

BIOCHEMICAL RISK FACTORS FOR MYOCARDIAL INFARCTION AMONG SOUTH ASIAN IMMIGRANTS AND ARABS

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Population migration from the Indian subcontinent to other parts of the world started around the middle of the 19th century. Irrespective of the areas they settled, epidemiological studies have shown that South Asian immigrants have a higher rate of coronary heart disease (CHD) than the indigenous population. This trend has been consistently demonstrated in Europe,¹⁻³ Africa,⁴⁻⁶ the Americas,⁷⁻⁸ the Caribbean,⁹ and even in other parts of Asia outside the Indian subcontinent.¹⁰ The causes of this increased susceptibility have not been clearly elucidated. In the past, diabetes mellitus¹¹⁻¹² and hypercholesterolemia¹³ were implicated, but there is now no evidence that either of these factors sufficiently explains the increased susceptibility of South Asians to CHD. The recent view is that South Asians are genetically predisposed to atherothrombotic risk factors which migration and westernization unmask and potentiate.¹³ But the genetic factors responsible for such a predisposition have not been identified. In order to explore further the reasons for the increased susceptibility of South Asians to CHD, we studied some of the recently reported CHD risk factors such as serum total protein, albumin, total cholesterol to albumin ratio, and total bilirubin.

Patients and Methods

This is a retrospective study of the case notes of all patients with chest pain who were seen at Mubarak Al Kabeer Hospital, Kuwait, between January 1992 and July 1995. Those in whom a diagnosis of myocardial infarction was confirmed clinically, electrocardiographically and biochemically (elevated cardiac enzymes) were selected for the study. The demographic data collected from each case note included age, sex, nationality and history of diabetes, while the biochemical data included blood glucose, serum triglyceride, total cholesterol, total protein, albumin and total bilirubin. Only patients with complete demographic and biochemical data were included in the study.

Apparently healthy subjects without any previous history of chest pain or myocardial infarction (MI) who visited the outpatient department for minor ailments or routine medical check-up served as controls. Data collected from the controls were similar to those collected from the patients.

Simple descriptive statistics (mean, standard deviation) were used to describe the findings observed in both patients and controls. Descriptive analysis of the triglyceride data showed some deviation from gaussian distribution, with significant values for skewness. For normalizing the values, a log transformation (to the base e) was carried out which resulted in an almost perfect gaussian distribution. Since age, sex, serum total cholesterol, triglyceride, albumin and total bilirubin are known to be independent risk factors for CHD, analysis of covariance with each of these risk factors as a covariate was used to test the difference between control and each ethnic population, and between South Asians and Arabs. To determine the relative risk of MI for different levels of serum albumin and serum total bilirubin, the odd ratios were calculated by taking a reference level of 45 g/L and above for albumin, and less than 5 $\mu\text{mol/L}$ for bilirubin. These statistical analyses were done on a computer using the statistical package SPSS Version 6.

Results

There were 250 cases of MI, of which 88 (35.20%) were Kuwaiti Arabs, 97 (38.80%) non-Kuwaiti Arabs (Egyptians, Palestinians, Lebanese, Jordanians), and 65 (26.0%) South Asian immigrants (Indians, Pakistanis, Bangladeshis and Sri Lankans). There was a male preponderance of cases in all the ethnic groups.

Table 1 shows that the mean age (46.80 ± 8.64 years) of South Asian patients with MI was significantly lower ($P < 0.0001$) than that of Kuwaiti Arabs (56.40 ± 11.50 years) or non-Kuwaiti Arabs (50.05 ± 9.25 years), suggesting that MI occurs at a younger age group among South Asians compared to Arabs. Also, 42.0% of Kuwaiti patients with MI gave a history of diabetes mellitus. This was significantly higher ($P < 0.0001$) than the 27.90% among non-Kuwaiti Arabs and 29.20% among South Asians. This observation suggests that diabetes mellitus

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TABLE 1. Comparison of some risk factors in patients with myocardial infarction (Arabs and South Asians) and healthy controls.

	Kuwaiti Arabs (mean±2SD) n=88	Non-Kuwaiti Arabs (mean±2SD) n=97	South Asians (mean±2SD) n=65	Healthy controls (mean±2SD) n=600	P-value
Age in years	56.40±11.5	50.5±9.25	46.80±8.64	44.8±10.2	a, b, ns
History of diabetes mellitus	42.04%	27.90%	29.23%	–	
Total cholesterol (mmol/L)	5.48±1.07	5.57±1.29	5.32±1.15	5.38±1.09	ns, ns, ns
Triglyceride (mmol/L)	2.08±1.56	2.06±1.27	2.06±1.06	1.59±0.96	a, b, c
Total protein (g/L)	66.58±5.31	68.49±4.84	68.06±9.52	73.63±6.08	a, b, c
Albumin (g/L)	36.85±3.68	39.54±3.56	38.75±4.81	42.49±3.46	a, b, c
Total bilirubin (µmol/L)	11.42±3.90	10.82±4.10	11.87±4.30	9.31±4.0	a, ns, c
Cholesterol to albumin ratio	0.16±0.04	0.14±0.03	0.14±0.04	0.13±0.03	a, b, c

There were no significant intrapopulation differences; a=significant difference between Kuwaiti Arabs and healthy controls; b=significant difference between non-Kuwaiti Arabs and healthy controls; c=significant difference between South Asians and healthy controls; patients and controls in the markers, ns=no significant difference between.

may be a more prominent risk factor for myocardial infarction in Kuwaitis than in non-Kuwaitis.

Table 1 shows that in each population, patients with MI had significantly higher serum triglyceride and serum total bilirubin but lower serum albumin and total protein than the healthy control population. However, there were no significant differences ($P>0.05$) in serum concentrations of total cholesterol, triglyceride, albumin, total protein, total bilirubin and total cholesterol to albumin ratio between South Asian immigrants and Arab patients with myocardial infarction. Table 2 shows that the serum triglyceride concentration in patients with MI (2.07 ± 1.33 mmol/L) was significantly higher than that in healthy controls (1.59 ± 0.96 mmol/L). On the other hand, there was no significant difference in serum total cholesterol concentration between patients with MI (5.47 ± 1.18 mmol/L) and controls (5.38 ± 1.09 mmol/L), suggesting that hypertriglyceridemia, but not hypercholesterolemia, is associated with MI in South Asians and Arabs.

Table 2 shows that the serum albumin (38.57 ± 4.06 g/L) and total protein (67.83 ± 6.41 g/L) in patients with MI were significantly lower ($P<0.0001$) than those in healthy controls. On the other hand, the serum total bilirubin (11.3 ± 4.1 µmol/L) in patients with MI was significantly higher ($P<0.0001$) than the mean value (9.31 ± 4.1 µmol/L) for healthy controls. Since serum total cholesterol to albumin ratio (TC:Alb) has been reported to be a better index of cardiovascular risk than serum total cholesterol,¹⁴ we examined this ratio and found that patients with MI had a significantly ($P<0.0001$) higher ratio (0.15 ± 0.04) than healthy controls (0.13 ± 0.03).

In order to find out if there is any relationship between MI, serum albumin and serum total bilirubin, we calculated the odds ratios by taking a reference level of 45 g/L and above for serum albumin, and less than 5 µmol/L for serum bilirubin. Based on the calculated odds ratios, a level of serum albumin below 40 g/L showed a significantly higher risk ($P<0.0001$) (OR=16.57, CI=7.1-38.7) for MI than a serum albumin concentration of 45 g/L

TABLE 2. Some biochemical risk factors in patients with myocardial infarction (MI), compared with those in healthy controls.

Risk factors	Cases with MI (mean±2SD) n=250	Controls (mean±2SD) n=600	P-value
Serum albumin (g/L)	38.57±4.06	42.49±3.46	0.0001
Serum total bilirubin (µmol/L)	11.30±4.10	9.31±4.0	0.0001
Serum total cholesterol (mmol/L)	5.47±1.18	5.38±1.09	0.872
Serum triglyceride (mmol/L)	2.07±1.33	1.59±0.96	0.0001
Serum total protein (g/L)	67.83±6.41	73.63±6.08	0.0001
Serum total cholesterol: albumin ratio	0.15±0.04	0.13±0.03	0.0001

and above, suggesting an inverse relationship between serum albumin concentration and risk for MI. On the other hand, there was a direct relationship between serum total bilirubin and risk for MI. For example, the risk for MI at a serum bilirubin level of less than 5 µmol/L was three times greater than the risk when serum bilirubin level was 8-17 µmol/L, and more than 6 times greater when serum bilirubin level was 17 µmol/L (OR=6.31, CI= 3.2-12.4).

Discussion

An important finding in this study is that MI appears to occur at a younger age in South Asians compared to Arabs. The results of this study did not show any significant differences in serum albumin, total protein and total bilirubin concentrations between South Asian immigrants and Arab patients with MI. Therefore, it would appear that the increased susceptibility of South Asians to MI is not due to any of these biochemical risk factors. However, a controlled prospective study is needed to investigate this further.

Patients with MI from both populations had significantly higher serum triglyceride than the controls, even after taking into account confounding factors such as age, sex, serum albumin and total cholesterol concen-

trations. For a long time, the association between serum triglyceride and CHD remained unclear. In a large number of both case control and cross-sectional studies, an association between hypertriglyceridemia and myocardial infarction was reported, but only in three of them¹⁵⁻¹⁷ did the association remain significant after controlling for other confounding factors. Recently, Bainton et al.¹⁸ reported that serum triglyceride was an independent risk factor for CHD. Our finding that both South Asian and Arab patients with MI had significantly higher serum triglyceride concentrations than the controls would seem to suggest that hypertriglyceridemia is associated with MI in these populations. Epidemiological, clinical and experimental studies suggest that hypertriglyceridemia predisposes an individual to thrombosis by increasing factor VII coagulant activity.^{19,20} It is, therefore, suggested that a prospective study of the relationship between hypertriglyceridemia, factor VII coagulant activity and MI be carried out in Kuwait.

We found in this study that patients with MI had significantly higher serum total bilirubin than controls, and that there was a direct relationship between serum total bilirubin and risk of MI. This finding does not support that of Schwertner et al.,²¹ who found that serum total bilirubin was an inverse and independent risk factor for CHD. Schwertner's study, however, involved a larger number of subjects. A prospective study of a large number of MI cases is necessary to test the association between serum total bilirubin and MI. We conclude that South Asian and Arab patients with MI had significantly higher serum triglyceride and total bilirubin, but lower serum total protein and albumin concentrations, than healthy controls.

References

- Balarajan R, Aldestein, AM, Bulusul SV. Patterns of mortality among migrants to England from the Indian subcontinent. *BMJ* 1984;289:1185-7.
- McKeigue PM, Marmot MG. Mortality from coronary heart disease in Asian communities in London. *BMJ* 1988;297:903.
- McKeigue PM, Miller GJ, Marmot MG. Coronary heart disease in South Asians overseas: review. *J Clin Epidemiol* 1989;422:597-609.
- Cosnet JI. Illness among Natal Indians: a survey of hospital admissions. *S Afr Med J* 1957;31:1109-15.
- Sharper AG, Jones KW. Serum cholesterol, diet and coronary heart disease in Africans and Asians in Uganda. *Lancet* 1959;2:534-7.
- Walker ARP. Extremes of coronary heart disease mortality in ethnic groups in Johannesburg, South Africa. *Am Heart J* 1961;66:291-5.
- Wattley GH. Myocardial infarction in south Trinidad. *W Ind Med J* 1959;8:33-6.
- Ramhal S, Poon King T. Unpublished report quoted by Ashcroft MT, Stuart KI. Acute myocardial infarction in the university hospital, Jamaica 1968-1970. *W Ind Med J* 1973;22:60-6.
- Miller GJ, Alexis SD, Beckles GLA, Byan NTA, Price SGL. Serum lipoproteins and susceptibility of men of Indian descent to coronary heart disease. The St. James Survey, Trinidad. *Lancet* 1982;ii:200-3.
- Danaraj TJ, Acker MS, Sanaraj W, Ong WH, Yam TB. Ethnic group differences in coronary heart disease in Singapore: an analysis of necropsy studies. *Am Heart J* 1959;58:516-26.
- Hughes LD, Cruikshank J, Wright J, Raftary EB. Disturbances of insulin in British Asian and white men surviving myocardial infarction. *BMJ* 1989;299:537-41.
- McKeigue PM, Shah B, Marmot MG. Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. *Lancet* 1991;337:382-6.
- Bhatnager D, Anand IS, Durrington PN, Patel DJ, Wander GS, Mackness MI, et al. Coronary risk factors in people from the Indian subcontinent living in West London and their siblings in India. *Lancet* 1995;345:405-9.
- Nanji AA, Reddy S. Use of total cholesterol/albumin ratio as an alternative to high-density lipoprotein cholesterol measurement. *J Clin Pathol* 1983;36:716-8.
- Fager G, Wiklund O, Olofsson, SO, Silhemsén L, Bondijmers G. Multivariate analyses of serum apolipoproteins and risk factors in relation to acute myocardial infarction. *Arteriosclerosis* 1981;1:273-9.
- Hamst AM, Walldius G, Dahlen G, Johansson B, De Faire U. Serum lipoproteins and apolipoproteins in young male survivors of myocardial infarction. *Atherosclerosis* 1989;77:131-8.
- Al-Mutaseb N, Hayat N, Al-Khafaji M. Lipoproteins and apolipoproteins in young male survivors of myocardial infarction. *Atherosclerosis* 1989;77:131-8.
- Bainton D, Miller NE, Botton CH, et al. Plasma triglyceride and high-density lipoprotein cholesterol as predictors of ischaemic heart disease in British men. *Br Heart J* 1992;68:60-6.
- Meade TW, North WRS, Chakrabarti R, et al. Haemostatic function and cardiovascular death: early results of a prospective study. *Lancet* 1980;1:1050-4.
- Meade TW, Mellows S, Brozovic M, et al. Haemostatic function and cardiovascular death: principal results of Northwick Park Heart Study. *Lancet* 1986;2:533-7.
- Schwertner HA, Jackson WG, Tolan G. Association of low serum concentration of bilirubin with increased risk of coronary artery disease. *Clin Chem* 1994;40:18-23.