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## Risk Factors and Outcome of Medically Treated Acute Coronary Syndromes

AISHA A. AL GHAMDI, FACP, Arab & Saudi Boards  
*Department of Internal Medicine, Faculty of Medicine,  
King Abdulaziz University, Jeddah, Saudi Arabia*

**ABSTRACT.** A retrospective study included patients admitted to an intensive care unit with a diagnosis of acute coronary syndrome from January 2000 to December 2003. Three hundred patients' medical histories were reviewed. The underlying risk factors such as a positive family history, diabetes mellitus, hypertension and hyperlipidemia were obtained. The cause for admission, hospitalization duration, complications and mortality were all taken into consideration and compared statistically. Mean age was  $55.2 \pm 11.9$  years with the male to female ratio of 5.8:1. Diagnoses at the time of admission were ST elevation myocardial infarction, unstable angina, and non-ST elevation myocardial infarction in 61%, 30%, 9% of the patients, respectively. Thrombolytic treatment had been the golden therapeutic option for ST elevation myocardial infarction available in King Abdulaziz University Hospital, used by 78% of the patients, followed by intravenous anticoagulants and other anti-ischemic medications. The procedures performed were percutaneous coronary angioplasty (3%), coronary bypass grafting (2%), and cardiac catheterization and angiography for further intervention (45%) for the 300 patients, respectively. 26% of patients developed complications. Mortality was higher among females compared to males (13.6% versus 5.9%). In conclusion male gender, *diabetes mellitus*, hypertension, hyperlipidemia, positive family history and smoking were the main associated risk factors in our study. ST elevation myocardial infarction was the predominant presentation in our patients. Thrombolytic treatment was the available therapeutic option in our hospital.

**Keywords:** Acute coronary syndrome, Risk factors, Thrombolytic treatment.

Correspondence & reprint requests to: Dr. Aisha A. Al Ghamdi  
P.O. Box 30598, Jeddah 21487 Saudi Arabia

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### Introduction

Acute coronary syndrome (ACS) is a wide spectrum of definitions covering three important cardiological emergencies; myocardial infarction (MI) whether ST elevation (Q-wave) MI (STEMI) or non-ST elevation (non-Q wave) MI (NSTEMI) and unstable angina (UA)<sup>[1]</sup>. The diagnosis of acute MI relies on the revised criteria established by the World Health Organization (WHO) in 1979<sup>[2]</sup>. Two of these criteria were required for diagnosis of an acute STEMI; history of ischemic chest pain, typical electrocardiogram (ECG) pattern including the development of Q waves and typical elevations in serum markers of myocardial injury, usually creatine kinase (CK MB).

Joint European Society of Cardiology (ESC) and American College of Cardiology Committee (ACC) proposed the following definition of an acute episode, evolving MI in 2000<sup>[3]</sup>. Typical rise and gradual fall (troponin) or more rapid rise and fall (CK MB) of biochemical markers of myocardial necrosis with at least one of the following: Ischemic symptoms, development of pathologic Q waves on the ECG, ECG changes indicative of ischemia (ST segment elevation or depression) and coronary artery intervention (e.g., angioplasty). According to this definition and guidelines published by the ACC and the American Heart Association (AHA) in 2002, UA and NSTEMI differ primarily in whether the ischemia is severe enough to cause sufficient myocardial damage to release detectable quantities of a marker of myocardial injury<sup>[3,4]</sup>.

UA and NSTEMI are frequently indistinguishable at initial evaluation. UA is considered to be present in patients with ischemic symptoms suggestive of an ACS and no elevation in troponins or CK MB, with or without ECG changes indicative of ischemia. Prevalence of ACS may be underestimated because of high percentage of silent ischemia which is thought to account for 75 percent of all ischemic episodes<sup>[5]</sup>. Males have higher incidence of ACS than premenopausal females, but after menopause the incidence in women reaches that in men.

The presence of ischemic heart disease in first degree relatives (before the age of 45-years in males and before 50-years in female) represents a fixed risk factor. Other strongly associated risk factors are hypertension, diabetes mellitus (DM), dyslipidemia, cigarette smoking, obesity, physical inactivity and adverse dietary pattern<sup>[6]</sup>. The ECG is a mainstay in the diagnosis of acute MI, it can also localize it<sup>[2,3]</sup>. Biomarkers of cardiac injury are troponin I and troponin T, creatine kinase (CK) and its isoform CK MB. An elevation in the serum concentration of one or more of the above markers is seen in virtually all patients with an acute MI<sup>[7,8]</sup>. Serum troponins are the marker of choice because of the high specificity to myocardial injury<sup>[9]</sup>, followed by CK MB. Total CK, lactate dehydrogenase and myoglobin no longer have a major role<sup>[7]</sup>, because they lack the specificity to the heart muscle.

Once the diagnosis of an acute STEMI is made management of the patient involves the early and simultaneous achievement of several goals, as outlined by a task force of the ACC & AHA<sup>[10]</sup>. Relief of ischemic pain, assessment of the hemodynamic state and correction of abnormalities that are present, initiation of reperfusion therapy with primary percutaneous coronary intervention (PCI) or thrombolysis and antithrombotic therapy to prevent rethrombosis of an ulcerated plaque or subtotal stenosis by angiotensin converting enzyme (ACE) inhibitor, beta blockers, statin and anticoagulation, if needed.

### Method

#### *Study Design, Population and Setting*

A retrospective study of the intensive care unit (ICU) at King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia included all patients with a diagnosis of acute coronary syndrome admitted to the ICU from January 2000 to December 2003. A total of three hundred and forty (340) patients were admitted during that period. Forty (40) patients were excluded from the study because of insufficient data and missing medical records.

#### *Data Collection and Statistical Analysis*

Three hundred (300) patients were included in the study. Their demographic features were recorded. It was difficult to calculate the body mass index (BMI) because height could not be assessed nor it was recorded due to critical patients' conditions in the ICU. Cardiac investigations were registered including cardiac enzymes; tryponin I, CK and CK-MB, ECG findings (interpreted by a cardiologist), echocardiography and chest radiography. Diagnosis at admission; STEMI (history of ischemic symptoms suggestive of an ACS with serum elevation in troponins or CK MB and ST elevation in ECG), NSTEMI (history of ischemic symptoms suggestive of an ACS, with serum elevation in troponins or CK MB with out ST elevation in ECG ), UA (history of ischemic symptoms suggestive of an ACS, with no serum elevation in troponins or CK MB, with or without ECG changes indicative of ischemia). Presence of risk factors was reviewed; positive family history of early deaths, (< 45-years in males, < 50-years in females), presence of DM which was diagnosed according to American Diabetic Association's criteria<sup>[11]</sup>. Hypertension (patient is known hypertensive or receiving antihypertensive agents or BP > 140/90 mmHg on more than one occasion), presence of Hyperlipidemia (known to have hyperlipidemia or on lipid lowering agent), smoking history (active or passive or 5-year ex-smoker). Other recognizable risk factors like obesity, physical inactivity were not registered because of insufficient data inside the patients' files. Their treatment (thrombolytic, anticoagulant medications and if they needed emergency or elec-

tive cardiac intervention). Period of ICU staying, pattern of complications and mortality all were recorded. Follow-up treatment by anti-ischemic medications (aspirin, nitrites, ACE inhibitors, beta blockers, calcium channel blockers) and lipid-lowering therapy with a statin was registered. Mortality, risk factors were studied and compared statistically in relation to the age and gender of the patients.

Data analysis was done using statistical package for social sciences (SPSS software)<sup>[12]</sup>. Mean  $\pm$  SD was calculated for quantitative data and proportions for categorical variables. One-way ANOVA and "student's" *t*-test were used for comparing means of continuous variables. Proportions were compared by Chi-square test and Mantel-Haenszel test if needed. Significance level was set at  $< 0.05$  throughout the analysis.

### Results

A total of 300 patients were studied. Their mean age was  $55.2 \pm 11.9$  years (Range was 20-87 years) with male to female ratio of 5.8:1. STEMI was found in 182 (61%) patients, NSTEMI was found in 27 (9%) patients and UA in 91 (30%) patients. Table 1 shows demographic features of each group. High serum tryponin and CK MB were found in all cases of MI (70%) of all cases. ST elevation was recorded as antroseptal MI in 42%, inferior MI in 42% and antrolateral in 16%. Chest radiography was abnormal in about one-third (32%) of all cases. The abnormalities included cardiomegaly, pulmonary congestion and edema.

TABLE 1. General characteristics of the patients.

Variable	Study Group N (%)	STEMI N (%)	NSTEMI N (%)	UA N (%)	P Value
Total Patients	300 (100.0)	182 (61.0)	27 (9.0)	91 (30.0)	
Age: (mean $\pm$ SD)	55.2 $\pm$ 11.9	54.8 $\pm$ 12.3	55.3 $\pm$ 10.0	56.0 $\pm$ 11.6	0.8
Sex					
Male	256 (85.3)	163 (89.6)	22 (81.5)	71 (78.0)	0.03
Female	44 (14.7)	19 (10.4)	5 (18.5)	20 (22.0)	
Nationality					
Saudi	91 (30.3)	54 (29.7)	10 (37.0)	27 (29.7)	0.7
Non-Saudi	209 (69.7)	128 (70.3)	17 (63.0)	64 (70.3)	

STEMI = ST elevation myocardial infarction.

NSTEMI = non-ST elevation myocardial infarction

UA = unstable angina

P  $< 0.05$  is significant

Associated risk factors are illustrated in Table 2 in relation to gender and age. Thrombolytic treatment was given to 142 (78%) of STEMI patients (those who presented within 6 hours of the onset of symptoms). Heparin, aspirin, nitrites were given to all 300 patients regardless of time of presentation. Other anti-ischemic medications were given which included ACE inhibitors to 245 (82%) patients, beta blockers to 243 (81%) patients and calcium channel blockers to 30 (10%) patients. Lipid lowering agents were used in 161 (54%) patients. Complications developed in 54 (30%) patients in STEMI, 8 (30%) patients in NSTEMI and in 17 (19%) patients in UA. Table 3 showed different types of complications and their respective ratios. Post MI unstable angina developed in 8% patients with STEMI, and in 4% patient with NSTEMI (P 0.02). Cardiogenic shock developed in 12% with STEMI, in 4% with NSTEMI and in 6% with UA (P 0.1). For those who developed post MI unstable angina, percutaneous coronary angioplasty (PTCA) was performed for 9 (60%) patients of them and coronary bypass grafting (CABG) for 6 (40%) patients. Cardiac catheterization and angiography were required for 135 (45%) patients for possible further interventions. The duration in ICU was  $3.3 \pm 3.8$  days (range 1-49 days). Mortality among males was 5.9% while amongst females was 13.6%. As shown in Table 4 the proportion of mortality among males and females aged less than 50 years was (5.7%, 0%), respectively, but it differs in those who are older (6%, 16.7%), respectively (P 0.7).

TABLE 2. Risk factors of acute coronary syndrome.

Risk Factors		Total Number N (%)	Age Groups N (%)	P Value
Gender	Male	256 (85.3)	88 (30.0) 168 (70.0)	0.03
	< 50 y			
	≥ 50 y			
	Female	44 (14.7)	8 (20.0) 36 (80.0)	
< 50 y				
≥ 50 y				
Family History	Male	42 (16.4)	24 (57.1) 18 (41.9)	0.07
	< 50 y			
	≥ 50 y			
	Female	5 (11.4)	2 (40.0) 3 (60.0)	
< 50 y				
≥ 50 y				
Diabetes Mellitus	Male	149 (58.2)	32 (21.5) 117 (78.5)	0.05
	< 50 y			
	≥ 50 y			
	Female	26 (59.1)	4 (15.4) 22 (84.6)	
< 50 y				
≥ 50 y				

TABLE 2. Contd.

Risk Factors		Total Number N (%)	Age Groups N (%)	P Value
Hypertension	Male	110 (43.0)	36 (32.7) 74 (67.3)	0.06
	< 50 y			
	≥ 50 y			
Female	25 (56.8)	3 (12.0) 22 (88.0)		
< 50 y				
	≥ 50 y			
Hyperlipidemia	Male	141 (55.1)	59 (41.8) 82 (58.2)	0.07
	< 50 y			
	≥ 50 y			
Female	20 (45.5)	4 (20.0) 16 (80.0)		
< 50 y				
	≥ 50 y			
Smoking	Male	156 (60.9)	68 (43.6) 88 (56.4)	0.5
	< 50 y			
	≥ 50 y			
Female	7 (15.9)	2 (28.6) 5 (71.4)		
< 50 y				
	≥ 50 y			

N = number of patients; % = percentage; y = years, P < 0.05 is significant.

TABLE 3. Complications and outcome of acute coronary syndrome.

Variable	STEMI N (%) 182 (100)	NSTEMI N (%) 27 (100)	UA N (%) 91 (100)	P Value
Complications	54 (29.7)	8 (29.6)	17 (18.7)	0.1
CHF	5 (2.7)	2 (7.4)	6 (6.6)	0.2
RHF	1 (0.5)	0 (0.0)	1 (1.1)	0.6
LHF	23 (12.6)	2 (7.4)	5 (5.5)	0.2
Arrhythmia	19 (10.4)	3 (11.1)	6 (6.6)	0.3
Cardiogenic Shock	22 (12.1)	1 (3.7)	5 (5.5)	0.1
Post MI UA	14 (7.7)	1 (3.7)	0 (0.0)	0.02
ICU Duration (mean ± SD)	3.5 ± 4.3 d	4.1 ± 3.7 d	2.8 ± 2.7 d	0.07
Mortality	15 (8.2)	2 (7.4)	4 (4.4)	0.5

STEMI = ST elevation myocardial infarction.  
 NSTEMI = non-ST elevation myocardial infarction  
 UA = unstable angina  
 P < 0.05 is significant  
 CHF = congestive heart failure  
 RHF = right-sided heart failure  
 LHF = left-sided heart failure  
 d = day/s

TABLE 4. Effect of age and gender on mortality of acute coronary syndrome.

Gender	Mortality N (%)	P Value
Male		
< 50 y = 88 (30%)	5 (5.7)	1.0
≥ 50 y = 168 (70%)	10 (6.0)	
Total*	15 (5.9)	
Female		
< 50 y = 8 (20%)	0 (0.0)	0.6
≥ 50 y = 36 (80%)	6 (16.7)	
Total**	6 (13.6)	

\*Total = N = 256; (%) = 100

\*\*Total = N = 44; (%) = 100

### Discussion

Angina is often characterized more as a discomfort than pain, and may be difficult to describe. Terms frequently used by patients included: discomfort, squeezing, tightness, pressure, constriction, burning, heartburn, fullness in the chest, band-like sensation, lump in the throat, ache and toothache (when there is radiation to the lower jaw). It is generally not described as sharp, dull-aching, knife-like, stabbing, or pins and needles-like<sup>[13,14]</sup>. Some patients with an ACS present with atypical symptoms rather than chest pain. In a review of over 430,000 patients with confirmed acute MI from the National Registry of Myocardial Infarction 2, one-third had no chest pain on presentation to the hospital. These patients may present with dyspnea alone, nausea and/or vomiting, palpitations, syncope, or cardiac arrest. They are more likely to be older, diabetic, and women<sup>[15]</sup>. Patients with silent MI are usually under treated and they have an increased in-hospital mortality<sup>[15]</sup>. A potential diagnostic problem is that myocarditis can mimic an acute MI in all major diagnostic features, including chest pain, ECG changes, and a rise in the concentration of serum markers. Myocarditis should be considered in young patients with a clinical presentation of an ACS, particularly those who have a normal coronary angiogram<sup>[16,17]</sup>. The ECG is a mainstay in the diagnosis of acute MI. Patients with a strong clinical history and ST segment elevation or new left bundle branch block should undergo immediate reperfusion therapy with thrombolysis or primary percutaneous coronary intervention.

In our study the majority were having STEMI was 61% of the study's patients. Two multi-center, international surveys published in 2002 determined the relative frequency of ACS in approximately 22,000 patients; STEMI in 33%, NSTEMI in 25%, and UA in 42%<sup>[18,19]</sup>. Different percentages were found in our study, which may reflect the different pattern of ACS in our part of



sidered. Follow-up by anti-ischemic medications is recommended for a better outcome. Mortality in our study was compared to that which was obtained by Furman *et al.*<sup>[26]</sup> from community-based multihospital study, less figures were found by our study (8% versus 14%) in STEMI patients and (7% versus 12%) in NSTEMI patients. Improvement in survival has been also observed by other studies<sup>[27-29]</sup>.

In our study, higher mortality rate was observed among females compared to males (13.6%, 5.9%), respectively. Females whose age 50-years and older showed higher mortality (16.7%) than younger age group (0%) of same gender, and it was about three times that in males at the same age group (6%), this finding does not agree with Vaccarino *et al.*<sup>[29]</sup>, who found that mortality rate of women less than 50-years of age was more than twice that for men and concluded that younger women with MI represent a high-risk group. Despite small numbers of females in our study group (15%) older women represent a high-risk group in contrast to males who represented the majority of our study group (85%) only (30%) of males represented a high-risk group; those who aged less than 50-years showed higher mortality rate compared to females of the same age group (5.7%, 0%) respectively, which does not go with (Stone *et al.*)<sup>[30]</sup> who found that males older than 75-years of age have three-fold increase in the incidence of death post MI. The gender, age based differences in risk factors, presentations, outcome and mortality were the main concern among our study group. We need larger number of patients to see the cause of these differences, which could not be entirely accounted for by differences in risk factors only and may reflect pathophysiological and anatomical differences between men and women.

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## عوامل الخطورة ونتائج علاج المتلازمة التاجية الحادة

عائشة عبده الغامدي

قسم الباطنة، كلية الطب، جامعة الملك عبدالعزيز،

جدة - المملكة العربية السعودية

المستخلص. كان الهدف هو دراسة عوامل الخطورة وعلاج ونتائج المتلازمة التاجية الحادة للمرضى الذين أدخلوا في العناية المركزة بمستشفى جامعة الملك عبد العزيز بجدة، وتمت مقارنة الموتى من حيث العمر، وما إذا كانوا ذكوراً أو إناثاً. كل المرضى الذين أدخلوا للعناية المركزة وكان تشخيص مرضهم المتلازمة التاجية الحادة (احتشاء عضلة القلب مع ارتفاع أو بدون ارتفاع في رسم القلب الكهربائي، الذبحة الصدرية) من يناير ٢٠٠٠م إلى ديسمبر ٢٠٠٣م، وكان عددهم ٣٠٠ حالة، وسجلت دراستهم الوصفية، والفحوصات التي أجريت لهم، وعوامل الخطورة لديهم، وما إذا حدث لديهم مضاعفات، ونسبة الموتى، وتمت دراستها ومقارنتها إحصائياً. كان متوسط أعمارهم ٥٥، ٩ ± ١١ سنة (٢٥٦ رجلاً، ٤٤ امرأة) تم إعطاء العلاج السريع للجلطة إلى ٧٨٪ من المرضى المصابين. وتم علاج المرضى كلهم بمضاد تخثر الدم وعلاجات القلة الدموية الموضعية للقلب. تم تقويم الأوعية عن طريق الجلد في ٣٪ من المرضى احتاجوا لقطرة وتصوير أوعية القلب. حدثت مضاعفات في ٢٦٪ من المرضى، وكانت نسبة الموتى أعلى في النساء مقارنة بالرجال (١٣، ٦٪، ٥، ٩٪). أما عند دراسة فرق العمر، فكانت نسبة موت النساء أقل منها في الرجال للمرضى الذين تقل أعمارهم عن ٥٠ عاماً، (٥، ٧٪، ٠٪). أما المرضى الذين أعمارهم أكثر من ٥٠ عاماً، فإن نسبة موت النساء أكثر منها في الرجال (١٦، ٧٪، ٦٪).

عوامل الخطورة التي وجدت من الدراسة كانت في الرجال والمرضى الذين كانوا يعانون من السكري، وارتفاع في ضغط الدم، والدهون، ووجود تاريخ المرض في عوائلهم. كان احتشاء عضلة القلب الأكثر تشخيصاً، ونسبة الموت في النساء أكثر.

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مجلة  
جامعة الملك عبدالعزيز  
العلوم الطبية

المجلد ١٢  
م ٢٠٠٥  
١٤٢٥-١٤٢٦هـ

مركز النشر العالمي  
جامعة الملك عبدالعزيز  
جدة