A Case-Control Study of the Incidence of Coronary Heart Disease Risk Factors in Saudis at Almadina Almounawarah

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A total of 136 Saudi subjects (68 patients with coronary heart disease (CHD) and an equal number of age- and sex-matched controls) were studied in detail for the incidence of CHD risk factors.

The following are the percentages of patients with risk factors found significantly more frequently than in controls (together with p-value and 95% confidence interval): hypertension 42%, <0.01 (6-37%); diabetes mellitus 41%, <0.046 (2-33%); cigarette smoking 24%, <0.046 (2-27%); hypertriglyceridaemia 32%, <0.001 (1-37%); hyperuricaemia 45%, <0.001 (19-50%).

The incidence of the following risk factors were not significantly different in patients and controls: alcohol consumption; family history of premature CHD; lack of physical activity; raised total cholesterol (TC) and low density lipoprotein (LDL) and obesity as assessed by the mean Body Mass Index (BMI).

Perhaps the recently reported qualitative blood lipid abnormalities, e.g. apolipoprotein, need to be investigated in Saudis with CHD.

The predictive variables for coronary heart disease (CHD) first suggested by Keys in 1949, now known as risk factors,1-2 are still the subject of discussion and debate to this day. Some workers doubted the presence of a clear cause and effect relationship between these factors and the presence of atherothrombotic plaque,3 and one study from this country found no significant relation between the extent of the disease on angiography or the asymptomatic status of the cases and the risk factor profile.4 Hypertriglyceridaemia as an independent risk factor, long doubted by some workers,5 was recently supported by others.6 Psychological factors such as ‘type A’ behaviour long held as a definite risk factor for CHD7-8 have recently been doubted.9 Regarding plasma lipids, qualitative abnormalities in the presence of normal plasma
levels\textsuperscript{16-11} are now considered as important if not more important than raised levels and at present the relationship between lipids and CHD is an area of intense research.

Diabetes mellitus as a risk factor for CHD has gained ground, as some authorities state that it actually increases the risk of CHD to at least the same level as any of the three already known major risk factors i.e. hypertension, smoking and hypercholesterolaemia.\textsuperscript{12} Actually a particularly high incidence of diabetes mellitus as a risk factor of CHD was reported from Japan,\textsuperscript{13} Jordan,\textsuperscript{14} Sudan\textsuperscript{15} and Saudi Arabia.\textsuperscript{4}

With this background and in the light of our impression of a lack of consistency in the occurrence of these risk factors in our patients we studied their incidence for CHD in a group of Saudi patients compared with sex- and age-matched controls.

Materials and Methods

Patients and their age- and sex-matched controls were studied in detail for the following risk factors: hypertension; filter cigarettes and ‘shisha’ smoking; lipid profile (total cholesterol (TC), low density lipoproteins (LDL), high density lipoproteins (HDL), triglycerides (TG)); diabetes mellitus; obesity (assessed by Body Mass Index); hyperuricaemia; alcohol; family history of premature CHD; physical activity; psychological factors e.g. type A behaviour.\textsuperscript{15}

Index patients

Saudi patients diagnosed or suspected to have CHD at Ohud hospital and King Fahad hospital were considered for study according to the following manifestations of the disease:

1. \textit{Angina pectoris} defined for this study as positive Grade I or Grade II angina on the London School of Hygiene Cardiovascular Questionnaire,\textsuperscript{16} plus an electrocardiogram showing Minnesota Code\textsuperscript{16} ST/T items 4.1–4; 5.1–3; 7.1.

2. \textit{Myocardial infarction} defined by presence of at least two of the following:
   (a) positive ‘possible infarction’ on the London School of Hygiene Cardiovascular Questionnaire;
   (b) electrocardiogram showing Minnesota Code Q/QS items 1.1–3 (usually on serial ECGs);
   (c) raised cardiac enzymes.

The upper age limit was 60 years. Patients with significant valvular lesions were excluded even if they satisfied the above criteria. Concomitant liver disease, pregnancy, hypothyroidism and cancer also disqualified the patient from being included in this study.

Control subjects

We made use of a study we were conducting in the primary health care centres on the prevalence of hypertension in Almadina Almounawarah\textsuperscript{17} to draw a random sample of subjects matched for sex and age with the cases. The sole criterion for selection of a subject at the primary health care centre as a control, was the absence of a history of chest pain. These patients were seen in hospital where they were finally included as controls after they satisfied the following criteria:

(a) negative London School of Hygiene Cardiovascular Questionnaire;
(b) an electrocardiogram that did not contain codable items suggestive or diagnostic of CHD.

(i) London School of Hygiene Cardiovascular Questionnaire was administered by the researchers after it had been translated into Arabic.

(ii) A purpose-made questionnaire, was administered to obtain data about residence (rural, suburban or urban), work history, educational level, smoking habits of filter cigarettes (smoking questionnaire)\textsuperscript{16} and shisha (hubbly bubbly), alcohol consumption, history of diabetes mellitus, hypertension, gout or premature CHD in the family. Type A behaviour was evaluated by scoring ‘JAS Form N’-short type A scale.\textsuperscript{15}

(iii) A physical examination was conducted and included: height and weight (a Stadiometer and beam balance scale were used); blood pressure measured with a mercury sphygmomanometer with the diastolic (BP) read at Phase five with standardization precautions.\textsuperscript{18} The heart was examined to exclude significant valvular disease.

(iv) Twelve lead electrocardiogram at rest.

(v) A blood sample was drawn taking care of the standardization precautions;\textsuperscript{16} 10 ml of whole blood – 2 ml in a fluoride bottle and 8 ml in a plain tube. The laboratory investigations were centralized at Ohud hospital laboratory. On the day of receiving the specimens the fasting blood sugar was estimated using an enzymatic method (glucose oxidase and peroxidase) and serum uric acid was estimated after deproteinization by phosphatungstic reduction in alkaline medium. The lipid profiles were processed in batches. All estimations were done manually.\textsuperscript{19}

The data were analysed by computer; the raw data were fed into Lotus software\textsuperscript{20} and descriptive statistics performed. Further statistical tests were done by CIA software.\textsuperscript{21} Different parameters were analysed by Student’s t-test and individual variables were examined with a $\chi^2$-test and finally the 95% confidence interval was estimated.

Results

A total of 136 subjects (68 patients and an equal number of sex- and age-matched controls) were studied. The patients were 43 males; mean (SD) age 51.5 (8.5) years and 25 females; mean (SD) age 52.5 (5.2) years.

Both social factors and physical activity were remarkably comparable in the two groups with 50% and and 52% of patients and controls respectively having
Table 1

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Proportion of known hypertensive and/or hypertensive BP 160/95 mmHg (n=68)</th>
<th>Mean systolic BP (mmHg)</th>
<th>Mean diastolic BP (mmHg)</th>
<th>Proportion with raised lipoprotein (LDL) lipoprotein (HDL) Triglycerides (TG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>27/64 (n=164)</td>
<td>127/79.5</td>
<td>4.9</td>
<td>7/59 (n=55)</td>
</tr>
<tr>
<td>Control</td>
<td>14/68 (n=68)</td>
<td>133/81</td>
<td>5.0</td>
<td>8/68 (n=68)</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.01</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>95% confidence interval</td>
<td>0.06–0.37</td>
<td>–13.0–</td>
<td>–5.3–</td>
<td>–1.3–</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.0</td>
<td>2.5</td>
<td>0.11</td>
</tr>
</tbody>
</table>

BP: blood pressure; NS: not significant.
*There is no agreed high level of HDL, but ‘normal’ is usually higher than 1.2.
*Raised TG = 2.2 for males and 1.8 for females.

Table 2

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Obesity</th>
<th>Diabetes mellitus</th>
<th>Hyperuricaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>26.6 (4.3)</td>
<td>28/68</td>
<td>24/53</td>
</tr>
<tr>
<td>(n=68)</td>
<td></td>
<td></td>
<td>n=57</td>
</tr>
<tr>
<td>Controls</td>
<td>28 (6.6)</td>
<td>16/68</td>
<td>7/68</td>
</tr>
<tr>
<td>(n=68)</td>
<td></td>
<td></td>
<td>n=68</td>
</tr>
<tr>
<td>p-value</td>
<td>NS</td>
<td>&lt;0.046</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>95% confidence interval</td>
<td>–3.3–0.49</td>
<td>0.02–0.33</td>
<td>0.19–0.50</td>
</tr>
</tbody>
</table>

*Obesity is assessed by Quetelet’s Index. (Body mass index) = kg/m² (wt./ht.²).
*Hyperuricaemia for males = 427.7 and for females = 297 μmol/litre.
NS: not significant. DM: Diabetes mellitus.

Table 3

<table>
<thead>
<tr>
<th>Drugs used</th>
<th>Non-proprietary names</th>
<th>Proprietary names</th>
<th>No. of patients</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atenolol</td>
<td>tenormin</td>
<td></td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Chlorothiazide+ triamterine</td>
<td>dyazide</td>
<td></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Chlorothiazide</td>
<td>esidrex</td>
<td></td>
<td>2</td>
<td>–</td>
</tr>
<tr>
<td>Glibenclamide</td>
<td>daonil</td>
<td></td>
<td>21</td>
<td>10</td>
</tr>
<tr>
<td>Insulin</td>
<td>humulin (R)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td>adalat</td>
<td></td>
<td>8</td>
<td>–</td>
</tr>
<tr>
<td>Methyldopa</td>
<td>aldomet</td>
<td></td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Reserpine + Clopamide + Ergot</td>
<td>brinerdin</td>
<td></td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>
The study of cigarette smoking showed that both the total number of smokers and of those who smoked more than one pack (20 filter cigarettes) per day in the patient group (18/68 and 16/68 respectively) were significantly more than in the control group; p-value <0.046 and <0.046. For shisha smoking 10 and 8 of the patients and controls respectively reported the use of shisha.

Finally, Table 3 shows the drugs used by patients and controls at the time of the study.

Discussion

The risk factors for coronary heart disease include irreversible factors; advancing age, male sex and family history of premature CHD; and potentially reversible factors; hypertension; cigarette smoking; hypercholesterolaemia, hypertriglyceridaemia and recently qualitative lipid abnormalities; diabetes mellitus; lack of physical exercise; obesity; alcohol (in excess) and hyperuricaemia. Psychological factors, type A behaviour and chronic stress, although recent reports have doubted type A behaviour as a risk factor.

The results of comparisons of the social factors such as physical activity, alcohol consumption and family history of premature CHD and obesity as assessed by Body Mass Index showed no significant difference between patients and controls. This was a welcome finding as it reduced the number of variables to be compared.

A history of hypertension was significantly more prevalent in patients (42%). However, the mean systolic and diastolic BP were not significantly different from controls as the BP of patients was lowered by the drug treatment (Table 2) and by the fact that most myocardial infarction patients drop their BP and never regain the pre-myocardial infarction BP levels. The type of anti-hypertensive drug is important as β-blockers and diuretics can offset the benefit of control of BP through their adverse effect on plasma lipids and blood glucose and insulin secretion.

Comparing the patients and control groups for lipid profiles (Table 1) both the mean plasma triglyceride level and the proportion of subjects with hypertriglyceridaemia were significantly raised in the patients group. However, hypertriglyceridaemia as a risk factor of CHD is debated. This lipid abnormality is a recognized dyslipidaemia secondary to the diabetic state, and we have significantly excess diabetes in the patients group (Table 2). As far as plasma total cholesterol (TC), low density lipoproteins (LDL) and high density lipoprotein (HDL) no significant difference was noted and the means of both groups were very close to the mean value for Saudi males and females. Our data on lipids did not cover the recently recognized qualitative lipid abnormalities which would be an interesting area to investigate.

The total number of smokers as well as those who smoked more than one pack (20 filter cigarettes) per day in the patients group were significantly more than in the controls. The incidence of smoking as a risk factor for CHD in our series (26.5%) is less than that reported from Riyadh (39%), reflecting the well known geographical variation in risk factor even within the same country. Smoking has been demonstrated beyond reasonable doubt as a cause of CHD in men and recent evidence has shown that women are as vulnerable. A new area of interest is the risk to passive or involuntary smokers e.g. non-smokers exposed to smoking spouses; where most studies suggest that they share an increased risk of developing heart disease.

Diabetes mellitus evaluated in this study by the history and/or fasting blood sugar > 7.7 mmol/litre (140 mg/dl); was significantly more prevalent in the patient population (41%) compared with the controls (Table 2). Diabetes mellitus as a risk factor for CHD was found consistently associated with CHD in reports from industrialized countries and also in relatively low prevalence countries like Japan, Jordan, Sudan, and from this country where a study in Riyadh reported diabetes as the second most prevalent risk factor for CHD found in (24%) of patients. Diabetes mellitus has been reported by several researchers as increasing the risk of CHD by two- to three fold. Recent work showed that this excess risk is related, partly, to excess of hypertension in diabetics with some recent work claiming hyperinsulinaemia, the hallmark of insulin-resistance, a common finding in obese subjects as the link between non-insulin dependent diabetes mellitus and hypertension. In part, the excess risk of CHD in diabetics is related to the associated dyslipidaemia such as hypertriglyceridaemia and low levels of HDL cholesterol. The risk is also increased in insulin-dependent diabetes mellitus (IDDM) patients in the absence of other risk factors; and recently it has been found that perfectly normal plasma lipid levels in such patients were associated with disturbance in lipoprotein composition and function. The specific constituent responsible is Lp(a) which is associated with apolipoprotein B, the principal apoprotein of atherogenic LDL. The low density lipoproteins have homologies with plasminogen and its association with increased cardiovascular risk probably relates at least in part to its activating
thrombosis.55 The excess of smoking in the patient population noted in this study will surely increase the risk for diabetics.54–56

Both the mean serum level and the proportion of subjects with hyperuricaemia were significantly higher in patients than in controls. This could not be accounted for by the drug therapy (Table 2); perhaps the normal reference value for Saudis is higher than those of Western countries.

In conclusion, this study showed that, in Saudis, hypertension, diabetes mellitus and smoking were consistently associated with CHD. Of the plasma lipids, hypertriglyceridaemia (a controversial independent risk factor of CHD)5,6 was consistently associated with CHD; whereas raised plasma levels of the other lipids showed no such association. The recently reported qualitative plasma lipid abnormalities need to be investigated. Hyperuricaemia (considered a minor risk factor for CHD) was remarkably associated with CHD in Saudis which is an interesting but unexplained finding.

Acknowledgement

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References


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