Coronary artery disease in Saudi Arabia

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ABSTRACT

Objectives: Coronary artery disease (CAD) is a major public health problem worldwide. To our knowledge, there is no national data available from community based studies on prevalence of CAD in the Kingdom of Saudi Arabia (KSA). Therefore, we designed this study with the objective to determine the prevalence of CAD among Saudis of both sexes, between the ages of 30-70-years in rural as well as urban communities. Further, to determine the prevalence and clinical pattern of the major modifiable risk factors for CAD among the same population. This work is part of a major national study on CAD in Saudis Study (CADISS).

Methods: This is a community based study conducted by examining subjects in the age group of 30-70-years of selected households during 5-year period between 1995 and 2000 in KSA. Data were obtained from history using a validated questionnaire, and electrocardiography. The data were analyzed to provide prevalence of CAD and risk assessment model.

Results: Nine hundred and forty-four subjects, out of 17232 were diagnosed to have CAD. Thus, the overall prevalence of CAD obtained from this study is 5.5% in KSA. The prevalence in males and females were 6.6% and 4.4% ($P<0.0001$). Urban Saudis have a higher prevalence of 6.2% compared to rural Saudis of 4% ($P<0.0001$). The following variables are found to be statistically significant risk factors in KSA: age, male gender, body mass index (BMI), hypertension, current smoking, fasting blood glucose, fasting cholesterol and triglycerides.

Conclusions: The overall prevalence of CAD in KSA is 5.5%. A national prevention program at community level as well as high risk groups should be implemented sooner to prevent the expected epidemic of CAD that we are seeing, beginning. Measures are needed to change lifestyle and to address the management of the metabolic syndrome, to reduce modifiable risk factors for CAD. A longitudinal study is needed to demonstrate the importance of reducing modifiable risk factors for CAD in KSA.

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Coronary artery disease (CAD) is a major public health problem in industrialized nations.[1] In the United States of America (USA), for example, CAD is the leading cause of death in adults, accounting for approximately one-third of all deaths in subjects over the age of 35-years.[2] Hence, emphasis on its primary as well as secondary prevention was given great attention by health authorities in western countries. While age adjusted mortality from CAD is gradually falling in developed countries, it is set to become an epidemic in developing countries, and over the next 20-years will probably become the

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most important global health problem.[3] As more developing countries adopt similar lifestyles to the west that result in increasing overweight and obesity, tobacco use, along with the rapid increase in diabetes that is occurring in aging population, it would be expected that their CAD patterns parallel that of the industrialized nations. In the Kingdom of Saudi Arabia (KSA), the information on CAD prevalence is very scratchy. Only few limited scaled, hospital based studies are published.[4,5] Currently, no data are available in KSA, obtained from community based studies, on the prevalence of CAD. However, one hospital-based study showed that the leading cause of admission to major hospitals was due to CAD.[5] Therefore, to our knowledge, no published data exist on the precise magnitude of the prevalence of CAD in KSA. As this nation benefits from its thriving economy, changes in lifestyle conducive to enhanced atherosclerosis are inevitable. Therefore, a project was designed to study the problem of CAD and its related risk factors in a comprehensive and encompassing fashion at the national level. It was divided into 3 different sub-projects: community based study, hospital based study, and metabolic basis of CAD. The objectives of community based study were: to determine the prevalence of CAD among Saudis of both sexes, between the ages of 30-70-years in rural as well as urban communities. Further, to determine the prevalence and clinical pattern of the major modifiable risk factors for CAD among the same population. These include: obesity, hypertension, diabetes mellitus, hypercholesterolemia and smoking.

This article reports the prevalence of CAD among Saudis, categorized by gender, area of residence and age group; and shows the mean and percentage values of known risk factors among patients with CAD and those without CAD. Furthermore, a risk assessment model is developed with statistically significant risk factors.

Methods. The Kingdom of Saudi Arabia encompasses approximately four-fifths of the Arabian Peninsula has inhabitants of 20.8,000.000 people with 15.6,000,000 of local population (Saudis).[6] A 5-year National Epidemiological Health Survey regarding CAD was conducted between 1995 and 2000. Male and female Saudi adults aged (30-70-years), in rural and urban areas of KSA formed the target population for this study. For the purpose of the study, a Saudi is identified as a person holding (or a dependent of a holder) of a Saudi Nationality Identification Card (SNIC). Most previous studies on CAD from other part of the world focused on similar population that allows for inter countries comparison. A sample size of 20,000 participants was the target of the study to ensure a high reliability of our estimates of the prevalence of CAD. The subjects were selected using a 2 stage, stratified cluster sampling procedure, urban and rural areas being the stratifying factors. For practical and logistic reasons, the study population was drawn from the local primary health care centers'catchments areas. The catchments population of each primary care center was taken as a cluster. The KSA is subdivided into 14 administrative regions and samples were selected from each region. The first stage sampling units were 1,623 primary health centers (PHC) uniformly distributed in KSA. Since the establishment of the primary health centers was dictated by the population in each region, the allocation of the required number of PHCS were made proportional to be the number of PHCS in each region. Then, each region was stratified into urban and rural communities and a simple random sample of PHCS was selected. The number of PHCS to be selected from each community was based on the total number of PHCS in each rural and urban community. A total of 66 PHCS were selected from urban and 58 from rural areas. Then block (blocks) was randomly selected from the catchments areas of each selected primary care center and used as cluster. One hundred households from urban PHCS and 50 households from rural PHCS were selected from these blocks. All subjects (males and females) of age group of 30-70-years of selected households were interviewed and examined. The study protocol consisted of interviews, clinical examinations, laboratory tests, Electrocardiograms (ECGs), and measurements. The questionnaire used, included basic demographic and socio-economic data, a detailed history of CAD and its risk factors. Well trained primary care physicians were responsible for filling the questionnaire. This has been shown to increase the yield of positives for angina and history of possible myocardial infarction (MI).[7,8] A person was defined as having anginal chest pain of ischemia if the chest pain was typical in character, occurred on effort (exertional) and relieved by rest or sublingual nitroglycerin, therefore, fulfilling all world health organization (WHO) criteria.[9] The questionnaire was developed, pre-tested, and validated in a pilot study. A complete physical examination was conducted at the primary health care center, included height, weight, BP, waist and hip circumferences as well as signs of hyperlipidemia. Laboratory data included a fasting blood sample for glucose (FBG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL). Also, a 12 leads electrocardiographic tracing was carried out for every participant. Trained primary care physicians, using mercury sphygmomanometers to the nearest 2 mm, measured blood pressure of the subjects. Participants were seated, and the right arm

was placed on the tabletop; the appropriate cuff size was used. For systolic blood pressure, the first Korotkoff sound (K1) was used defined as appearance of 2 consecutive beats. For diastolic blood pressure, the fifth Korotkoff sound (K5) was used defined as the last beat before disappearance of the sound. Two blood pressure measurements were taken with 30 seconds rest in between. The 2 readings were averaged. Weight was measured with ordinary scales with indoor clothing on without shoes on to the nearest 0.1 kg. Height, waist and hip measurements were carried out to the nearest mm by using measuring tape. Trained technicians, under the supervision of primary care physicians, collected a 20 cc of fasting blood (12 hour fasting), in 2 tubes of 10 cc each. Tubes were immediately kept in refrigerator for at least 30 minutes and no more than 4 hours before centrifugation. Centrifugation was carried out for 30 minutes at 3000 RPM in refrigerated centrifuger at 4°C. Plasma and serum were separated and were frozen at -20°C immediately. These samples were transported frozen in ice to the coordinating laboratory in the region where they were kept frozen at -20°C. At the end of the sample collection from all participants in the region, it was transferred frozen in ice in incubators to the central laboratory at the College of Science, King Saud University, Riyadh. All biochemical parameters were analyzed on a clinical analysis (Konelab, Intelligent Diagnostics system, Helsinki, Finland). The instrument was calibrated prior to analysis using quality control samples provided with the solutions. Standard International Units (mmol/L) was used to record the results. The intra and inter assay coefficients of variation were 0.3% and 0.4%. Electrocardiograms tracings were carried out at the primary care centers by primary care physicians or trained technicians and were interpreted by 2 independent cardiologists from the investigator team according to the Minnesota Code.[10] The diagnosis of previous MI was based on WHO MONICA Project (monitoring trends and determinants in cardiovascular disease).[11] In case of difference in readings between them, a third cardiologist opinion was sought. The number of patients who were diagnosed to have CAD was established in finding of one or more of the following criteria: either physician's clinical assessment of the chest pain as anginal, previous MI, or findings of evidence of previous MI by ECG.

The data were analyzed using the Statistical Package for Social Sciences (Version 10.0) on PC. Both univariate and multivariate analysis were carried out. The frequency distribution tables of the variables measured in various age groups, gender, rural, and urban areas are presented. The estimate of CAD prevalence rate is calculated for the total sample, and sub-groups of gender, area of residence and age groups. A risk assessment model is developed using logistic regression.

Results. Nine hundred and forty-four subjects (944), out of 17232 were diagnosed to have CAD. Thus, the prevalence of CAD obtained from this study is 5.5%. **Table 1** shows the prevalence of angina and MI used to determine the prevalence of CAD. The prevalence was categorized into 2 main groups: prevalence by history and ECG defined MI. Prevalence by history shows that 4.9% of the subjects has reported anginal chest pain and 0.4% gave history consistent with previous MI. Male subjects have reported significantly more cases of MI than female subjects (p=0.027). The prevalence of MI diagnosed by ECG was 1.1%. Male subjects had significantly higher MI than female subjects (p <0.0001). A total of 5.5% of the subjects were diagnosed to have CAD. The prevalence of CAD in males and females were 6.6% and 4.4%, and it was statistically different (p<0.0001). The age adjusted prevalence of CAD according to Saudi population during the year 2000 was 5.9% and 4.4%, for males and females and 5.1% as aggregate. **Table 2** discusses the prevalence of CAD by residence (urban/rural) and age groups. The prevalence was 6.2% in urban areas, and 4% in rural areas. This difference was statistically significant (P<0.00001). The prevalence was in increasing order from youngest to eldest groups when considering the ages of the subjects. These percentages are statistically different from each other (P<0.00001). The overall percent prevalence of different risk factors for CAD in KSA is shown in **Table 3**. These risk factors will be discussed in detail in subsequent publications. **Table 4** shows the descriptive statistics and significance differences of demographic variables and risk factors for the patients with CAD and without CAD. The prevalence of CAD increases with ageing (p<0.0001). Male gender showed more risk to have CAD than female (p< 0.00001). The body mass index (BMI) of patient with CAD had higher values than patients without CAD (p=0.013). Patients with CAD showed wider waist circumference than patients without CAD (p< 0.0001). Waist-height ratio was statistically greater in patients with CAD (p=0.006). Systolic and diastolic blood pressures (BP) were significantly higher in patients with CAD than without those of CAD (p <0.0001). The percentage of smokers and ex-smokers (quit smoking at least one year) were significantly higher in subjects with CAD category than the subjects without CAD (p=0.001). Mean fasting blood sugar and serum TG level were significantly higher in subjects with CAD than without CAD (p<0.0001). Mean TC level was also significantly higher in subjects with CAD (p=0.034). Mean high density

lipoprotein-cholesterol (HDL-C) values were statistically lower in subjects with CAD as compared to subject without CAD (p=0.024). Mean low-density lipoprotein (LDL-C) values were almost the same in both with CAD and without CAD groups (p=0.853).

A risk assessment model was developed by loading CAD as dependent variable and all statistically significant risk factors as independent variables, namely age, gender, BMI, waist circumference, waist-height ratio, systolic BP, diastolic BP, ex-smokers, current smokers, fasting blood sugar, fasting TG, fasting serum cholesterol and HDL-C, in bivariate logistic regression analysis. **Table 5** shows the final model developed by logistic regression using 'likelihood forward method'. Seven factors, namely age (OR: 1.02, p<0.0001), gender (OR: 0.770, p<0.0001), BMI (OR: 1.015, p=0.014), systolic BP (OR: 1.009, p<0.0001), current smokers (OR:0. 797, p=0.017), fasting blood sugar (OR: 1.020, p=0.027) and fasting TG (OR: 1.082, p=0.001), had combined significant relationship with CAD.

Discussion. Community based epidemiological data provide a real assessment of CAD as it is less encumbered by selection bias observed in clinical studies. The data presented in this study report 5.5% overall prevalence of CAD in KSA. The diagnosis of CAD is determined by history of angina, MI, or by documented evidence based on ECG interpretation of previous MI according to Minnesota code. Therefore, avoiding underestimation due to silent ischemia, which is thought to account for up to 75% of all ischemic episodes.[12-15] The results of our study show prevalence of CAD in males of 6.6% and in females of 4.4%, a lower prevalence than reported figures from Asian Indians (11%), Americans (6.9%), however, higher than Chinese (2%) and Europeans (5%).[16-23] Nonetheless, it is expected to observe a dramatic increase in the prevalence of CAD in KSA over the coming 2 decades due to increasing prevalence of risk factors, increasing aging population as better heath care is provided and change to western lifestyle.

Our data demonstrate an increasing prevalence of CAD with age ranging from 3.9% at ages 30-39 years to 4.6% at 40-49-years, 6.3% at 50-59-years, and 9.3% at 60-70-years (p<0.0001). These results are concurring with the reported increasing prevalence of CAD with age in the USA as estimates for men are from 7% at ages 40-49-years to 13% at 50-59-years, 16% at 60-69-years, and 22% at 70-79-years. The corresponding estimates for women are substantially lower than for men: 5, 8, 11, and 14%.[24] Among Indians, an ethnic population with high existing rate of CAD, the

Table 1 - Prevalence of angina, MI and total CAD.

Prevalence	Male n	(%)	Female n	(%)	p value	Total n	(%)
History							
Prevalence of angina	401	(4.9)	440	(4.8)	0.760	**841**	**(4.9)**
Prevalence of previous MI	42	(0.5)	27	(0.3)	0.027	**69**	**(0.4)**
ECG							
Prevalence of previous MI	113	(1.4)	74	(0.8)	<0.0001	**187**	**(1.1)**
Total CAD prevalence	542	(6.6)	4.2	(4.4)	<0.0001	**944**	**(5.5)**
Age adjusted CAD prevalence*		(5.9)		(4.4)			**(5.1)**

* CAD was adjusted on year 1420H (2000G) saudi population
MI - myocardial infarction, CAD - coronary artery disease
ECG - electrocardiogram

Table 2 - Prevalence of CAD by area of residence and age group.

Area	Sample	CAD prevalence		Age group	Sample	CAD prevalence	
Urban	11707	722	(6.2)	30-39	5877	232	(3.9)
Rural	5525	222	(4)	40-49	4858	222	(4.6)
				50-59	3479	220	(6.3)
				60-70	2918	270	(9.3)
p value <0.0001				p value <0.0001			

CAD - coronary artery disease

Table 3 - Prevalence of risk factors for CAD in KSA.

Risk factor	Prevalence
Diabetes mellitus (FBG ≥ 7.0 mmol/l)	23.7%
Hypertension (BP ≥ 140/90)	26%
Current smoking	12.8%
Hypercholesterolemia (TC ≥ 5.2 mmol/l)	53.9%
Hypertriglyceridemia (Trig ≥ 1.7 mmol/l)	39.9%
Obesity (BMI ≥30)	35.6%

FBG - fasting blood glucose, BP - blood pressure
TC - fasting total cholesterol
Trig - fasting trglycerides, BMI - body mass index

prevalence of CAD has been affected by migration to western countries, and the reported figures on prevalence of CAD in urban or migrant Indians range from 7-17%.[25-30] Urban Saudis have 6.2% prevalence of CAD, which is significantly higher, as one would expect, than rural Saudis of 4% ($P<0.0001$), a price one pays for a modern lifestyle .

Our study confirms that CAD occurs much more common in diabetics than in the general population, as shown by our results of fasting blood glucose of 7.5 mmol/l in subjects with CAD compared to 6.7 mmol/l for subjects without CAD ($P<0.0001$). The concept of diabetes mellitus being a major risk factor for CAD is in agreement with previous studies.[31-36] The data obtained from our study showed that BMI is found to be significantly higher among patients with CAD compared to subjects without CAD (BMI=29.1 versus 28.5 kg/m^2) ($P=0.01$). It is known that obesity or overweight promotes or aggravates all the atherogenic risk factors predisposing subjects of all ages to coronary events.[37,38] There is current evidence that in patients with established coronary atherosclerosis, BMI is independently associated with acute coronary syndromes, and the risk is increased even at mildly elevated BMI levels.[39] We found the features of the metabolic syndrome correlates well with the clinical and biochemical features of Saudi patients with CAD in this study. It is of paramount importance to recognize the metabolic syndrome with its classical clinical features as part of risk assessment for CAD.[40] The term metabolic syndrome refers to a virulent and lethal group of atherosclerotic risk factors, including dyslipidemia, insulin resistance, obesity, and hypertension. Dyslipidemia in the metabolic syndrome is characterized by hypertriglyceridemia, low HDL cholesterol, in the context of normal or slightly elevated LDL cholesterol. Guidelines from Adult Treatment Panel (ATP) III suggest that the clinical diagnosis of the metabolic syndrome be based upon the presence of any 3 of the following: abdominal obesity, TG >1.7 mmol/L, HDL cholesterol <1 mmol/L in men and <1.3 mmol/L in women, BP >130/85 mm Hg, fasting glucose > 6.1 mmol/L.[41] This syndrome affects some 47,000,000 people in the USA, placing them at increased risk for CAD, and has an estimated age adjusted US prevalence of 23.7%.[42-44] Our data clearly demonstrate a statistically significant correlation of CAD with hypertriglyceridemia, elevated total serum cholesterol, and lower HDL-cholesterol. Furthermore, other classical risk factors such as hypertension and cigarette smoking are shown in this study to be significantly associated with CAD among Saudi patients. Previous studies have shown that elevated serum TC concentration as well as elevated LDL-cholesterol, low HDL cholesterol, increased total to HDL cholesterol ratio, hypertriglyceridemia, hypertension, and smoking are clear risk factors for CAD.[45-54] It is likely, as stated earlier, that the metabolic syndrome, considering its widespread prevalence, plays a significant role in the development of CAD seen in our patients. Therefore, it is evident that management of the metabolic syndrome constitutes a cornerstone measure for the prevention of CAD in KSA. On multivariate regression analysis, the following variables have been shown in our study to have significant association with CAD: age, male gender, BMI, hypertension, current smoking, diabetes mellitus, and hypertriglyceridemia. Clearly, our community, as demonstrated by our findings, is not different than western communities having similar risk factors for CAD. Therefore, we suggest adopting a national program promoting primary prevention of CAD in

Table 4 - Clinical and biochemical characteristic of with and without coronary artery disease subjects.

Parameters	Parameters	Without CAD (n=16288)	*p* value
Age (year)	500±12.27	45.92 ± 11.52	<0.0001
Men n (%)	542 (57.4)	7646 (46.9)	<0.0001
Body mass index (kg/m2)	29.052 ± 6.055	28.570 ± 5.756	0.013
Waist circumference (cm)	94.09 ± 14.83	91.93 ± 14.67	<0.0001
Waist-height ratio	0.5869 ± 9.373	0.5782 ± 9.243	0.006
Systolic BP (mm Hg)	126.39 ± 20.18	78.22 ± 10.37	<0.0001
Diastolic BP (mm Hg)	80.33 ± 11.19	120.88 ± 17.42	<0.0001
Ex smokers n (%)	114 (12.1)	1418 (8.8)	0.001
Current smokers n (%)	153 (16.3)	2012 (8.8)	0.001
Fasting blood surgar (mmol/L)	7.4535 ± 4.1698	6.6841 ± 3.4642	<0.0001
Serum cholesterol (mmol/L)	5.4723 ± 1.6774	5.3516 ± 1.4832	0.034
Serum triglycerides (mmol/L)	2.0906 ± 1.6178	1.8255 ± 1.2688	<0.0001
High density lipoprotein (mmol/L)	0.9168 ± 0.3197	0.9419 ± 0.4222	0.024
Low density lipoprotein (mmol/L)	3.8015 ± 1.3713	3.7923 ± 1.2133	0.853

BP - blood pressure, CAD - coronary artery disease

Table 5 - Logistic regression of determinant of coronary artery disease.

Variables	β	SE	*P* value	Odd ratio
Age	0.020	0.003	<0.0001	1.021
Gender	-0.262	0.075	0.014	0.770
BMI	0.015	0.006	<0.0001	0.015
SBP	0.009	0.002	0.017	1.009
Current smokers	-0.227	0.095	0.027	0.797
FBS	0.020	0.009	0.001	1.020
Fasting triglycerides	0.079	0.024	<0.0001	1.082

SE - standard error, BMI - body mass index
SBP - systolic blood pressure, FBS - fasting blood sugar

KSA. The experience from other countries in this regard showed positive correlations between the outcome of CAD and population mean risk factor changes.[55] It is important to emphasize an early intervention, particularly, educating our children for healthier habits, which can be achieved by implementing a strategy targeting children's schoolteachers as well as mothers at home. A longitudinal study may be needed to demonstrate the effect of modifying lifestyle by reducing weight, increasing physical activity, quitting smoking, controlling hypertension, controlling diabetes, as well as taking active steps for managing the metabolic syndrome in reducing the risk of CAD in KSA.

In conclusion, the overall prevalence of CAD in KSA is 5.5%, a figure midway to those reported from other countries. Classical risk factors for CAD; namely, older age, male gender, overweight, hypertension, current smoking, diabetes mellitus, hypertriglyceridemia, and hypercholesterolemia are important risk factors in Saudi population. Moreover, the metabolic syndrome is taking an active role in the development of CAD in this population. Measures are needed to change lifestyle and to address the management of the metabolic syndrome, as preventive method to reduce modifiable risk factors for CAD. A longitudinal study is needed to demonstrate the importance of reducing modifiable risk factors for CAD in KSA.

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