Abnormal glucose tolerance and lipid abnormalities in Indian myocardial infarct survivors

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Summary

Glucose tolerance and lipid levels in a random sample of 103 Indian patients (96 males and 7 females) with coronary artery disease (CAD) aged between 20 and 55 years were compared with those in a healthy Indian control group matched as regards age and sex. Previous episodes of myocardial infarction were taken as evidence of CAD. Of the patients 44% were overweight.

Glucose tolerance was abnormal in 55% of the patients. Both cholesterol and triglyceride values in the patients with CAD were significantly higher than those in the control group. Serum cholesterol levels were over 6,5 mmol/l in 62% of the patients with CAD and serum triglyceride levels were over 2,0 mmol/l in 53%. Males with CAD tended to have lower plasma high-density lipoprotein (HDL) cholesterol levels than the control group ($P < 0,01$).

There was a significant negative correlation between body mass index and HDL cholesterol, and no correlation was demonstrated between body mass index and total cholesterol or triglyceride levels. Furthermore, when the patients were subgrouped according to their glucose tolerances it was found that only the triglyceride levels were significantly different (values were higher in those with abnormal glucose tolerance). Our data suggest that abnormal glucose tolerance and lipid aberrations are significant risk factors in Indian patients with CAD.

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Hyperlipidaemia[1] and hyperglycaemia[2] have long been implicated in the pathogenesis of coronary artery disease (CAD). Whereas hypercholesterolaemia and hyperglycaemia are well-recognized risk factors for the development of CAD, the relationship between hypertriglyceridaemia[3] and CAD is less well defined. Recently a further risk factor has emerged; an independent inverse relationship between high-density lipoprotein (HDL) cholesterol and CAD, which has been established by many studies.[4,5] The relative frequency of these risk factors varies geographically and among different racial groups.[6]

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The high incidence of CAD and its accompanying mortality in the South African Indian population have been highlighted by previous workers.[7,8] It has previously been shown that the frequency of abnormal glucose tolerance (impaired glucose tolerance and diabetes mellitus) in Indian patients with CAD is similar to that in White patients.[9] However, with respect to the lipid profile there have been conflicting reports; hypercholesterolaemia was present in 37% of the series described by McKechnie and Davidson,[10] while Thandroyen *et al.*[9] have reported hypercholesterolaemia in 63% of their Indian patients. No study has compared lipid levels in healthy Indian controls with those in CAD survivors, nor have there been any reports on HDL cholesterol levels in Indian patients with CAD.

This study was therefore undertaken to assess the status of lipid aberrations with respect to fasting plasma cholesterol, triglyceride and HDL cholesterol values and abnormal glucose tolerance (impaired glucose tolerance and diabetes mellitus) in Indian patients with CAD compared with those in a healthy Indian control group.

Patients and methods

Patients

The patients selected for this study were 103 Indian subjects attending the Ischaemic Heart Disease Clinic at the R. K. Khan Hospital, Durban. All had had at least one acute myocardial infarction (MI). The criteria for the diagnosis of MI were a history of chest pain supported by unequivocal electrocardiographic findings of abnormal Q waves and raised ST segments and/or sequential ST-T-wave changes, accompanied by a transient rise in aspartate amino transferase, lactate dehydrogenase and creatine kinase levels. The MI was presumed to be due to coronary atherosclerosis.

The patients (96 males and 7 females) were matched as regards age and sex with a control group of apparently healthy Indian hospital staff numbers. Informed consent was obtained from all the participants in the study.

Methods

In all cases investigations were carried out a minimum of 3 months after MI. The specimens for lipid analyses were taken after a 14-hour fast according to the precautions set out by Lewis.[11] After centrifugation, the sera were stored at 4°C and assays were undertaken within 3 days. Cholesterol and triglycerides were measured by enzymatic methods, utilizing commercial kits (Boehringer Mannheim, GmBH Diagnostica). A control serum sample was included in each assay (Preclip). HDL cholesterol levels were measured by a polyanion precipitation method, using phosphotungstic acid and magnesium chloride.[12] Serum cholesterol levels above 6,5 mmol/l and triglyceride levels above 2,0 mmol/l were arbitrarily defined as abnormal, according to the criteria of Stamler *et al.*[13]

Oral glucose tolerance tests were performed on all patients except those who were already known to have diabetes. The diagnosis of diabetes mellitus and impaired glucose tolerance was based on 1980 World Health Organization criteria: diabetes was considered to be present if the fasting plasma glucose level was ⩾ 8 mmol/l and/or the 2-hour plasma glucose level after a 50 g oral glucose load ⩾ 10 mmol/l; impaired glucose tolerance was diagnosed if the fasting plasma glucose level was < 8 mmol/l and the 2-hour plasma glucose level after a 50 g oral glucose load ⩾ 8 and < 10 mmol/l. All the controls had fasting plasma glucose levels of < 6 mmol/l.

Body mass indices were calculated according to Bray.[14] Males with a body mass index of ⩾ 25 and females with a body mass index of ⩾ 27 were considered to be overweight.[15] Lipid levels were compared using the Mann-Whitney U test. Correlation coefficients between variables were also calculated. All data are expressed as mean ± SE.

Results

One hundred and eighty-four subjects between the ages of 20 and 55 years participated in the study; 103 (96 males and 7 females) were MI survivors and the rest (74 males and 7 females) were healthy controls. Mean ages and body mass indices of the 103 patients are set out in Table I. It can be seen that there were no major differences between the males and females as regards mean ages and body mass indices; 45 patients (44%) were overweight according to the criteria defined earlier.

TABLE I. MEAN AGES AND BODY MASS INDICES OF MI SURVIVORS

	Males (96)	Females (7)
Age (yrs)	**45,2**	**47,3**
	(20 - 55)	**(42 - 55)**
Body mass index	**24,7**	**26,4**
	(19 - 39)	**(25 - 30)**

Ranges in parentheses.

Impaired glucose tolerance was present in 14 patients (14%) and diabetes mellitus was diagnosed in a further 42 (41%). A total of 55% (56 patients) of the entire group therefore had abnormal glucose tolerance (impaired glucose tolerance and diabetes mellitus).

Comparisons of the results of lipid analyses in controls and MI survivors were undertaken separately for males and females. Total plasma cholesterol, triglyceride and HDL cholesterol levels for male and female MI survivors compared with those in controls are shown in Tables II and III. As can be seen from these tables, cholesterol and triglyceride levels in male MI survivors (6,99 ± 0,15 mmol/l and 2,36 ± 0,13 mmol/l respectively) and in females (7,0 ± 0,57 mmol/l and 2,89 ± 0,73 mmol/l) were significantly higher than those in controls (5,56 ± 0,13 mmol/l and 1,63 ± 0,16 mmol/l in males; 5,21 ± 0,39 mmol/l and 1,22 ± 0,10 mmol/l in females). There was no significant difference between the HDL cholesterol levels in the female patients and controls. However, male patients had significantly lower HDL cholesterol levels (0,83 ± 0,02 mmol/l) than male controls (0,95 ± 0,03 mmol/l).

Using the cut-off points of 6,5 mmol/l for cholesterol and 2,0 mmol/l for triglycerides[13] it was found that 62% of our patients had hypercholesterolaemia and 53% hypertriglyceridaemia; combined hyperlipidaemia (hypercholesterolaemia and hypertriglyceridaemia) was present in 37% of the patients. These findings contrasted sharply with those in the control group (hypercholesterolaemia 17%; hypertriglyceridaemia 19% and combined hyperlipidaemia 10%).

TABLE II. LIPID LEVELS IN MALE MI SURVIVORS

	Controls	MI survivors
Cholesterol (mmol/l)		
N	**74**	**96**
Mean	**5,56**	**6,99**
SE	**0,13**	**0,15**
	P < **0,001**	
Triglycerides (mmol/l)		
N	**73**	**96**
Mean	**1,63**	**2,36**
SE	**0,16**	**0,13**
	P < **0,001**	
HDL cholesterol (mmol/l)		
N	**69**	**78**
Mean	**0,95**	**0,83**
SE	**0,03**	**0,02**
	P < **0,01**	

TABLE III. LIPID LEVELS IN FEMALE MI SURVIVORS

	Controls	MI survivors
Cholesterol (mmol/l)		
N	**7**	**7**
Mean	**5,21**	**7,00**
SE	**0,39**	**0,57**
	P < **0,005**	
Triglycerides (mmol/l)		
N	**7**	**7**
Mean	**1,22**	**2,89**
SE	**0,10**	**0,73**
	P < **0,001**	
HDL cholesterol (mmol/l)		
N	**7**	**6**
Mean	**1,11**	**1,06**
SE	**0,12**	**0,09**
	NS (*P* > 0,05)	

Because of the small number of female MI survivors, the effect of obesity and abnormal glucose tolerance on lipid levels was studied in the male patients only. There was no significant correlation between body mass index and triglycerides ($r = 0,03$; $P > 0,05$) or between body mass index and cholesterol ($r = 0,11$; $P > 0,05$). However, there was a significant inverse correlation between body mass index and HDL cholesterol ($r = -0,22$; $P < 0,05$).

In Table IV lipid levels in male MI survivors with normal glucose tolerance and in those with abnormal glucose tolerance are compared. There was no significant difference between these two subgroups as regards total cholesterol and HDL cholesterol levels ($P > 0,05$); however, triglyceride levels were significantly higher in those with abnormal glucose tolerance ($P < 0,05$).

Discussion

Regardless of varying diagnostic classification, abnormal glucose tolerance is a well-documented risk factor.[16] Abnormalities in

TABLE IV. COMPARISON OF LIPID LEVELS IN MALE MI SURVIVORS WITH NORMAL AND ABNORMAL GLUCOSE TOLERANCE

	Glucose tolerance	
	Normal	Abnormal
Cholesterol (mmol/l)		
N	46	50
Mean	6,97	7,01
SE	0,22	0,21
	NS ($P > 0,05$)	
Triglycerides (mmol/l)		
N	46	50
Mean	2,03	2,67
SE	0,14	0,21
	$P < 0,05$	
HDL cholesterol (mmol/l)		
N	41	44
Mean	0,88	0,89
SE	0,03	0,05
	NS ($P > 0,05$)	

carbohydrate metabolism have been described in approximately 60% of patients with CAD.[17] Our results show that 55% of patients who had had an MI had abnormal glucose tolerance. This is consistent with the findings of Thandroyen *et al.*[9] (47%) and McKechnie[10] (53%) and with the published data.

The association between hyperlipidaemia and CAD is well established.[1] In previous studies of lipid abnormalities in Indian patients with CAD arbitrary cut-off points were used to define hyperlipidaemia.[9,10] The Framingham study[1] suggested that the serum cholesterol level is related to risk of CAD as a continuous function. In an angiographic study of patients with and without CAD Cohn *et al.*[18] were unable to establish any critical serum level for either cholesterol or triglycerides which would separate risk from non-risk. In a similar study Gotto *et al.*[19] concluded that it was misleading to define hyperlipidaemia using arbitrary cut-off values.

Without defining hyperlipidaemia, the present study shows that both cholesterol and triglyceride levels in Indians who had had an MI were significantly higher than those in a control group. This finding was also clearly demonstrated when using arbitrary criteria for the definition of hyperlipidaemia. This was done in order to compare our results with those of previous investigators.[9,10] Hypercholesterolaemia was present in 62% of our patients, a prevalence similar to that reported by Thandroyen *et al.*[9] (63%) but much higher than that reported by McKechnie[10] (37%). Hypertriglyceridaemia was present in 53% of our patients, also a prevalence similar to that reported by Thandroyen *et al.* (47%); in McKechnie's series triglyceride levels were not measured. However, it should be stressed that neither of these workers used normal Indian controls for comparison.

The role of HDL cholesterol in CAD has been examined extensively.[4,5] It is generally thought that HDL cholesterol levels are lower in subjects with CAD than in controls. The difference is often small, but is statistically significant and independent of other risk factors. Our findings in male patients are in keeping with this general trend (this relationship was not seen in the female patients, possibly because of the small number studied). Furthermore, the significant negative correlation between HDL cholesterol and body mass index is in accordance with previously published literature.[4] However, it seems that there is no significant relationship between body mass index and cholesterol and triglyceride levels.

Hyperlipidaemia is frequently associated with diabetes and is often considered a major determinant of its atherosclerotic sequelae. The commonest lipid abnormality is hypertriglyceridaemia,[20] but hypercholesterolaemia[21] has also been reported. Information on HDL cholesterol levels in the diabetic state is somewhat conflicting.[22] Since 55% of our patients had abnormal glucose tolerance, the interrelationship of this disorder with cholesterol, triglyceride and HDL cholesterol levels is of relevance. The finding of significantly higher triglyceride levels in our patients with abnormal glucose tolerance than in subjects with normal glucose tolerance would suggest that the abnormal glucose tolerance contributes significantly to the higher triglyceride levels in our patients with CAD.

The fact that total cholesterol levels and HDL cholesterol levels were similar in the two subgroups would suggest that these variables are apparently independent of glycaemic status.

This study has demonstrated that abnormal glucose tolerance, hyperlipidaemia and low HDL cholesterol levels are significant risk factors in Indian MI survivors.

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