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Association between education and major adverse cardiac events among patients with acute coronary syndrome in the Arabian Gulf

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ABSTRACT

Introduction The objective of this study was to evaluate the association between education and major adverse cardiac events in patients with acute coronary syndrome (ACS) in the Arabian Gulf.

Methods Data were analysed from 3874 consecutive patients diagnosed with ACS admitted to 29 hospitals in four Arabian Gulf countries from January 2012 to January 2013. Education was defined as any type of formal training from primary school and above. MACE included stroke/ transient ischaemic attack (TIA), myocardial infarction (MI), all-cause mortality and readmissions for cardiac reasons.

Results The overall mean age was 60±13 years and 67% (n=2579) were men. A total of 53% (n=2039) of the patients had some form of school education. Adjusting for demographic and clinical characteristics as well as socioeconomic measures (insurance type and employment), at 12-month follow-up, educated patients were significantly less likely to have had MACE (adjusted OR (aOR): 0.55; 95% CI 0.44 to 0.68; p<0.001) than those with no formal education. The lower rate of events was also consistent across all MACE components: stroke/TIA (aOR: 0.56; 95% CI 0.33 to 0.94; p=0.030), MI (aOR: 0.58; 95% CI 0.38 to 0.86; p=0.008), all-cause mortality (aOR: 0.58; 95% CI 0.39 to 0.87; p=0.009) and readmissions for cardiac reasons (aOR: 0.61; 95% CI 0.48 to 0.77; p<0.001). MACE outcomes were consistent across men and women and across countries.

Conclusions Education was associated with lower MACE events in patients with ACS in the Arabian Gulf. Interventions promoting healthy lifestyles and management of clinical risk factors for patients with low health literacy are urgently required.

Key questions

What is already known?
► Most of the patients with acute coronary syndrome (ACS) in the West are literate.
► Education has been inversely associated with major adverse cardiac events (MACEs) in patients with ACS in the West.

What are the new findings?
► Compared with their illiterate counterparts, literate Arabian Gulf patients with ACS were associated with fewer MACEs, namely: stroke/transient ischaemic attack, myocardial infarction, mortality and readmissions for cardiac reasons.
► All patients in the Arabian Gulf received free universal health insurance including free medications.

What do the new findings imply?
► Interventions promoting healthy lifestyles and management of clinical risk factors for patients with low health literacy are urgently required.

INTRODUCTION

Cardiovascular diseases (CVDs) are one of the leading causes of death and disability in the Arabian Gulf and worldwide despite remarkable advances in their management.[1–4] An inverse association between measures of socioeconomic status, like educational attainment, and CVDs has been known for decades.[5][6] Education has been associated with significantly lower cardiovascular events (ie, cardiovascular mortality, coronary heart disease (CHD), myocardial infarction (MI) and stroke) in various regions of the world including USA, Europe, Australia, New Zealand, China and Asia Pacific.[5–10] Although, most of these studies were done in the West, it is likely that the positive association of education is universal. Also, it is possible that economic inequality within a country may magnify the disparity in cardiovascular outcomes between the least and highest educated groups.[11]

However, similar studies on the association of education with major adverse cardiac events (MACEs) in the Arabian Gulf are scarce. The effect of potentially modifiable risk factors associated with myocardial infarction (INTERHEART) study evaluated the effect of education on the risk of developing

first non-fatal MI, while Doulah *et al* only looked at the association between education and severity of coronary artery disease (CAD) in patients undergoing coronary angiography.[12 13] Furthermore, access to healthcare, a concern raised in studies regarding socioeconomic associations with CVD,[7 9 11] is unlikely to have limited effect given the high universal health coverage in the Arabian Gulf.[14] Hence, the aim of this study was to evaluate the potential association of education with MACE in patients with acute coronary syndrome (ACS) in the Arabian Gulf, using the Gulf COAST dataset, a prospective, multicentre, multinational registry of consecutive Gulf citizens hospitalised with ACS in four Arabian Gulf countries.[15]

METHODS

The methods of the Gulf COAST registry have been previously reported.[15] In summary, the Gulf COAST registry was a prospective, multicentre, multinational, longitudinal, cohort study of consecutive citizens with a diagnosis of ACS, from four Arabian Gulf countries (Bahrain, Kuwait, Oman and United Arab Emirates) and admitted to 29 hospitals between January 2012 and January 2013. The registry enrolled patients ≥18 years of age and diagnosed according to the American College of Cardiology clinical data standards.[16] Only those that were able to provide informed consent were included into the study.

Education was defined as any formal education from primary school and above. MACE included stroke/transient ischaemic attack (TIA), MI, all-cause mortality and readmissions for cardiac reasons.

Data collected included patient demographics (age, gender, employment status, marital status, health insurance, body mass index and tobacco and alcohol use), medical history and risk factors related to MACE, prior medication use, laboratory data, clinical presentation and management during hospital stay including medications, reperfusion therapy and procedures and discharge medications. Follow-up was performed at 1 month, 6 months and 12 months from the date of enrolment and was carried out by clinic visits or telephone interviews.

Statistical analysis

For categorical variables, frequencies and percentages were reported. Differences between educated and non-educated groups were analysed using Pearson's χ^2 tests (or Fisher's exact tests for cells <5). Mean and SD were used to summarise the data for continuous variables and analyses performed using Student's t-test. The relationships between education (yes/no) and MACE (stroke/TIA, MI, all-cause mortality, readmissions for cardiac reasons and overall MACE) were evaluated using multiple logistic regression using the simultaneous method and adjusting for Global Registry of Acute Coronary Events (GRACE) risk score for in-hospital mortality, which has been validated in an Arabian Gulf ACS Registry.[17] Apart from from GRACE risk score, the logistic models were also adjusted for gender, employment status, marital status, insurance

type, demographic and clinical characteristics. Interaction terms between education and employment status as well as between education and gender were also tested.

The goodness-of-fit of the multivariable logistic models was examined using the Hosmer-Lemeshow goodness-of-fit statistic[18] as well as the *G*-index.[19] An a priori two-tailed level of significance was set at the 0.05 level. Statistical analyses were conducted using STATA V.13.1.

RESULTS

The Gulf COAST registry enrolled 4044 patients. The present analysis included only patients who were discharged alive from the index admission (n=3784). The overall mean age of the cohort was 60±13 years, of which 67% (n=2579) were males. A total of 29% of the patients were employed (n=1117) and 85% (n=3281) were married. Forty per cent of the patients (n=1537) were current or prior smokers, and 3.1% (n=121) of the patients were alcohol consumers. Comorbid conditions were common in this cohort particularly hypertension (n=2510; 65%), dyslipidaemia (n=2189; 57%) and diabetes mellitus (n=2071; 53%).

A total of 53% (n=2039) of the patients had any formal education (24% had below secondary school (high school), 16% had completed secondary school (high school), 4.2% had some sort of vocational training, 6.4% graduated from college while 1.7% had postgraduate training). Those with formal education (compared with those that were illiterate) were younger (54 years vs 66 years; p<0.001) and more likely to be male (82 vs 49%; p<0.001), employed (49% vs 6.2%; p<0.001), married (91% vs 77%; p<0.001), current or prior smoker (54% vs 23%; p<0.001) and alcohol consumers (4.6% vs 1.5%; p<0.001) but less likely to have a prior MI (24% vs 29%; p=0.001), hypertension (57% vs 73%; p<0.001), diabetes mellitus (50% vs 57%; p<0.001) and prior stroke/TIA (4.7% vs 9.3%; p<0.001) than those without formal education. Educated patients were also more likely to present with a lower heart rate (84 vs 86 beats/min; p<0.001), systolic blood pressure (141 vs 144 mm Hg; p<0.001), serum creatinine (81 vs 84 µmol/L; p<0.001) and GRACE risk score (114 vs 139; p<0.001), and had higher left ventricular ejection fraction (50% vs 48%; p<0.001). They were also less likely to present with a high Killip class (p<0.001) (table 1).

Table 2 shows medication utilisation prior to admission and postdischarge stratified by education status. While 98% (n=3623) of the cohort was treated optimally with the dual antiplatelet combination (aspirin and clopidogrel concurrently), only 52% (n=1922) of the patients were prescribed the five-drug regimen (aspirin, clopidogrel, ACE inhibitor/angiotensin receptor blocker (ARB), statin and beta blocker) concurrently, which was significantly higher among educated participants in contrast to their illiterate counterparts (59% vs 45%; p<0.001).

The overall MACE rate was 32.9% (n=1276) with significant differences among the groups as shown in

Table 1 Demographic and clinical characteristics of patients with acute coronary syndrome in the Arabian Gulf stratified by education status: findings from Gulf Coast registry

Characteristic, n (%) unless specified otherwise	All (N=3874)	Educated		P value
		No (n=1835)	Yes (n=2039)	
Demographic				
Age, mean±SD, years	60±13	66±10	54±12	<0.001
Male gender	2579 (67)	898 (49)	1681 (82)	<0.001
Employed	1117 (29)	114 (6.2)	1003 (49)	<0.001
Married	3281 (85)	1418 (77)	1863 (91)	<0.001
BMI, mean±SD, kg/m^2	29.1±9.0	28.7±9.6	29.5±8.4	0.005
Smoking (current or prior)	1537 (40)	430 (23)	1107 (54)	<0.001
Alcohol	121 (3.1)	28 (1.5)	93 (4.6)	<0.001
Medical history				
Prior MI	1007 (26)	523 (29)	484 (24)	0.001
Dyslipidaemia	2189 (57)	1057 (58)	1132 (56)	0.191
Premature CAD	597 (15)	147 (8.0)	450 (22)	<0.001
Hypertension	2510 (65)	1344 (73)	1166 (57)	<0.001
Diabetes mellitus	2071 (53)	1051 (57)	1020 (50)	<0.001
Stroke/TIA	266 (6.9)	171 (9.3)	95 (4.7)	<0.001
Clinical (parameters) at presentation				
HR, mean±SD, bpm	85±21	86±21	84±20	<0.001
SBP, mean±SD, mm Hg	142±27	144±27	141±27	<0.001
DBP, mean±SD, mm Hg	81±16	80±16	82±16	<0.001
Crea, p50 (IQR), µmol/L	82 (66–104)	84 (66–114)	81 (68–98)	<0.001
LVEF, mean±SD, %	49±13	48±13	50±13	<0.001
GRACE risk, mean±SD	126±40	139±39	114±37	<0.001
Killip class				<0.001
I: no heart failure	3099 (80)	1340 (73)	1759 (86)	
II: rales	493 (13)	307 (17)	186 (9.1)	
III: pulmonary oedema	260 (6.7)	174 (9.5)	86 (4.2)	
IV: cardiogenic shock	22 (0.6)	14 (0.8)	8 (0.4)	
Discharged diagnosis				<0.001
LBBB MI	30 (0.8)	20 (1.1)	10 (0.5)	
NSTEMI	1820 (47)	1022 (56)	798 (39)	
STEMI	928 (24)	341 (19)	587 (29)	
Unstable angina	1094 (28)	452 (25)	642 (32)	

BMI was missing in 35 subjects, HR in 2 subjects, SBP in 3 subjects, DBP in 3 subjects, creatinine in 19 subjects, LVEF was missing in 1335 subjects, GRACE in 21 subjects and 2 subjects in discharged diagnosis.
Percentages might not add up to 100% due to rounding off.
BMI, body mass index; CAD, coronary artery disease; Crea, first serum creatinine; DBP, diastolic blood pressure; HR, heart rate; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; LBBB MI, myocardial infarction; NSTEMI, non-ST myocardial infarction; SBP, systolic blood pressure; STEMI, ST myocardial infarction; TIA, transient ischaemic attack; bpm, beats per minute; p50, median.

table 3. Adjusting for demographic and clinical characteristics as well as socioeconomic measures (insurance type, employment and marital status), at 12-month follow-up, educated patients with ACS were significantly less likely to have had MACE (adjusted OR (aOR): 0.55; 95% CI 0.44 to 0.68; p<0.001). The lower rate of events was also consistent across all MACE components: stroke/TIA (aOR: 0.56; 95% CI 0.33 to 0.94; p=0.030), MI (aOR: 0.58; 95% CI 0.38 to 0.86; p=0.008), all-cause mortality (aOR: 0.58; 95% CI 0.39 to 0.87; p=0.009) and readmissions for cardiac reasons (aOR: 0.61; 95% CI 0.48 to 0.77; p<0.001). The interaction terms between education and employment status as well as between education and gender were not significant in all the

Table 2 Medication utilisation of the patients with acute coronary syndrome in the Arabian Gulf stratified by education status: findings from Gulf Coast registry

Characteristic, n (%) unless specified otherwise	All (N=3874)	Educated		P value
		No (n=1835)	Yes (n=2039)	
Prior medications (N=2878)				
Aspirin	2288 (80)	1247 (83)	1041 (76)	<0.001
Clopidogrel	834 (29)	451 (30)	383 (28)	0.212
ACEIs	1490 (52)	833 (55)	657 (48)	<0.001
ARBs	557 (19)	267 (18)	290 (21)	0.023
Beta blockers	1755 (61)	935 (62)	820 (60)	0.172
Statins	2319 (81)	1240 (82)	1079 (79)	0.008
Other LLDs	60 (2.1)	14 (0.9)	46 (3.4)	<0.001
Oral nitrates	995 (35)	633 (42)	362 (26)	<0.001
CCBs	578 (20)	300 (20)	278 (20)	0.848
Discharged medications (N=3681)†				
Aspirin	3559 (97)	1682 (96)	1877 (97)	0.028
Clopidogrel	2698 (73)	1146 (65)	1552 (80)	<0.001
ACEIs	2475 (67)	1189 (68%)	1286 (67)	0.439
ARBs	558 (15)	269 (15)	289 (15)	0.758
Beta blockers	3123 (85)	1426 (81)	1697 (88)	<0.001
Statins	3568 (97)	1699 (97)	1869 (97)	0.951
Other LLDs	87 (2.4)	32 (1.8)	55 (2.9)	0.041
Oral nitrates	2212 (60)	1197 (68)	1015 (53)	<0.001
CCBs	570 (15)	289 (17)	281 (15)	0.108
Dual antiplatelets	3623 (98)	1726 (99)	1897 (98)	0.670
Five-drug regimen	1922 (52)	784 (45)	1138 (59)	<0.001

Percentages might not add up to 100% due to rounding off.

Dualantiplatelets, aspirin and clopidogrel concurrently; five drug regimen, concurrentprescribing of aspirin, clopidogrel, ACEI/ARB, statin, beta blocker.

*In the prior history, 996 patients had missing medications, while during †hospital discharge, 193 patients had missing medications.

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CCB, calcium channel blocker; LLD, lipid lowering drug.

various outcome models (p>0.05 in all the logistic regressions).

DISCUSSION

The present analysis of a large, prospective, multicentre, multinational study from the Arabian Gulf demonstrated that education was associated with significantly lower risk of MACE at 1-year follow-up among patients with ACS. The apparent protective effect of education was consistent across several outcomes including stroke/TIA, recurrent MI, all-cause mortality and readmissions for cardiac reasons. The findings are even more unique given the fact that all patients had free universal access to healthcare unlike in the prior studies, which had varying degrees of access to care.

The association of education with CVD, stroke, MI and CVD risk factors is well known.[5–10] Evidence demonstrates that less educated patients have increased comorbidities,[20] as seen in our study. Furthermore, less educated patients are more likely to experience worse clinical presentation, less likely to receive secondary prevention therapies and attend cardiac rehabilitation.[7 9] Despite patients presenting with a clinical history that portend a poor prognosis, a large Global Utilization of Streptokinase and tPA for Occluded Coronary Arteries III (GUSTO-III) study found that education was independently inversely correlated with 1-year mortality confirming findings from smaller studies.[9] Our study is the first to demonstrate this association in the Arabian Gulf.

Individuals with less education also tend to have increased number of behavioural risk factors like smoking, unhealthy diet and physical inactivity. The Monitoring Project on Risk Factors and Chronic Diseases in the Netherlands (MORGEN) study found that behavioural and biological factors like smoking, obesity, physical inactivity and hypertension explained more than half of the increased risk of CHD among people with low education.[21] Controlling for these risks factors has been found to attenuate but not eliminate the association of education on health and thus calls for further examination of these associations.[11] Addressing

Table 3 Association between education (Edu) and major adverse cardiac events (MACEs) in patients with acute coronary syndrome in the Arabian Gulf: findings from Gulf Coast registry

Outcome	Univariate statistics				Multivariate logistic regression			
	All (N=3874), n (%)	No Edu (n=1835), n (%)	Edu (n=2039), n (%)	P value	Adjusted OR (95% CI)	Adjusted P value	HL	ROC
Stroke/TIA								
12 months	143 (3.7)	105 (5.7)	38 (1.9)	<0.001	0.56 (0.33 to 0.94)	0.030	0.333	0.72
Myocardial infarction								
12 months	282 (7.3)	203 (11.1)	79 (3.9)	<0.001	0.58 (0.38 to 0.86)	0.008	0.264	0.75
All-cause mortality								
12 months	317 (8.2)	236 (12.9)	81 (4.0)	<0.001	0.58 (0.39 to 0.87)	0.009	0.791	0.79
Readmissions for cardiac reasons								
12 months	990 (25.6)	572 (31.2)	418 (20.5)	<0.001	0.61 (0.48 to 0.77)	<0.001	0.613	0.64
MACE								
12 months	1276 (32.9)	783 (42.7)	493 (24.2)	<0.001	0.55 (0.44 to 0.68)	<0.001	0.221	0.69

MACE included stroke/TIA, myocardial infarction, mortality and readmissions for cardiac reasons. For 6-month and 12-month follow-up, the events were cumulative.

Multivariate analyses were conducted using logistic regression models using the simultaneous method. The covariates in the models included GRACE risk score (derived from age, heart rate, systolic blood pressure, serum creatinine, cardiac arrest at admission, ST segment deviation on electrocardiogram (EKG), abnormal cardiac enzymes and Killip class) as well as gender, smoking status, marital status, employment status, body mass index, diabetes mellitus, peripheral artery disease, left ventricular ejection fraction, acute coronary syndrome type and use of evidence-based cardiac medications at hospital discharge (aspirin, clopidogrel, beta blocker, statin, ACE inhibitor (ACEI) or angiotensin receptor blocker (ARB)).

Over the 1-year follow-up period, a total of 20 patients (0.5%) were lost to follow-up.

HL, Hosmer-Lemeshow p value; ROC, area under the receiver operating curve (also known as c-statistic); TIA, transient ischaemic attack.

these risks remains critical for primary and secondary prevention.

Our findings indicate that a significantly higher proportion of educated patients were prescribed the recommended five-drug regimen compared with their uneducated counterparts. Although all patients were provided free healthcare including medications in the Arabian Gulf, this inequity in prescribing practice is concerning and may explain, in part, the poorer outcomes for less educated groups. Studies have shown that people with lower socioeconomic levels receive inferior treatment.[20] For example, a retrospective study in Taiwan found that low-income coronary artery bypass surgery was associated with poorer quality of services.[22] Further research is needed to better understand the observed inequality in prescribing practices in the Arabian Gulf.

Finally, health literacy, which is strongly correlated with education, may explain the education-associated differences in the observed cardiovascular outcomes.[20] Poor health literacy is associated with increased risk behaviours (ie, physical inactivity and unhealthy diet),[23] decreased medications adherence[24] and health interventions[25 26] and poor outcomes.[20] In their study on health literacy in Danish individuals with CVD, Aaby et al[23] found significant positive associations between health literacy and physical activity, healthier diet and higher self-reported health status. A prospective study of patients with heart failure in the USA reported that low health literacy was associated with increased risk of hospitalisation and mortality.[26] A nurse-coordinated intervention carried out in the Netherlands for patients with CAD appears to be effective among patients with poor health literacy. It involved four patient visits with a trained nurse focusing on promoting healthy lifestyles, managing biometric risk factors and increasing medication adherence and resulted in similar reductions in CVD risk profiles regardless of level of health literacy.[27] This promising initiative could be adapted and tested for patients with CVD in the Arabian Gulf; this is particularly important since nearly half of the patients are illiterate.

Our study has limitations. First, due to the inherent nature of uncontrolled observational study design, its ability to assess causal relationships is limited. Second, the analysis relies only on patients admitted to the hospital with a diagnosis of ACS and hence cannot be generalised to the entire population of patients with ACS that do not end up being hospitalised. Third, the study also only analysed those patients with ACS who survived following an ACS event. Fourth, the utilisation of the five-drug regimen did not take into account the contraindications and/or side effects of any of the components of this combination. Fifth, we reported all-cause 12 month mortality where, if data were available, cardiovascular mortality would have been more pertinent.

CONCLUSIONS

To our knowledge, this is the first study from the Arabian Gulf region to demonstrate that any formal patient education was less likely to be associated with 12 months

cumulative stroke/TIA, MI, all-cause mortality, readmissions for cardiac reasons and overall MACE in ACS patients compared with no education. Since a high proportion of patients with ACS have limited, if any education, interventions that promote healthy lifestyles and management of risk factors for this group are urgently required.

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