Socioeconomic Factors and Severity of Coronary Artery Disease in Patients Undergoing Coronary Angiography: A Multicentre Study of Arabian Gulf States

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Abstract:

Coronary artery disease (CAD) is a leading cause of death worldwide. The association of socioeconomic status with CAD is supported by numerous epidemiological studies. Whether such factors also impact the number of diseased coronary vessels and its severity is not well established.

Introduction:

Coronary artery disease (CAD) is a leading cause of death worldwide. The association of socioeconomic status with CAD is supported by numerous epidemiological studies. Whether such factors also impact the number of diseased coronary vessels and its severity is not well established.

Materials and Methods:

We conducted a prospective multicentre, multi-ethnic, cross sectional observational study of consecutive patients undergoing coronary angiography (CAG) at 5 hospitals in the Kingdom of Saudi Arabia and the United Arab Emirates. Baseline demographics, socioeconomic, and clinical variables were collected for all patients. Significant CAD was defined as ≥70% luminal stenosis in a major epicardial vessel. Left main disease (LMD) was defined as ≥50% stenosis in the left main coronary artery. Multi-vessel disease (MVD) was defined as having ≥1 significant CAD.

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Results:
Of 1,068 patients (age 59 ± 13, female 28%, diabetes 56%, hypertension 60%, history of CAD 43%), 792 (74%) were from urban and remainder (26%) from rural communities. Patients from rural centres were older (61 ± 12 vs 58 ± 13), and more likely to have a history of diabetes (63 vs 54%), hypertension (74 vs 55%), dyslipidaemia (78 vs 59%), CAD (50 vs 41%) and percutaneous coronary intervention (PCI) (27 vs 21%). The two groups differed significantly in terms of income level, employment status and indication for angiography. After adjusting for baseline differences, patients living in a rural area were more likely to have significant CAD (adjusted OR 2.40 [1.47, 3.97]), MVD (adjusted OR 1.76 [1.18, 2.63]) and LMD (adjusted OR 1.71 [1.04, 2.82]). Higher income was also associated with a higher risk for significant CAD (adjusted OR 6.97 [2.30, 21.09]) and MVD (adjusted OR 2.49 [1.11, 5.56]), while unemployment was associated with a higher risk of significant CAD (adjusted OR 2.21, [1.27, 3.85]).

Conclusion:
Communal and socioeconomic factors are associated with higher odds of significant CAD and MVD in the group of patients referred for CAG. The underpinnings of these associations (e.g. pathophysiologic factors, access to care, and system-wide determinants of quality) require further study.

Keywords: Arabian Gulf, Cross sectional study, Coronary artery disease, Coronary angiography, Cardiac epidemiology, CAD.

INTRODUCTION
CAD is the leading cause of death globally and in the Middle East [1, 2]. Development of CAD has been attributed to known modifiable risk factors [3]. Other factors such as physiological, psychological, emotional, social, and stress both acute and chronic have been studied [4 - 22]. Acute and chronic psychological stressors increase haemostatic factors and acute phase proteins, leading to CAD [23]. In addition, the interaction between risk factors has consequences [24].

The association between socioeconomic factors and CAD has been supported by numerous epidemiological studies [25 - 31]. Since the mid-1970s, the rate of major cardiovascular disease (CVD) and death has shifted from high-income to low-income countries [32 - 36]. In addition, rural rather than urban communities from low-income countries have a higher rate of major CVD and death, whereas no such difference was found in high-income countries [36]. Despite the fact that the risk factor burden was lower in low-income countries compared with high-income countries, the rates of major CVD and death were higher in the low-income countries [36]. This difference may be due to the presence of socioeconomic inequalities in access to treatment for CAD [37]. It is expected by 2020 that >80% of CVD will occur in low-income countries [38].

Therefore, we conducted a study examining the association between urbanization, income level, education and employment status with severity of CAD in the group of patients undergoing CAG for clinical indications in two Arabian Gulf regions.

MATERIALS AND METHODS

Study Population
The details regarding the design, methods, and endpoints of this multicentre, observational study came from the Polygamy and Risk of Coronary Artery Disease in Men Undergoing Angiography [39]. In the current study the data were collected prospectively from five hospitals in two Arabian Gulf regions (The Kingdom of Saudi Arabia and The United Arab Emirates), during the period April 1, 2013 to March 30, 2014. Two separate data forms (general and angiographic) were completed by the assigned physician. Both forms were completed before the patients were discharged from hospital. All data forms were reviewed by the respective cardiologist, then sent online to the principal investigator, who also checked the forms before submission for analysis. The study was approved by King Faisal Specialist Hospital and Research Center Institutional Review Board, and an invitation letter was given to all participants who affirmed verbal consent prior to their enrolment. All patients undergoing CAG were recruited; none refused to participate. There were no exclusion criteria.

Contents of Personal Data Form
Data were collected on demographics (age, ethnic background), physiological status (hypertension, diabetes, dyslipidaemia, BMI), life style (smoking history), past medical history (CAD, PCI, coronary artery bypass graft
Socioeconomic Factors and Severity of Coronary (CABG), cerebral vascular disease, peripheral arterial disease, congestive heart failure, atrial fibrillation and chronic kidney disease), and urban vs rural residence. Rural residence was defined by national statistical offices in Saudi Arabia and was last measured on 17.07.2014, according to the World Bank [40]. It was calculated as the difference between total population and urban population. Socioeconomic data included occupation (unemployed, private sector, government sector, self-employed), highest level of education completed (illiterate, secondary school, undergraduate, masters, PhD), and monthly income (<1300, 1300 to 2600, 2600 to 5300, 5300 to 7900, 7900 to 10600, >10600 US Dollars).

Contents of Angiographic Data Form

Data collected included; reason for coronary angiography (elective vs urgent/emergent), number of vessels involved (severity), and treatment (medical vs revascularization).

Definitions

Significant CAD was defined as ≥70% luminal stenosis in a major epicardial vessel. LMD was defined as ≥50% stenosis in the left main coronary artery. MVD was defined as having ≥1 coronary artery with significant disease. Non-ST-segment-elevation acute coronary syndrome (NSTEACS) includes non-ST-segment-elevation myocardial infarction (NSTEMI) and unstable angina.

Statistical Analysis

Continuous variables are summarized using means and standard deviations, and compared with the Student’s t-test. Categorical variables are summarized using percentages and compared with the Chi-square test. The associations between urbanization and other socioeconomic factors such as income, employment, education level and severity of CAD, MVD and LMD were assessed using logistic regression models and quantified with odds ratios. Adjusted regression models included the following explanatory variables: age, gender, baseline risk factors, past history of CAD/PCI or CABG, ethnicity, marital status, and indication for angiography (elective vs urgent/emergent). All statistical tests were two-sided and significance was set at the conventional 0.05. No adjustments for multiple comparisons were made.

RESULTS

Descriptive

Overall characteristics of patients and coronary angiogram findings are shown in (Table 1). A detailed description can be found in Polygamy and Risk of Coronary Artery Disease in Men Undergoing Angiography [39].

Table (1) shows the patients characteristics stratified by urbanization and other socioeconomic factors. We enrolled 1,068 patients, 792 (74%) were from urban areas, and 276 (26%) from rural areas. Patients from rural areas were older (61 ± 12 vs 58 ± 13), and more likely to have a history of diabetes (63 vs 54%), hypertension (74 vs 55%), dyslipidaemia (78 vs 59%), CAD (50 vs 41%), and PCI (27 vs 21%). The two groups did not differ significantly in terms of smoking, cerebral vascular disease, chronic kidney disease, peripheral arterial disease, atrial fibrillation, or history of depression. The indications for CAG differed significantly between the two groups. Of the rural population, 59% had CAG for non-urgent/emergent indication as opposed to 44% of the urban population, p <0.0001. Both groups did not differ when compared according to the number of vessel involved during CAG; overall, 67% of the urban population and 72% of the rural population had CAD. The presence of single or multi-vessel CAD in both populations not differ significantly. Presence of LM disease was higher in rural population compared with the urban population (16 vs 10%), p=0.0065. Types of intervention differed significantly between the two groups. Of the urban population, 38% received medical therapy compared with 33% of the rural population. However, 48% of the rural population had PCI as compared with 43% of the urban population, p<0.0001.

Multivariate logistic analysis was used to adjust data for baseline differences and characterize the odds of significant CAD, MVD, and LMD as it relates with the socio-economic factors under study. Tables (2-4) summarize the results of this regression analysis for significant CAD, MVD and LMD, respectively. Patients living in a rural area were more likely to have significant CAD (OR 2.40 [1.47, 3.97]), MVD (OR 1.76 [1.18, 2.63]) and LMD (OR 1.71 [1.04, 2.82]). Higher income was also associated with higher odds for significant CAD (OR 6.97 [2.30, 21.09]) and MVD (OR 2.49
while unemployment was associated with a higher risk of significant CAD (OR 2.21 [1.27, 3.85]). There was no clear association between significant CAD and level of education.

**DISCUSSION**

The association between socioeconomic factors and CAD has been demonstrated by many epidemiological studies of both developed and developing countries [25 - 31]. O’Connor et al. examined the rural-urban differences in the prevalence of CAD in >214,000 respondents using data from the US Centers for Disease Control and Prevention’s (CDC’s) 2008 Behavioral Risk Factor Surveillance System. They found a higher prevalence of CAD in rural populations [41]. In another study, rural rather than urban communities from low-income countries have a higher rate of major CVD and death whereas no such difference was found between rural and urban communities in high-income countries [36]. Our study reported a higher risk of significant CAD (OR 2.40), MVD (OR 1.76) and LMD (OR 1.71) in those living in a rural area compared with those living in urban area. This could be attributed to the delay in seeking health care, even when experiencing symptoms of a suspected heart attack [42] or due to poor access to medical facilities and regular screening programs in these areas [43 - 45].

The rate of CVD during the period from the 1930s to the 1950s was low in low-income countries and high in high-income countries [32, 33]. Since the mid-1970s the rate of CVD has declined in several high-income countries, owing to reductions in risk factors and better management of CVD [34]. In contrast, the rate of CVD increased in some low-income countries [46, 47] with 80% of the global burden estimated to occur in these countries [38]. This may be due to the presence of socioeconomic inequalities in access to treatment for CAD. Patients with low socioeconomic status are less frequently referred for CAG and subsequent management (i.e. revascularization and secondary prevention) [37]. In addition, there is a delay in hospital presentation after onset of symptoms of acute myocardial infarction [48]. However, our study demonstrated a link between higher income and higher odds for significant CAD (OR 6.97) and MVD (OR 2.49). We speculate that this finding could be explained by poor lifestyle (physical inactivity and a sedentary lifestyle, unhealthy dietary intake, tobacco use both smoking and non-smoking, and second hand tobacco smoke) [49 - 51] and the higher stressful events related to work and daily activities that individuals with higher income living in the Gulf region exhibit. Previous studies among men linking stress-related health risks with substantial losses in income and wealth [52, 53] help support our speculation. Based on our study, we believe further investigation is required to understand the effect of income and wealth on CAD and to evaluate the underlying mechanisms that lead to its effects.
Table 2. Multivariate logistic regressions [adjusting for age, gender, baseline risk factors, past history of CAD/PCI or CABG, ethnicity, marital status, and indication for CAG (elective vs urgent/emergent)] calculating odd of any coronary artery disease.

|                          | Adjusted | 95% Confidence       | P    |
|--------------------------|----------|----------------------|------|
|                          | Odds Ratio | Limits               |      |
| Rural vs Urban           | 2.4      | [1.47, 3.97]         | 0.0005|
| Income > $5300 vs $1300  | 6.97     | [2.3, 21.09]         | 0.0007|
| Job                      |          |                      | 0.0029|
| Self-employed vs Unemployed | 0.24   | [0.10, 0.55]         |      |
| Government vs Unemployed  | 0.49     | [0.27, 0.91]         |      |
| Private sector vs Unemployed | 0.87   | [0.37, 2.04]         |      |
| Education                |          |                      | 0.1141|
| PhD vs Illiterate        | 0.52     | [0.06, 4.31]         |      |
| Master vs Illiterate     | 0.21     | [0.06, 0.75]         |      |
| Undergraduate vs Illiterate | 0.94  | [0.46, 1.90]         |      |
| Secondary school vs Illiterate | 0.68 | [0.40, 1.14]         |      |
### Table 3. Multivariate logistic regressions [adjusting for age, gender, baseline risk factors, past history of CAD/PCI or CABG, ethnicity, marital status, and indication for CAG (elective vs urgent/emergent)] calculating odds of multi-vessel disease.

|                          | Adjusted | 95% Confidence Limits | p     |
|--------------------------|----------|------------------------|-------|
|                          | Odds Ratio |                       |       |
| Rural vs Urban           | 1.76     | [1.18, 2.63]           | 0.0058|
| Income > $5300 vs ≤ $1300| 2.49     | [1.11, 5.56]           | 0.0015|
| Job                      |          |                        | 0.5159|
| Self-employed vs Unemployed | 0.67    | [0.39, 1.16]           |       |
| Government vs Unemployed  | 0.79     | [0.49, 1.26]           |       |
| Private sector vs Unemployed | 0.87    | [0.48, 1.59]           |       |
| Education                |          |                        | 0.086 |
| PhD vs Illiterate        | 1.79     | [0.32, 10.05]          |       |
| Master vs Illiterate     | 0.36     | [0.13, 1.03]           |       |
| Undergraduate vs Illiterate | 1.13    | [0.65, 1.98]           |       |
| Secondary school vs Illiterate | 0.72   | [0.50, 1.05]           |       |

### Table 4. Multivariate logistic regressions [adjusting for age, gender, baseline risk factors, past history of CAD/PCI or CABG, ethnicity, marital status, and indication for CAG (elective vs urgent/emergent)] calculating odds of left main disease.

|                          | Adjusted | 95% Confidence Limits | p     |
|--------------------------|----------|------------------------|-------|
|                          | Odds Ratio |                       |       |
| Rural vs Urban           | 1.71     | [1.04, 2.82]           | 0.0355|
| Income > $5300 vs ≤ $1300| 0.57     | [0.20, 1.61]           | 0.4311|
| Job                      |          |                        | 0.3886|
| Self-employed vs Unemployed | 1.14    | [0.51, 2.53]           |       |
| Government vs Unemployed  | 1.02     | [0.55, 1.90]           |       |
| Private sector vs Unemployed | 1.95    | [0.86, 4.42]           |       |
| Education                |          |                        | 0.6484|
| PhD vs Illiterate        | 1.63     | [0.25, 10.65]          |       |
| Master vs Illiterate     | 0.28     | [0.04, 2.25]           |       |
| Undergraduate vs Illiterate | 0.91    | [0.43, 1.32]           |       |
| Secondary school vs Illiterate | 0.79   | [0.47, 1.32]           |       |

Our study demonstrated a higher risk of CAD (OR 2.21) associated with unemployment, which is in agreement with previous studies [54 - 57]. Socioeconomic factors also seem to be implicated in the relationship between education and cardiac health [58, 59]. Recently, the US National Bureau of Economic Research stated that each additional 4 years of education lowered all-cause mortality by almost 1.8% and reduced the risk of heart disease by 2.2% [60]. However, our current study failed to show the association between education level and risk of CAD, and this could be explained by similar distribution of education levels in the rural and urban population, and the large number of illiterate people in our study population.

It has been suggested that socioeconomic factors exert their impact on the heart through affecting the central nervous system, increasing output from the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis. Chronic stimulation from these outputs can induce a wide variety of pathophysiologic responses, including inflammation and platelet activation [11, 61 - 63]. They may also affect health related behaviours such as smoking, diet, alcohol consumption and physical activity, and affect access to health care which might be affected by social support [64]. Further study is required to understand the underlying mechanisms that lead to the association of high income in the gulf region with higher CAD risk. This might suggest that the well-accepted socioeconomic-CAD gradient might not be applicable to all regions of the world. Such differences in risk factors between different ethnicities are not uncommon and have been seen for instance in the South Asian and African population in the UK [65 - 67]. Another possible explanation of such differences might be attributed to the way socioeconomic status was taken into account. It is important for the health care providers when discussing traditional risk factors, to incorporate discussion of different aspect of socioeconomic factor management as part of the overall cardiovascular health [11, 30].
Study Strengths

This study is the first to look at the association between socioeconomic factors and severity of CAD in the group of patients referred for CAG for clinical indications in two gulf regions.

Study Limitations

First, it is surprising that almost half the cohort were illiterate and approximately 90% had a low monthly income: this is likely due to a small sample size and referral bias. One possible explanation is the nature of the enrolled hospitals, which tend to receive referrals from poorer areas. Second, the time interval from the socioeconomic factors to the cardiac catheterization was not recorded; this interval may have influenced the findings. Third, our study population was selected to undergo CAG if clinically indicated, and as such, cannot be generalized to all the population in the Gulf Region. Fourth, we relied on self-reporting history of depression, without using a formal objective screening tool, thus the incidence of depression in our cohort may not be accurate. Fifth, we did not look at unmeasured confounding variables such as dietary habits, physical activity, inflammatory markers, and other unconsidered variables. Chronic stress was found to reduce the levels of leptin receptors [68] and increase levels of peripheral neuropeptide Y [69] which might change dietary habit and lead to consumption of high fat diet and increase risk of CAD. Several studies also indicate that the stress impedes individual efforts to be more physically active, increasing risk of CAD [70]. Stress has been associated with higher levels of inflammatory markers such as C-reactive protein (CRP), TNF-α [71 - 73] and pro-inflammatory cytokines [72], which contribute to increased risk of CAD. Six, we did not obtain information specifically regarding retirement or those receiving industrial injury benefit in defining employment status.

CONCLUSION

Communal and socioeconomic factors are associated with severity of CAD and MVD in the group of patients referred for CAG for clinical indications in two gulf regions. The well-accepted socioeconomic-CAD gradient might not be applicable to all regions of the world. We suggest that the interpretation of socioeconomic status should take in account the differences in risk factors between different ethnicities and the difference of cultural life style in individuals from the same socioeconomic status. The underpinnings of these associations (e.g. pathophysiologic factors, access to care, and system-wide determinants of quality) require further study.

LIST OF ABBREVIATIONS

| Abbreviation | Definition                      |
|--------------|---------------------------------|
| BMI          | Body Mass Index                 |
| CAD          | Coronary Artery Disease         |
| PCI          | Percutaneous Coronary Intervention |
| CABG         | Coronary artery bypass grafting |
| CHF          | Congestive Heart failure        |
| CVA          | Cerebrovascular accident        |
| CKD          | Chronic Kidney Disease          |
| PAD          | Peripheral Arterial disease     |
| $            | USA Dollars                     |
| PhD          | A Doctor of Philosophy          |
| STEMI        | ST Segment Elevation Myocardial Infarction |
| NSTEACS      | Non–ST-Segment Elevation Acute Coronary Syndromes |
| CAG          | Coronary Angiography            |

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None.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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