sedimentation rate-SE, blood count, C-reactive protein; Risk factors: diabetes, hypertension and current smoking.

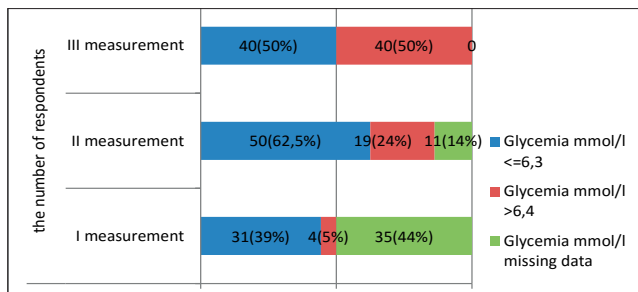
**4. RESULTS**

The sample included 80 respondents. Men dominated with a total prevalence of 77.5%. The subjects were at mean age of 62.8±13.8 years with the youngest aged 27 and the oldest 80 years. The most frequent age group was 75 to 80 years 21%. The percentage of patients with angina pectoris in relation to the percentage of patients with MI was significantly different p<0.0005. In the study dominated respondents with the IM (Table1). All respondents

		N	Per-cent	Valid percent	Cumulative percent
Referral diagnosis	Angina pectoris	6	7.5	7.5	7.5
	MI	74	92.5	92.5	100.0
	Total	80	100.0	100.0	

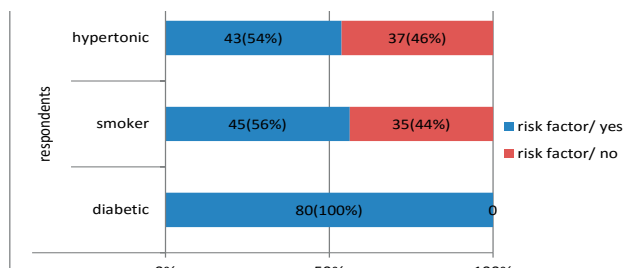
**Table 1.** Sample structure by referral diagnosis

before ACI had normal glycemia. During the first measurement, immediately after hospital admission, 50% of respondents had increased blood glucose value and after the second measurement 62% of them. During the third measurement in 56% data was missing-discharged (Figure 1).



**Figure 1.** Stress diabetes during I, II and III measurements.

Hypertension as a risk factor had 54% and 56% are smokers (Figure 2). The incidence of stress diabetes after ACI does not depend on the diagnosis of hypertension,  $\chi^2=0.050$ ;  $p=0.823$ . Of 43 patients without hypertension after ACI, 51% had elevated blood glucose levels, and 59% reference value blood glucose. Of the 37 patients with hypertension after ACI, 49% had elevated values of blood glucose, while 51% had the values in normal range. The



**Figure 2.** The cigarette consumption and hypertension as a risk factor for ACI are approximately 45%.

percentage is almost identical to  $p>0.05$ . Almost identical to the statistics and smoking as a risk factor ( $p>0.05$ ).

The differences of BMI mean values (median) between examined respondents with or without stress DM are not statistically significant,  $p=0.402$ . Subjects with DM had a BMI=25.25 (23.8 to 27) kg/m<sup>2</sup> and respondents without DM BMI=25.25 (from 23.78 to 27.8) kg/m<sup>2</sup>. The differences of mean values (median) in systolic and diastolic blood pressure between the examined patients with or without stress DM were not statistically significant (systolic/DM,  $p=0.522$ ; diastolic/DM,  $p=0.899$ ).

Independent t-test showed that there was no statistically significant difference in the average values of HDL and LDL in patients with stress diabetes than in patients without stress diabetes after ACI  $p>0.05$ . Also, differences in the mean value (median) of cholesterol ( $p=0.776$ ), triglycerides ( $p=0.658$ ) and CRP ( $p=0.124$ ) between the examined persons with/without stress diabetes were not statistically significant. Significant difference was established for variable-HbA1c between the examined patients with/without the stress diabetes ( $p=0.019$ ). Subjects with elevated blood sugar had an average HbA1c=5.8 (5.37 to 6.1%), and those without high blood sugar had an average HbA1c = 5.2 (5.0 to 5.9%).

Binary logistic regression examined the influence of age, sex and BMI at the occurrence of “stress diabetes yes/no” after ACI. In the two-step method Backward Wald showed that age and gender have a statistically significant effect of which has a greater impact -Wald age=9.0,  $p = 0.003$  by half Wald = 5.25,  $p = 0.22$ . For each year of age Odds ratio that the subject develop “stress diabetes” increases by 7% and 95% CI = 2% -12%. Men have a higher risk to develop “stress diabetes” for 78% and 95% confidence interval = 94% -20% (Table 2).

		B	S.E.	Wald	df	p.	Exp(B)	95.0% C.I. for EXP(B)	
								Lower	Upper
Step 1(a)	Gender	-1.477	.671	4.841	1	.028	.228	.061	.851
	Age	.065	.022	8.428	1	.004	1.067	1.021	1.116
	BMI	-.040	.112	.130	1	.719	.960	.770	1.197
	Constant	-1.270	3.221	.155	1	.693	.281		
Step 2(a)	Gender	-1.517	.662	5.251	1	.022	.219	.060	.803
	Age	.067	.022	9.000	1	.003	1.069	1.023	1.117
	Constant	-2.345	1.245	3.547	1	.060	.096		

**Table 2.** Impact of dependent variables (age, sex, BMI) on outcome (stress diabetes yes/no) after ACI

Binary logistic regression examined the impact of SE, Er, hemoglobin, hematocrit, MCV, Tr, Le, cholesterol, triglycerides, HDL, LDL and HbA1c at the occurrence of “stress diabetes yes/no” after acute coronary artery disease. In eight step method Backward Wald turned out that none of these variables have statically significant influence  $p>0.05$ .

**5. DISCUSSION**

Medical history and clinical status are important prognostic indicators in patients with stable angina pectoris or other verified coronary disease. Diabetes, hypertension, cigarette smoking and high cholesterol (untreated or unregulated despite treatment) are considered predictors

of poor outcome. A large number of authors believe that stress–hyperglycemia is an independent predictive factor for such complications after acute coronary artery disease in diabetics and non-diabetics (7, 8).

In our study, 77.5% of patients were male. The incidence of stress diabetes after ACI is not dependent on sex ( $\chi^2=1.147$ ,  $p=0.284$ ). Similar results were presented by other authors (9). The average age of our respondents was  $62.8\% \pm 13.8$  years. The most frequent age group was 75 to 80 years–21%. By binary logistic regression we examined the influence of age and gender of the occurrence of stress diabetes. Both variables have a statistically significant impact on the development of the disease with higher influence of age. For each year of age odds ratio that the respondent develop stress diabetes increases by 7%. Results are compared with other studies, since the older age is more prone to developing complications examined in our study, due to weaker immunity in the elderly, but also because of comorbidity that burdens them (10, 11). Jimenez et al. examined the risk factors in the development of de novo DM after cardiac transplantation. Age, obesity, ischemic MI, hypertension and kidney failure are marked as the main factors in the development of diabetes. Unlike them, Moro et al. as a dominant risk factor cited hypertension and old age, while there was no statistically significant difference in relation to BMI, dyslipidemia, smoking and acute kidney disease. Rafel et al. also show that there were no statistically significant differences in risk factors such as age, sex, smoking, cholesterol, triglycerides and creatinine in three categories of patients (newly developed hyperglycemia, earlier diabetics and those with normoglycemia). So, followed are different risk factors depending on which aspect of acute coronary events are analyzed (11, 12, 13). A study we present was designed differently in relation to risk factors for other studies because there was no control group to test the statistically significant difference. All subjects had a value before ACI of blood glucose in reference values–80 (100%), hypertension had 54% and the smoking as a risk factor 56%. Systolic blood pressure and frequency were significantly increased in the group of newly established diabetics in a study presented Marfella and colleagues. Our results are not in this sense, considering that there was no statistical significance in the values of blood pressure in the study population (13).

In the post-hospital period patients who have had proper glycemia after discharge should be followed once a year, while those with elevated glycemia more often. Also, a number of studies suggesting that persistent hyperglycemia during hospital follow-up or non-diabetic patients represent a predictor of poor prognosis after acute coronary artery disease (14, 15, 16, 17, 18).

Goyal et al. evaluated the effect of changes in glucose levels after admission of the patient with respect to mortality and found that elevated glucose during the first 24 hours of hospitalization was associated with higher mortality rate after 30 and 180 days and lower blood glucose value is reflected as a predictor of a good prognosis. This correlation is present in non-diabetics but not in diabetics (13, 19).

## 6. CONCLUSION

Measuring blood glucose, both during admission and hospital monitoring should be part of the regular program of evaluation of patients with ACI. The incidence of hyperglycemia ranges from 3 to 71% according to different threshold that is set for the diagnosis of acute coronary patients. Fox and colleagues emphasized that the need for monitoring the effectiveness of therapies or the discovery of new diabetes after disease (stress diabetes) (14).

**CONFLICT OF INTEREST: NONE DECLARED.**

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