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The Epidemiology of Acute Coronary Syndrome in Oman

Results from the Oman-RACE study

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وبائيات متلازمة الشريان التاجي الحادة في سلطنة عمان

نتائج دراسة عمان– ريس

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الملخص: **الهدف**: تقييم وبائية وعوامل الخطر لمتلازمة الشريان التاجي الحادة في سلطنة عمان. **المنهجية**: تحليل البيانات التي تم جمعها من خلال دراسة متعددة المراكز في عدة دول، بين المرضى اللذين أدخلوا على التوالي الى المشافي والذين تتراوح أعمارهم 20 عاما أو أكثر بتشخيص متلازمة الشريان التاجي الحادة في خمس من دول الخليج العربي (عمان والبحرين والكويت وقطر والإمارات العربية المتحدة)، واليمن على مدى فترة 5 أشهر. هذا التحليل يلخص بيانات المرضى العمانيين الذين أدخلوا المستشفى بتشخيص مبدئي بمتلازمة الشريان التاجي الحادة. **النتائج**: تم تأكيد 1,340 حالة لمتلازمة الشريان التاجي الحادة منها 748 بين الرجال 592 بين النساء حيث بلغ العمر الوسيط 61 سنة. وكان معدل الإصابة للمتلازمة 338.9 حالة لكل 100,000 شخص– سنة. بينما بلغت 779 و 674 حالة لكل100,000 شخص– سنة بين الرجال والنساء على التوالي. وكان نسبة الذكور إلى الإناث أعلى بين مرضى إرتفاع مقطع ST في رسم قلب الإحتشاء التجلطي (2.26، بفاصل ثقة 95% 1.63 الى 3.15) ويليه إحتشاء عضلة القلب غير المرتبط بمقطع ST 86.1، بفاصل ثقة 95% 1.28 الى 2.21)، والذبحة الصدرية غير المستقرة (0.79 بفاصل ثقة 95% 0.66 الى 0.99). وشكلت الذبحة الصدرية غير المستقرة 55% من الحالات، وإحتشاء عضلة القلب الناجم عن ارتفاع مقطع ST 26% وإحتشاء عضلة القلب غير المرتبط بمقطع ST 19% من الحالات. من بين عوامل خطرالأصابة بمتلازمة الشريان التاجيزيادة معدل انتشار ارتفاع ضغط الدم (68%) وداء السكري (36%)، وارتفاع الدهون (63%) وزيادة الوزن / السمنة (65%)، مع معدل منخفض نسبيا من استخدام التبغ في الوقت الحاضر (11%) و**الخلاصة**: دراستنا تؤكد حدوث معدلات مرتفعة لمتلازمة الشريان التاجي الحادة بين العمانيين ويدعم فكرة أن وباء مرض القلب والأوعية الدموية تجتاح البلدان النامية.

مفتاح الكلمات: متلازمة الشريان التاجي الحادة، أمراض القلب والأوعية الدموية، نقص تروية القلب، عوامل الخطر، وسلطنة عمان.

abstract: ***Objectives:*** **T**his study aimed to evaluate the epidemiology and coronary risk factors of acute coronary syndrome (ACS) in Oman. ***Methods:*** Data were collected through a prospective, multinational, multicentre survey of consecutive patients, hospitalised over a 5-month period in 2007 with a diagnosis of ACS, in Yemen and five Arabian Gulf countries (Oman, Bahrain, Kuwait, Qatar, United Arab Emirates). Here we present data of Omani patients aged ≥20 years who received a provisional diagnosis of ACS and were consequently admitted to 14 different hospitals. ***Results:*** There where 1,340 confirmed ACS episodes in 748 men and 592 women (median age 61 years). The overall crude incidence rate of ACS was 338.9 per 100,000 person-years (P-Y). The age-standardised rate (ASR) of ACS was 779 and 674 per 100,000 P-Y for men and women, respectively. The ASR male-to-female rate ratio was highest in the ST-elevation myocardial infarction (STEMI) group (2.26, 95% confidence interval ([CI], 1.63 to 3.15) followed by the non-STEMI (NSTEMI) group (1.68, 95% CI 1.28 to 2.21) and unstable angina (0.79, 95% CI 0.66 to 0.99). Unstable angina accounted for 55%, STEMI for 26% and NSTEMI for 19% of ACS cases. Among the coronary risk factors, there was a high prevalence of hypertension (68%), diabetes mellitus (DM) (36%), hyperlipidaemia (63%), and overweight/obesity (65%), with a relatively low rate of current tobacco use (11%). ***Conclusion:*** Our study confirms a high incidence of ACS in Omanis and supports the notion that the cardiovascular disease epidemic is also sweeping developing countries.

Keywords: Acute coronary syndrome; Incidence; Cardiovascular disease; Ischemic heart disease; Risk factors; Oman.

Advances in knowledge

- *This paper provides nationwide population-based incidence rates of acute coronary syndrome in a large prospective cohort recruited from multiple centres in Oman.*
- *A comparable methodology was used, assessing the Omani population against other Arab Gulf states, and based upon an international comparison with other Arab, Asian, and European populations.*

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Application to Patient Care

- *With the recognition of the high incidence of acute coronary syndrome (ACS) in Oman, the government and public health authorities should give higher priority to the control of the underlying cardiovascular disease risk factors which are shown to be highly prevalent in Omani patients.*

Current evidence indicates that cardiovascular diseases (CVD) make the largest contribution to mortality in most developing countries.[1] Of all CVD, ischaemic heart disease (IHD) is the single largest cause of death in such nations.[2] Worldwide, IHD was the second and third leading cause of disability-adjusted life years lost in men and women in 2002, respectively.[1] Although rates of IHD have fallen by up to 70% in the past three decades in some industrialised countries, it is likely to remain as the undisputed leading cause of death globally until the year 2030.[2,3]

Since the early 1990s, CVDs have been the leading cause of in-patient mortality in Oman.[4] In 2006, IHD was Oman's leading cause of morbidity and fourth cause of mortality among patients aged 45-60 years.[5] Although clinical management patterns of acute coronary syndrome (ACS) have been reported in Oman,[6] to the best of our knowledge, the epidemiology of IHD and/or ACS has not been studied. Through a joint collaborative effort, the Gulf Registry for Acute Coronary Events (Gulf RACE) was established in 2006 to study such events in five Arabian Gulf countries and Yemen.[7] The aim of this registry was to estimate the incidence of ACS in the participating countries, the distribution of CVD risk factors among affected patients, and types and practice patterns for the management of ACS.[7] This study details the epidemiology and coronary risk factors of ACS patients throughout Oman.

Methods

The Gulf Registry of Acute Coronary Events (Gulf RACE) study was organised as a prospective, multinational, multicentre survey of consecutive patients over 20 years-old who had been hospitalised with the final diagnosis of acute coronary syndrome (ACS) in Yemen and five Arabian Gulf countries—Oman, Bahrain, Kuwait, Qatar, and the United Arab Emirates (UAE)—over a period of 6 months. The pilot phase lasted throughout May 2006 and is described in detail elsewhere.[7] Enrolment for the study itself commenced on 29 January 2007, and continued for 5 months. An attempt was made to include all admissions that had been given a provisional diagnosis of ACS with no exclusion criteria. Patients who were admitted for non-ACS causes to general wards but later developed ACS in hospital were also included in the study. Of the 16 requested centres (15 secondary and one tertiary care hospital, all with facilities to manage ACS patients), 14 participated in the registry and enrolled patients according to the survey's inclusion criteria. The study thus covered at least 85% of the total population of Oman. Ethical approval for the study was granted by the national or institutional ethical bodies in all participating countries.

During the study period, all recruiting hospitals managed their patients independently. However, patients were referred to Royal Hospital in Muscat, the capital of Oman, on an emergency basis for primary angiography and/or angioplasty. Study forms initiated in the parent institution, or secondary care hospital, were sent with patients during transfer to the Royal Hospital to complete data collection procedures and avoid duplicate reporting. All medical services, including ACS management, are provided free of charge to Omani nationals throughout government institutions in the country.

Data collected included patient demographics, past medical history, provisional diagnosis on admission, final discharge diagnosis, clinical features at hospital presentation, electrocardiogram (ECG) findings, laboratory investigations, medications administered within 24 hours of admission and those prescribed on discharge, use of cardiac procedures and interventions, in-hospital outcomes, and in-hospital mortality. All management decisions were at the discretion of the treating physician. The external auditor visited 20% of the centres where filled forms and source documents (i.e. patients' case notes) were inspected to verify that data collected in the case report form matched source documents. No attempt was made to validate the accuracy of discharge diagnosis of

the attending physician.

Diagnosis of the different types of ACS and definitions of data variables were based on the American College of Cardiology clinical data standards published in December 2001.[8] These definitions are based on clinical presentations, ECG findings, and cardiac biomarkers. The biomarkers were measured locally at each hospital's laboratory using its own assays and reference ranges. Only two centres used troponin (T) as routine assays in the diagnosis of myocardial injury. Body mass index (BMI) was used to characterise overweight (BMI 25–29.9 Kg/m^2) or obese patients (BMI ≥30 Kg/m^2).[9] A waist circumference ≥94 cm in males and ≥80 cm in females was considered abnormal. Diagnosis of diabetes mellitus (DM) was based on past diagnosis by a physician, intake of anti-diabetic medications, or post-admission fasting plasma glucose (FPG) values using the 1999 diagnostic criteria recommended by the World Health Organization (WHO).[10] Hypertension was diagnosed if systolic and/or diastolic arterial blood pressure exceeded 130/85 mmHg, or if a patient was on anti-hypertensive medication. Subjects were classified as having high total cholesterol if fasting levels exceeded 5.2 mmol/L; hypertriglyceridaemia if levels exceeded 1.69 mmol/L, and/or abnormal levels of high density lipoproteins if levels were <1.04 in males and <1.29 mmol/L in females.[11]

Data were entered in Epi Info, Version 6 (Centers for Disease Control, Atlanta, Georgia, USA). Categorical variables were presented as a number of cases and percentages and compared using the chi-square test. The K-sample equality-of-medians test was used to examine differences between groups of median age. Incidence rates of coronary events were calculated from index episodes during the study period using the mid-year 2007 population estimates for Oman obtained from the Omani Ministry of National Economy.[12] To facilitate comparisons with other published rates, age-standardised incidence rates (ASR) were calculated by direct method within 10-year bands for ages 20 years and above, using the world standard population.[13] For comparisons with World Health Organization - Monitoring Trends and Determinants in Cardiovascular Disease (WHO-MONICA), MONICA age weights in the 5-year age bands for ages 35–64 years were used.[14,15] A 95% confidence interval (CI) for ASR ratio (RR) was calculated using the standard error of the natural logarithm of the RRs.[16] Observed differences were expressed as *P* values. A value of *P* <0.05 was considered statistically significant. Analyses were performed with Intercooled Stata, version 9.1 (Stata Corporation, Texas, USA) and Microsoft Excel 2003 (Microsoft Corporation, Redmond, Washington, USA). Completeness of data was 98% for all the analysed variables. Patients with a diagnosis of left bundle branch block (n = 9) were grouped with the ST-elevation myocardial infarction (STEMI) patients.

Results

The baseline characteristics of the ACS patients enrolled in the study are given in Table 1. Over the 153-day recruitment period, 1,340 cases of ACS were reported with complete core data. The median age of ACS patients was 61 years (males 60 years and females 61 years; *P* = 0.39). Among the risk factors, a high prevalence of hypertension (56%), DM (38.2%), and hyperlipidaemia (36.4%) was reported on admission. When fasting blood sugar, blood pressure, and total cholesterol were measured 24 hours post-admission, there was a significant increase in the detection of hypertension (56–69%; *P* <001) and hyperlipidaemia (36.4–63.3%, *P* <001). The prevalence of DM was around 32% using random blood sugar, and increased to 46% when using fasting plasma glucose levels in patients with STEMI (*P* <001). One-half to two-thirds of ACS patients were either overweight or obese according to WHO criteria.[9] Current tobacco use was relatively low (11.1%).

Of the total ACS patients, 741 (55.3%) were discharged from hospitals with unstable angina, 345 (25.7%) with non-ST elevation myocardial infarction (NSTEMI) and 254 (18.9%) with STEMI [Table 1]. Unstable angina was also the most common diagnosis across all 10-year age strata, followed by NSTEMI and STEMI. Patients with unstable angina and NSTEMI were also more likely to report a medical history of percutaneous coronary intervention, DM, hypertension, and hyperlipidaemia. On the other hand, STEMI patients were more likely to be current tobacco users. Women were more likely to present with unstable angina compared to men (54% versus 46%, *P* <03) [Table 2], while men were twice as likely to present with STEMI and NSTEMI compared to

Table 1: Baseline characteristics of patients admitted with acute coronary syndrome (Oman RACE study, 2006)

Characteristic	STEMI % (n = 254)	NSTEMI % (n = 345)	Unstable Angina % (n = 741)	All % (n = 1,340)
Median age (yrs)	61	61	61	61
Age groups				
20–29	0.8	0.6	0.9	0.8
30–39	4.7	4.6	3.5	4.0
40–49	12.6	13.9	13.9	13.7
50–59	22.0	26.1	25.9	25.2
60–69	29.5	33.0	33.3	32.5
70+*	30.3	21.7	22.4	23.7
Men*	73	65	46.0	56.0
Medical history				
Angina pectoris*	30.3	52.2	60.9	52.8
MI	16.1	22.6	19.5	19.6
PCI*	3.9	9.0	9.1	8.0
CABG*	3.1	7.0	9.5	7.6
Aspirin use*	31.6	54.2	60.2	53.2
Current tobacco use*	23.6	12.5	6.2	11.1
Diabetes*	30.3	37.4	41.3	38.2
Hypertension*	39.4	55.6	61.8	56.0
Hyperlipidaemia*	23.2	35.6	41.3	36.4
Measurements 24 hours post-admission				
RBG ≥ 11.1 mmol/l	32.4	30.7	28.7	29.9
FBG ≥ 7.0 mmol/l*	46.0	41.9	30.7	36.5
Hypertension*	61.0	68.0	71.8	68.8
TC >5.2mmol/l	63.3	63.4	63.3	63.3
Abnormal HDL	51.6	57.3	57.7	56.4
Abnormal TG	33.5	30.1	36.8	34.4
BMI 25-29.9 Kg/m2	33.5	40.3	38.3	37.9
BMI ≥30 kg/m2	25.2	26.4	28.9	27.5
Abnormal WC (cm)*	43.7	57.2	66.1	59.8

STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft; RBG = random blood glucose; FBG = fasting blood glucose; TC = total cholesterol; HDL = high density lipoprotein; TG = triglycerides; BMI = body mass index; WC = waist circumference.

** = P < 0.05; Chi-square tests were utilised to examine the statistical significance of differences between the respective comparison groups with regards to the distribution of categorical variables. A K-sample equality-of-medians test was used to examine between group differences in median age.*

For cut-off points for each variable, see Methods section.

women.

Table 2 demonstrates the crude and ASR of incidence of ACS in Oman in patients aged 20 years and above, and in a subgroup aged 35–64 years. The period of case ascertainment (5 months) encompassed 395,389 person-years (P-Y) of observations in 748 men and 592 women (all Omanis) with episodes of ACS. The overall crude incidence of ACS was 338.9 per 100,000 P-Y. The ASR of ACS was 779 and 674 per 100,000 P-Y for men and women, respectively. The ASR of ACS were significantly higher in men than women with

Table 2: Crude and age-standardised annual incidence rates (all per 100,000 person-years) of acute coronary syndrome and its components in Omani men and women aged 20 years and above (Oman RACE study, 2006)

Age group	All ACS	STEMI	NSTEMI	Unstable Angina
Male (20+ years)				
No. of cases	748	184	224	340
P-Y	198,324	198,324	198,324	198,324
Crude rate (95% CI)	377.2 (350.6 to 405.1)	92.8 (79.9 to 107.2)	112.9 (98.6 to 128.8)	171.4 (153.7 to 190.6)
ASR (95% CI)	779.7 (723.2 to 836.2)	184.9 (164.6 to 221.5)	239.5 (200.5 to 262.3)	355.3 (723.2 to 836.2)
Female (20+ years)				
No. of cases	592	70	121	401
P-Y	197,065	197,065	197,065	197,065
All crude (95% CI)	300.4 (276.7 to 325.6)	35.5 (27.7 to 44.9)	61.4 (50.9 to 73.4)	203.5 (184.1 to 224.4)
All ASR (95% CI)	674.3 (619.5 to 729.1)	81.7 (64.1 to 103.8)	142.2 (114.7 to 165.3)	450.4 (619.5 to 729.1)
Male (35-64 years)				
No. of cases	448	139	103	206
Person-years	63,543	63,543	63,543	63,543
ASR for ages 35–64	835.0 (757.3 to 912.8)	189.7 (152.6 to 226.8)	256.9 (213.7 to 300.2)	388.3 (335.0 to 441.7)
Females (35-64 yrs)				
No. of Cases	350		39	241
P-Y	64,644	64,644	64,644	64,644
ASR for ages 35–64	691.6 (618.7 to 764.5)	81.1 (55.5 to 106.7)	138.9 (106.0 to 171.7)	471.6 (411.4 to 531.7)
Male:Female				
Rate ratio, 20+ years (95% CI)	1.16 (1.01 to 1.32)	2.26 (1.63 to 3.15)	1.68 (1.28 to 2.21)	0.79 (0.66 to 0.99)
Rate ratio, 35–64 years (95% CI)	1.21 (1.01 to 1.45)	2.34 (1.47 to 3.73)	1.85 (1.28 to 2.68)	0.82 (0.65 to 1.05)

ACS = acute coronary syndrome; STEMI = ST-elevation myocardial infarction; NSTEMI = Non ST-elevation myocardial infarction; P-Y = person-years; ASR = age-standardised rate; CI = confidence interval.
For age-standardising, see reference no. 13.

a rate ratio of 1.16 (95% CI: 1.01 to 1.32). The male to female age-standardised incident rate ratio was highest in the STEMI group (2.26, 95% CI: 1.63 to 3.15) followed by the NSTEMI group at 1.68 (95% CI: 1.28 to 2.21) and that with unstable angina at 0.79. (95% CI: 0.66 to 0.99). When data were analysed in a subgroup aged 35–64 years for broad comparisons with the MONICA project cohort, there were 448 events in males and 350 events in females within 128,187 P-Y.[14] Age-standardised ACS event incident rates were higher in men than in women in this age band with a rate ratio of 1.21 (95% CI: 1.01 to 1.45).

Discussion

We provide the first age-standardised population-based incidence rates of ACS and associated risk factors in Oman. The ASR of ACS in Omanis (men 779, women 674 per 100,000 P-Y) were similar to rates reported among Palestinian Arabs of Jerusalem (796 and 503 per 100,000 men and women P-Y, respectively).[17] These incidence rates are markedly higher than those reported in industrialised nations such as Denmark (men 331 and women 137 per 100,000 P-Y), Greece (both genders 226 per 100,000 P-Y), and France (men 262 and women 55 per 100,000 P-Y), thus confirming the double burden of already existing communicable diseases and the present non-communicable diseases in

middle and low-income developing countries.[18–21]Notwithstanding the differences in the definitions of coronary events between the present study and the MONICA populations studied between 1981 and 1995, the coronary event incidence rate in Omani men aged 35–64 years (835 per 100,000 P-Y) are comparable to the highest rates recorded in the MONICA project (907 per 100,000 P-Y among Finnish men).[22] Similarly, in the 35–64 year old cohort, the incidence rate of ACS among Omani women (692 per 100,000 P-Y) was more than double the rate in their Scottish counterparts in the UK (241 per 100,000 P-Y), although, the latter was the highest rate reported among MONICA women.[22] When compared with other Arabs in the same age group of 35–64 years, the ACS incidence rate among Omanis surpassed the rate reported in Palestinian men (799 per 100,000 P-Y) while the rate in Omani women was three times the rate in Palestinian women (234 per 100,000 P-Y).[17]

The high incidence of ACS among Omanis (and other Arab ethnic groups) may stem from greater susceptibility and excess exposure to established CVD risk factors.[23] In Asian populations, morbidity and mortality appear to occur at lower cut-off point values for some CVD risk factors such as BMI and waist circumference than in Caucasians, possibly indicating greater susceptibility at a lower threshold for adverse health outcomes.[24–26] In our study, Omani patients appeared to experience ACS at an earlier age (mean 60.7 years; median 61 years) than their counterparts from Europe, Australia, the United States, and Brazil (median range 63.4–68.1) by an average of 2 to 7 years.[27]The difference in age can extend up to 11 years if compared with Europeans with unstable angina.[28] Arab patients with ACS from other countries were also reported to be younger (mean age: Saudi Arabia 57.1, Kuwait 56.7, and Palestine 57.9),[17,29,30] The INTERHEART study also showed Arab patients to be a decade younger at presentation with acute myocardial infarction than Europeans, Chinese, or Latin American patients.[31] The earlier onset of ACS in Arabs has not been studied systematically. However, greater susceptibility to CVD risk factors may be implied, in a similar way suspected to occur among South Asians through genetic differences or a mismatch of metabolic processes during early or middle age.[23] Other findings like low levels of high density lipoproteins and a lack of regular physical activity among Omanis may have contributed further to their susceptibility to adverse coronary outcomes.[32]

Our study's main strength lies in the fact that it is the first to provide nationwide estimates of incidence and risk factors of ACS in a large prospective cohort recruited from multiple centres in Oman using a methodology comparable with other Arab Gulf states. On the other hand, the lack of a vital registration system within the country implies that sudden cardiac deaths due to ACS could not be estimated and thus are not included in the current incidence estimates presented here. Further, due to limited resources, out of 1,340 patients, T assays were used in less than 21% (277 patients) to diagnose myocardial injury. However, this is unlikely to have biased results towards the under-diagnosis of STEMI and NSTEMI as proportions of the later two in Oman are similar (42% and 58%, respectively) to the overall Gulf-RACE (39% and 61%, respectively) and Gulf-RACE 2 (46% and 54%, respectively) studies after discarding results from unstable angina patients.[33,34] Finally, comparison data were presented with MONICA cohorts in spite of changes of some diagnostic criteria and temporality between the two studies, mainly due to wide use of T assays in the current survey.

Conclusion

The incidence of ACS among Omanis is one of the highest in the world and flags up an impending CVD epidemic that is yet to reach its peak. The need to address root causes of established CVD risk factors could not be more urgent.[35] Health reforms and prevention strategies are needed to counter a CVD epidemic, with a particular focus on reducing the high number of preventable risk factors.

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