

## Cardiogenic Shock Among Yemeni Patients Presented With Acute Coronary Syndrome (ACS). Data From Gulf Registry of Acute Coronary Events Phase (Gulf Race I)

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### ABSTRACT

**Introductions & Aims:** Acute Coronary Syndrome (ACS) and its magnitudes is one of the most common cardiac diseases worldwide. Yet in Yemen; GULF RACE I data are the first nation- wide information that highlight the magnitude of this problem. Cardiogenic shock is a miserable complication of ACS. Pointing out this problem among Yemeni with ACS, its prognostic importance and impact in patients outcomes is a major aim of this study.

**Methods and Patients:** Yemen data arm was a part from the GULF RACE I, which is a prospective, multinational, multicentres survey of consecutive patients hospitalized with the final diagnosis of ACS in six Arabian Peninsula/Gulf countries over a period of six month. Yemeni patients were 1054 patients included from 20 major hospitals all over the country with ACS including cases of ST Elevation Acute Myocardial Infarction (STEMI), non ST Elevation Acute Myocardial Infarction (NSTEMI), newly developed Left Bundle Branch Block (LBBB) and unstable angina pectoris (UA). Patients with Acute Heart Failure (AHF) and presented with cardiogenic shock were pointed out. The end point of this study was all causes of in-hospital mortality.

**Results:** Out of 1054 hospitalized with ACS, 181 patients (17.3%) had AHF on presenting to the hospital or during hospitalization itself. Out of those patients with AHF there were 74 patients who developed Cardiogenic Shock. They were relatively older  $64.7 \pm 9.7$  (SD) years ( $P < 0.001$ ) with male predominance (63.5%). In spite of Anterior/Anteriolateral STEMI was a common feature of presentation (70.2%), echocardiographic feature were more



consistent with cardiogenic shock, Left Ventricular Ejection Fraction (LVEF) was (36.5% Vs 51%  $P < 0.001$ ). Those patients were in co-morbid condition more than the rest of the group of ACS & evidently were less treated utilizing evidence based treatment. Cardiogenic shock was linked to higher in-hospital mortality (66.2% Vs 4.8% with  $P < 0.001$ ).

**Conclusion:** Yemeni patients with acute coronary syndrome complicated with cardiogenic shock had more worse prognosis regarding in-hospital morbidity and mortality.

**Key words:** Yemen, Acute Coronary Syndrome, Acute Heart Failure, Cardiogenic shock, Mortality.

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## BACKGROUND

Cardiogenic shock is defined as a systolic blood pressure of less than 90 mmHg for at least 30 minutes, which is secondary to myocardial dysfunction<sup>1</sup>. It is associated with clinical signs of hypoperfusion. Cardiogenic shock is state of reduced cardiac output and signs of tissue hypoxia. Cardiogenic shock complicates 5% to 10% of cases with ACS and remains the leading cause of death in patients hospitalized with AMI.<sup>2,3</sup> It is a consequence of Acute Heart Failure (AHF); AHF is a complex syndrome that can result from any structural or functional cardiac disorder leading to inability of the left ventricle to fill with or eject blood. It is a result of many conditions including cardiovascular diseases. Its high morbidity and mortality represent a major economic burden<sup>4</sup>. Yemen is one of the low income country group where rheumatic heart disease is still highly prevalent<sup>5</sup>, while in more developed the most common cause of HF is no longer hypertension or valvular heart disease, but coronary artery disease (CAD)<sup>6</sup>. Data from phase I of The *gulf registry* of acute coronary events (*GULF RACE I*), indicate that CAD is a leading health problem that cause AHF in the gulf countries including Yemen<sup>7</sup>. Cardiogenic shock complicating ACS was not studied before in Yemen. A major aim of this study is to highlight the magnitude of this condition among ACS Yemeni population participated in phase I *GULF RACE*. As well as to describe the incidence, patient characteristics, treatment patterns and in hospital outcomes of cardiogenic shock complicating ACS in those patients.

## METHODS

### Design and Study Population

*GULF RACE I* is an initiative from the Gulf Heart Association; it is a prospective, multinational, multicentre survey of consecutive patients hospitalized with the final diagnosis of ACS in six Arabian Peninsula/Gulf countries (Kuwait, Oman, United Arab Emirates, Yemen, Qatar, and Bahrain). Patients were enrolled in a pilot phase that lasted for 1 month in May 2006 and a subsequent study phase from January 2007 to June 2007. All patients were included in the present analysis<sup>8,9</sup>. All patients with ACS were eligible with no upper age cap or other restrictions on study sample. Patients were managed according to the judgment of the treating physician. An institutional review board or equivalent at each participating hospital approved the protocol. All hospitals that care for patients with ACS in Kuwait, Bahrain, and Qatar participated, as did the majority of such hospitals (serving 85% of the population) in Yemen, United Arab Emirates, and Oman. Over this period of six months, 1054 Yemeni patients were included from 20 major hospitals all over the country with ACS including cases of ST Elevation Acute Myocardial Infarction (STEMI), non ST

Elevation Acute Myocardial Infarction (NSTEMI), newly developed Left Bundle Branch Block (LBBB) and unstable angina pectoris (UA) with manifestations of CHF. The determinants of CHF in those patients and the impact of CHF on their outcome were studied. The ACS with HF cohort included patients with CHF at presentation (Killip class II/III), cardiogenic shock and death.

#### **Data Collection & statistical analysis:**

All patients gave informed consent to process their anonymous data. Data were collected on record forms by treating physicians. Completed data sheets were sent to the central data-processing center for uniform monitoring and registration. Patients' characteristics are presented as proportions, medians, or mean  $\pm$  SD as appropriate. Whenever possible, rates were used to describe patient populations. The frequencies of categorical variables were compared using the chi-square test and by calculating odds ratios (ORs) and 95% confidence intervals (CIs). Continuous variables were compared using the 2-tailed Student's *t* test. Variables influencing in-hospital mortality were assessed using multiple logistic regression after adjustment for all confounders (i.e., age, gender, heart rate, blood pressure, and diabetes mellitus). ORs, 95% CIs, and *p* values are reported for significant predictors. A *p* value 0.05 was considered significant. All *p* values were the results of 2-tailed tests. All data analyses were carried out using SPSS version 20 (SPSS, IBM, California).

## **RESULTS**

1054 patients were documented to have ACS during study period, heart failure was a result of ACS in 181 patients (17.3%). Patients who developed manifestations of cardiogenic shock were pointed out 74 patients (40.9%) of patients with AHF developed this consequence. The base line characteristics of those group of cardiogenic shock patients was illustrated in table 1. The mean age (SD) was 64.7 years ( $\pm$ 9.7 SD). Male gender was mostly affected than female, 47 males (63.5%) with *P* value < 0.001. The risk factors predisposing to IHD and cardiogenic shock were prominent in those with hypertension & DM type II was 34 (45.9%) in each group and *P* value was significant in both < 0.001. Hyperlipidemia was seen in 20 (27%) patients with *P* value of 0.001. Smoking of different forms of tobacco was recorded in 24 patients (32.4%) with *P* value of 0.210. Khat chewing habit was very prominent (49) patients was chewers with a *P* value of 0.061.

Previous history of AMI, CABG & Stroke worsen the patient's condition and enhances cardiogenic shock representing 28 patients (37.8%), 9 patients (12.2%) and 14 patients (18.9 %) correspondingly and *P* value for all was < 0.001. History of angina pectoris was noted in 32 (43.2%) with *P* value of 0.001. History of PVD 7 patients (9.5%) with *P* value 0.04. History of previous PCI was least to develop cardiogenic shock Five patients were post PCI (6.8%) with *P* value 0.910. All patients with cardiogenic shock were symptomatic at presentations and the most frequent symptoms were: angina chest pain 43 patients (58.1%), Dyspnea 17 patients (23%) & Atypical chest pain 2 patients (2.7%) with *P* value <0.001. ST elevation MI (STEMI) was a noticeable category of ACS with *P* value < 0.001; The patients number at presentation with those subtypes were; STEMI 59 (79.4%), NSTEMI 6 (8.1%), UA 1 (1.4%) & LBBB MI 8 (10.8%).

**Table 1:** Cardiogenic shock complicated ACS Patients characteristics.

Variables	CARDIOGENIC SHOCK	Rest of AHF	Total ACS	P VALUE
Number (%)	74(40.9%)	107 (59.1%)	1054 (100%)	
Mean Age in Years (SD)	64.7±9.7	62.1±11.2	58.7±11.5	< 0.001
Male (%)	47(63.5%)	84 (78.5%)	836 (79.3%)	< 0.001
Female (%)	27(36.5%)	23 (21.5%)	218 (20.7%)	0.005
Khat chewing	49(66.2%)	70 (65.4%)	757 (71.8%)	0.061
Smoking	24(32.4%)	47 (43.92%)	501 (47.5%)	0.140
Arterial Hypertension	34(45.9%)	49 (45.8%)	353 (33.5%)	< 0.001
Diabetes Mellitus	34(45.9%)	47 (43.9%)	282 (26.8%)	< 0.001
Hyperlipidemia	20(27.0%)	15 (14.3%)	126 (12%)	0.001
History of angina	32(43.2%)	39 (36.4%)	308 (29.2%)	0.001
History of MI	28(37.8%)	31 (29%)	201 (19.1%)	< 0.001
Post CABG	9(12.2%)	(5 (4.6%)	36 (3.4%)	< 0.001
Post PCI	5(6.8%)	(8 (7.5%)	80 (7.6%)	0.910
Post Stroke	14(18.9%)	6 (5.6%)	46 (4.4%)	< 0.001
History PVD	7(9.5%)	4 (3.7%)	31 (2.9%)	0.04
Symptoms at presentation				< 0.001
IHD chest pain	43(58.1%)	77 (72%)	870(82.5%)	
Dyspnea	17(23.0%)	24 (22.4%)	86 (8.2%)	
Atypical chest pain	2(2.7%)	4 (3.7%)	68 (6.5%)	
ACS diagnosis				< 0.001
STEMI	59(79.4%)	(67 (62.6%)	751 (71.3%)	
NSTEMI	6(8.1%)	(17 (15.9%)	117 (11.1%)	
UA	1(1.4%)	(15 (14%)	151 (14.3%)	
LBBB MI	8(10.8%)	(8 (7.5%)	31 (2.9%)	
Site of STEMI –ECG				< 0.001
Anterior / anteriolateral	52(70.2%)	58 (54.2%)	574 (54.5%)	
Inferior / inferoposterior	12(16.2%)	20 (18.7%)	289 (27.4%)	
Echocardiography				
Done	30(40.5%)	97 (90.7%)	832 (78.8%)	
LVEF%	36.5% (19-59)	(40 % (31-49)	49.5 (40-61)	< 0.001
LVEF ≤40%	18 (24.3%)	57 (53.2%)	153 (14.5%)	< 0.001

STEMI population showed ECG changes of anterior/anteriolateral in 52 patients (70.2%) while inferior / inferoposterior 12 patients (16.2%) giving P value of <0.001. LBBB was a prominent ECG feature with cardiogenic shock (10.8% Vs. 2.9%). Echocardiographic features were mainly reduced EF% and LVEF ≤40% were noted in 18 patients (24.3%). Cardiogenic shock especially that due to ACS is one of the emergency situations thrombolytic therapy utilization either pharmacologic or mechanical should started as soon as possible. In this study utilizing such agents were very low among all the patients especially those with cardiogenic shock; 10 patients with cardiogenic shock (13.5%) in contrast with 15 with AHF but no manifestations of cardiogenic shock (14.1%) P value 0.912.

Asprin was used in most of the patients with cardiogenic shock 69 patients (93.2%) in contrast with 101 patients (94.3%) with AHF but without cardiogenic shock, Clopidogrel was used in 66.2% and 73.8% in both groups and P value was not significant for both medications, Anticoagulation by IV heparin was used widely in cardiogenic shock group 91.9% while AHF without cardiogenic shock group was used in 78.5% with significant P value of 0.004. Using inotropes as Dopamine, Dobutamine, Epinephrine & Norepinephrine in cardiogenic shock was abundant; 69 patient (93.2%) with cardiogenic shock in

comparison of 18.7% patient with AHF without cardiogenic shock. Mechanical ventilation was employed in 68.9% of cases with cardiogenic shock and intra-aortic balloon pump in 8.1 % of the cases with significant P value < 0.001 (Table 2). Morbidity and mortality were high among cardiogenic shock population, P value was <0.001; strokes were noted in 18.9 % of those patients, while major bleeding was seen in 2 patients. Death was very high among cardiogenic shock patients 66.2% to 5.6 % for AHF without cardiogenic shock patients. (Table 2).

**Table 2:** Cardiogenic shock complicating ACS patients; management and in-hospital outcome.

Variables	Cardiogenic shock	Rest AHF	P value
<b>Thrombolytic therapy</b>	10(13.5%)	15 (14.1%)	0.912
<b>Treatment on admission</b>			
<b>Aspirin</b>	69(93.2%)	101 (94.3%)	0.834
<b>Clopidogrel</b>	49(66.2%)	79 (73.8%)	0.023
<b>IV Heparin</b>	68(91.9%)	84 (78.5%)	0.004
<b>LMW Heparin</b>	3 (4.1%)	(12 (11.2 %	0.002
<b>Beta Blockers</b>	14(18.9%)	40 (37.4%)	0.003
<b>ACE I / ARBs</b>	33(44.6%)	102 (95.3%)	< 0.001
<b>Calcium CB</b>	0	1 (0.9%)	0.110
<b>Statins</b>	60(81.1%)	98 (91.6%)	0.031
<b>Nitrates</b>	39(52.7%)	94 (87.9%)	< 0.001
<b>Diuretics</b>	33(44.6%)	65 (60.7%)	< 0.051
<b>Inotropes</b>	69(93.2%)	20(18.7%)	< 0.001
<b>IABP</b>	6(8.1%)	1 (0.9%)	< 0.001
<b>Ventilation</b>	51(68.9%)	4 (3.7%)	< 0.001
<b>Morbidity &amp; mortality</b>			
<b>Acute MR</b>	2(2.7%)	22(20.6%)	<0.001
<b>Stroke</b>	14(18.9%)	20 (18.7%)	< 0.081
<b>Major bleeding</b>	2 (2.7%)	0	< 0.001
<b>Death</b>	49(66.2%)	6 (5.6%)	< 0.001

## DISCUSSIONS

A evident outcome of this study is that Acute Coronary Syndrome in Yemen is a major underlying cause for acute heart failure and its resultant cardiogenic shock. As a first of its kind study in the country, this study shows that in between every 5-6 patients one will develop AHF. Patients present late for any thrombolytic methods. Older males are more predisposed to AHF and cardiogenic shock. The morbidity in form of strokes & major bleedings were extremely high while mortality was the fate of most of the patients with cardiogenic shock. Framingham Heart Study suggests that the most common cause of AHF is no longer hypertension or valvular heart disease, as it was in previous decades, but rather CAD<sup>10</sup>. Cardiogenic shock in this study shows its gloomy face where its high prevalence was recorded in contrast of some of the neighborhood registries (Table 3) in Yemen 40.9% of the patients with AHF developed cardiogenic shock, while the whole Gulfrace I was 11.6%. The prevalence was low 4.3% as mentioned in SPACE<sup>11</sup> registry (The Saudi Project for Assessment of Coronary Events). GRACE<sup>12,13</sup> (Global Registry of Acute Coronary Events Investigators) showed slightly higher prevalence than SPACE data but less than

Yemen data (4.6%) with older male predominance. Kolte et al 2014 had reported that the incidence of cardiogenic shock in USA complicating STEMI has increased during the past 8 years together with increased use of early mechanical revascularization and intra-aortic balloon pumps. There has been a concomitant decrease in risk adjusted in-hospital mortality<sup>14</sup>. Investigators from GUSTO-I trial had reported occurrence of cardiogenic shock in STEMI population as 8.3% but after the first year, 2% to 4% of patients died each year regardless of whether they had cardiogenic shock or not<sup>15</sup>. In-hospital medications in Yemeni patients was shown in Table 2 pointed out inadequate cardiogenic shock management especially in lacking the facilities of performing primary PCI , which shows good improvement in management and prognosis of cardiogenic shock in particular in developed countries<sup>15</sup>.

The in-hospital prognosis and its outcomes concerning the morbidity and the mortality among cardiogenic shock group pointed out a sad outcome of the Yemeni patients and was a big complications in cases of AHF as Strokes in 11% , cardiogenic shock 40.9% major bleeding 1.1% and death 30.4% in contrast to other registries especially Gulf Race I and SPACE (table 3). The Table reflect the quality of care in Yemeni tertiary hospital , late presentation of the patient to health facilities , adequacy of the emergency referral system and the performance of medical teams handling those patients.

### Limitations of the study

The results presented here are only from major hospitals in Yemen with or without a Catheterization Laboratory facility. This could have led to a higher contribution of patients with ACS and a low percentage of patients who had undergone coronary angiography and hence low utilization of primary PCI during hospitalization. The utilization of natriuretic peptides as a marker for HF and cardiogenic shock is nearly lacking were determined in only few patients. The absence of data about prior history of pre - hospitalization with HF represent a major limitation of the study and that surly affects the outcomes post- hospital discharge. The loss of contact with the patients after discharge represent another limitation to know the long run outcome in those groups.

**Table 3:** In-Hospital Major outcomes in some close neighborhood ACS registers.

OUTCOMES	YEMEN DATA	GULF RACE I	SPACE
<b>Stroke</b>	11.0%	1.3%	0.9%
<b>Cardiogenic shock</b>	40.9%	11.6%	3.5%
<b>Major bleeding</b>	1.1%	1.5%	0.7%
<b>Death</b>	30.4%	7.9%	4.4%

## CONCLUSION AND RECOMMENDATIONS

Acute coronary syndrome in Yemeni patients is a major cause for cardiogenic shock and had more worse prognosis regarding in-hospital morbidity and mortality. In this observational study, ACS patients with cardiogenic shock were older, more likely to have hypertension, diabetes, lower LVEF, and hemodynamically unstable status. These findings potentially explain the higher incidence of in- hospital adverse outcomes in ACS patients with cardiogenic shock. More aggressive treatment of these patients may be warranted to

improve prognosis. Introduction of heart failure biomarkers as natriuretic peptides is mandatory to improve the quality of clinical practice. Establishing a comprehensive primary PCI program after improving health systems is mandatory to overcome limitations in handling those patients. More studies on Khat as a potential risk factors are needed.

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## الصدمة القلبية بين مرضى متلازمة الشرايين التاجية الحادة في اليمن (معلومات مستقاة من السجل الخليجي لمتلازمة الشرايين التاجية الحادة – المرحلة الأولى)

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### ملخص

**المقدمة والأهداف:** متلازمة الشرايين التاجية الحادة ومدى انتشارها هي واحدة من أكثر امراض القلب شيوعا في العالم. وتعتبر المعلومات المستقاة من السجل الخليجي لمتلازمة الشرايين التاجية الحادة في اليمن هي اول معلومات صحية توضح الوضع لذلك المرض في اليمن. اما الصدمة القلبية فهي واحدة من اسوء المضاعفات التي يمكن حدوثها لمرضى متلازمة الشرايين التاجية الحادة. وتحديد هذه المضاعفة الخطيرة بين مرضى هذه المتلازمة في بلادنا وكذا اهمية التكهن الطبي بما قد يحدث لهؤلاء المرضى هو هدف رئيس لهذه الدراسة.

**طرق الدراسة والمرض:** تمثل معلومات اليمن الطبية في السجل الخليجي لمتلازمة الشرايين التاجية الحادة حجر الزاوية في المعلومات الكلية للسجل. وسجل الخليج لمتلازمة الشرايين التاجية الحادة هو سجل استقصائي مسبق ويشمل ست دول عربية في جزيرة العرب منها اليمن ومن كل دولة شمل عدة منشآت طبية رئيسية وشمل السجل كل الحالات المرقدة تحت تشخيص نهائي لحالتهم: متلازمة الشرايين التاجية الحادة. تم تسجيل الحالات لمدة ستة أشهر من الاستقصاء وكان عدد الذين شملتهم الدراسة 1054 مريض تم حصرهم وتسجيل بياناتهم بعد ترقيدهم في المشافي وعمل الفحوصات الضرورية وذلك في 20 مشفى في عموم اليمن. وشملت متلازمة الشرايين التاجية الحادة كل المرضى الذين تم تشخيصهم على اساس احتشاء عضلة القلب ذو ارتفاع او انخفاض قطعة ST في تخطيط القلب الكهربائي وكذلك حالات احصار الحزمة اليسري حديثة المنشأ وايضا حالات الذبحة القلبية غير المستقرة. من بين كل هذه الحالات تم اختيار حالات الفشل القلبي الحاد والذين دخلوا في مضاعفة الصدمة القلبية. وكانت نقطة النهاية في هذه الدراسة هي تحديد كل الاسباب المؤدية للوفاة داخل المشافي محل الدراسة.

**النتائج:** من بين مجموع 1054 مريضا بمتلازمة الشرايين التاجية الحادة كان هناك 181 مريضا يعانون من فشل القلب الحاد (17.3%) وذلك عند دخوله المشفى محل الدراسة او عند ترقيده به. من 181 حالة فشل قلبي حاد تم حصر 73 حالة دخلت في مرحلة الصدمة القلبية وكانت معظم شريحة هؤلاء المرضى من الذكور (63.5%) كبار السن بمعدل عمري (64±9.7 سنة) وكانت الدالة الإحصائية ذات دلالة كبيرة (P < 0.001). وكان المصابون بإحتشاء عضلة القلب المتميز بارتفاع قطعة ST في الموقع الأمامي والأمامي الجانبي في تخطيط القلب الكهربائي الشريحة الأكبر من المرضى (70.2%) من اجمالي المرضى. وكان فحص القلب بالموجات الصوتية والدوبلر يتماشى مع معطيات المرضى المصابون بالصدمة القلبية فكان معدل قذف الدم من البطين الايسر 36.5% وحتى 51% وكانت الدلالة الإحصائية ذات مدلول كبير (P < 0.001). وكان الوضع الطبي لشريحة مرضى الصدمة القلبية أسوء بكثير من كل شريحة المرضى مع متلازمة الشرايين التاجية الحادة بدون صدمة قلبية وكانت مجموعة الصدمة القلبية عرضة للوفاة أكثر من بقية المجموعة بمعدل 66.2% مقابل 4.8% لكل المرضى وكانت الدالة الإحصائية ايضا كبيرة (P < 0.001).

**الاستنتاج:** المرضى اليمنيون والذين يعانون من متلازمة الشرايين التاجية الحادة وحصلت لهم مضاعفات في شكل الصدمة القلبية كان تطور الوضع الصحي والطبي لحالتهم سيئ جدا فيما يخص تعقيد هذا الوضع طبيا أو معدل الوفاة المرتفع جدا.