Genetic Association in Myocardial Infarction
Ethnicity; ABO, Rh, Le⁺, Xg⁺ Blood Groups; G6PD Deficiency; and Abnormal Haemoglobins

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Summary. Four hundred and eighty-six patients with myocardial infarction of both sexes comprising 213 Chinese, 53 Malays, 199 Indians, and 21 Europeans, resident in Singapore were investigated for differences in relative incidence, and for the ABO, Rh, Le⁺, and Xg⁺ blood groups, G6PD deficiency, and haemoglobin types. Relative incidence of myocardial infarction was appreciably higher among Indians than Chinese and Malays in all age groups, more so in younger people. There was no significant difference in the distribution of the genetic markers between patient and control series in either Chinese, Malays, or Indians.

Results of twin studies are suggestive of some genetic factor involved in the causation of coronary thrombosis (Hauge, 1969) and in recent years an association with ABO blood groups, with a higher incidence among group A persons, has been demonstrated in most of the populations studied and the literature has been reviewed recently by Mourant, Kopec, and Domaniewska-Sobczak (1971). From this it appears that there might be some epistatic genetic factor involved, though precisely how this might operate is not clear.

Several reports have shown that Chinese have a lower incidence of coronary thrombosis than do either Europeans or Indians (Danaraj et al, 1959; Toh, Low, and Tan, 1970; Barnes, 1972). The multiracial population of Singapore with a population of about two million made up of approximately 76% Chinese, 15% Malays, and 7% Indians seemed to us therefore to offer special opportunities to study some of the ethnic and genetic factors involved in the development of myocardial infarction by analysing the incidence of the disorder in different ethnic groups and looking for possible association of myocardial infarction with the ABO, Rh, Le⁺, Xg⁺ blood groups, G6PD deficiency, and abnormal haemoglobins.

Materials and Methods

Patients. Four hundred and eighty-six consecutive patients of both sexes comprising 213 Chinese, 53 Malays, 199 Indians, and 21 Europeans admitted to the Coronary Care Unit of Medical Unit II and to wards of Medical Unit I of the General Hospital, Singapore between December 1969 and December 1971, formed the sample. These were all cases of myocardial infarction as confirmed by clinical, electrocardiographic, and biochemical investigations.

Controls. For ABO blood groups the published data for blood donors of the Singapore Blood Transfusion Service was taken as control (Chan, 1962). For control series for abnormal haemoglobins, G6PD deficiency, and Xg⁺ blood group our data, previously published for healthy individuals (matched for race and sex) attending the Singapore Anti-Tuberculosis Association for Employees Health Insurance Scheme were used (Saha and Banerjee, 1971a and b; 1973). Another series of healthy individuals (matched for race and sex) from the same source was investigated for Rh and Le⁺ blood groups.

Methods. Blood was collected in fasting condition from each patient between the third and fifth day after the infarction using heparin as an anticoagulant. Blood was stored at 4°C and was tested within 48 hours of collection. Routine blood grouping was carried out by slide test using commercial antisera.* The details of Xg⁺ blood grouping, G6PD deficiency, and haemoglobin typing were the same as published previously (Saha, 1969 and 1970; Saha and Banerjee, 1973).

Received 30 May 1973.

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* Biotest, USA.
Genetic Association in Myocardial Infarction

Table I

DISTRIBUTION OF MYOCARDIAL INFARCTION

<table>
<thead>
<tr>
<th>Group</th>
<th>Population of Singapore (1970 Census)</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (in thousands)</td>
<td>%</td>
</tr>
<tr>
<td>Chinese</td>
<td>1579.8</td>
<td>76.15</td>
</tr>
<tr>
<td>Malays</td>
<td>311.4</td>
<td>15.01</td>
</tr>
<tr>
<td>Indians</td>
<td>145.2</td>
<td>7.00</td>
</tr>
<tr>
<td>Others</td>
<td>38.1</td>
<td>1.84</td>
</tr>
<tr>
<td>Total</td>
<td>2074.5</td>
<td>100.00</td>
</tr>
</tbody>
</table>

m = male; f = female.

Results and Discussion

Table I shows that Indians represent 40.9% of all myocardial infarction cases though they contribute to only 7.0% of the population. On the other hand, Chinese constitute only 43.8% of the patients though they represent 76.1% of the population and Malays represent 10.9% of the patient series against a population contribution of 15.0%. Patients of European descent form 4.3% of the patient series (in the total population Europeans are included in other ethnic groups which make up only 1.8%) but because of the small absolute number they have been excluded from further considerations. From the figures for the three main ethnic groups in the Singapore population it is very suggestive that the relative incidence of myocardial infarction is low among Chinese and Malays compared to that for Indians being 0.1 and 0.125, respectively.

The male/female ratio for myocardial infarction in the present series is 4:6 in Chinese, 12:2 in Malays, and 38:8 in Indians. Toh et al (1970) reported a lower male/female ratio for all three ethnic groups. However it may be noted that male/female ratio of Indians in the general population is disproportionately high in higher age groups, which may partly explain the high sex ratio in Indians.

Table II shows the relative age-specific incidence of myocardial infarction in different ethnic groups in males only. Females have been excluded as the number is too small. Relative incidences have been presented per thousand population in 10-year age groups. It is seen that in all age groups the relative incidence of myocardial infarction is higher in Indians than in Chinese and Malays. Another interesting aspect revealed is that there is a higher relative incidence of the disease in younger people among Indians than in Chinese and Malays. The significance of the higher relative incidence of myocardial infarction among Indians is not apparent at the moment, but is in agreement with previous reports (Danaraj et al, 1959; Toh et al, 1970; Barnes, 1972).

Plasma-cholesterol and plasma-triglycerides are known to be important risk factors for myocardial infarctions (Kannel, Gastelli, and McNamara, 1967; Carlson and Böttiger, 1972). It would be expected that Indians with higher relative incidence of myocardial infarction will have higher levels of those plasma lipids. However, in previous studies in Singapore and Malaya no significant differences of serum total cholesterol levels, lipid phosphorus, triglycerides, and lipoprotein levels were found between Chinese, Malay, and Indians.

Table II

AGE-SPECIFIC INCIDENCE OF MYOCARDIAL INFARCTION (MALES ONLY)

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>No./Thousand</td>
<td>No.</td>
<td>No./Thousand</td>
<td>No.</td>
<td>No./Thousand</td>
</tr>
<tr>
<td>20–29</td>
<td>135.2</td>
<td>1</td>
<td>0.007</td>
<td>21.3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30–39</td>
<td>95.1</td>
<td>16</td>
<td>0.168</td>
<td>17.0</td>
<td>10</td>
<td>0.588</td>
</tr>
<tr>
<td>40–49</td>
<td>68.0</td>
<td>37</td>
<td>0.544</td>
<td>15.8</td>
<td>23</td>
<td>1.456</td>
</tr>
<tr>
<td>50–59</td>
<td>51.9</td>
<td>64</td>
<td>1.233</td>
<td>8.3</td>
<td>8</td>
<td>0.964</td>
</tr>
<tr>
<td>60–69</td>
<td>33.9</td>
<td>47</td>
<td>1.386</td>
<td>3.8</td>
<td>7</td>
<td>1.842</td>
</tr>
<tr>
<td>70 and over</td>
<td>11.8</td>
<td>10</td>
<td>0.847</td>
<td>1.3</td>
<td>1</td>
<td>0.769</td>
</tr>
<tr>
<td>Total</td>
<td>395.9</td>
<td>175</td>
<td>0.442</td>
<td>67.5</td>
<td>49</td>
<td>0.726</td>
</tr>
</tbody>
</table>

* 1970 Census.

Table III shows the distribution of ABO blood groups in Chinese, Malay, and Indian patients compared to normal controls. There is no significant difference in the distribution of ABO blood groups between patient and control series in any of the ethnic groups. Most of the populations studied, including two Indian series (Bronte-Stewart, Botha, and Krut, 1962; Srivastava, Thakur, and Das, 1966) had a higher incidence of myocardial infarction among those with blood group A. There is no published data for Chinese and Malays. However, there is a higher incidence of myocardial infarction among Indians with blood group A, but the association is only significant at the 5% level if half of AB is taken into account (A:O = 1:42 \( p < 0.05 \); A+AB:O = 1:49 \( p < 0.05 \)). However, the possibility remains that there is higher mortality among A-group individuals compared to those who survived the attack of myocardial infarction. Furthermore, preliminary studies of prehospital deaths from acute myocardial infarction suggest that as many patients die outside the hospital as in hospital.

It has been reported that Le\(a^+\) individuals have higher serum cholesterol than Le\(a^-\) persons (Langman et al., 1969) and one would expect therefore higher incidences of Le\(a^+\) persons amongst myocardial infarction patients. However, Table IV shows the distribution of Le\(a^+\) blood group in 184 patients with myocardial infarction and 425 healthy individuals of three ethnic groups with no significant differences in any of the ethnic groups between the disease and control series. Further work with larger series is needed for a valid conclusion.

Table V shows the distribution of the Rh(D) blood group of 354 patients with myocardial infarction and 615 healthy individuals. There was again no significant difference in the frequency of Rh(D) between patient and control series. Out of these, 64 patients and 165 controls were tested with five anti-sera (D, C, E, c, and e): there was no significant difference in the frequency distribution of the Rh subtypes.

Tables VI, VII, and VIII show the distribution in patients and controls of abnormal haemoglobins, G6PD deficiency, and Xg\(a^+\) blood groups, respectively. There was also no significant difference in the frequency distribution of these genetic parameters between myocardial infarction and control series in any of the three ethnic groups.
Two aspects of the results emerging from the present study require clarification. The first concerns the striking difference in the relative incidence of myocardial infarction among Indians when compared with Chinese and Malays living in the same urbanized environment; the second concerns the failure to demonstrate the excess of blood group A among myocardial infarcted patients in any of the three ethnic groups studied here. High incidence of myocardial infarction has been reported in Indians in India also (Padmavati, Gupta, and Pantulu, 1959; Sarvotham and Berry, 1968).

The increased incidence of myocardial infarction amongst Indians confirms reports by other investigators, but it does not elucidate the reasons for this striking difference in the present report and other instances between the Indians on one hand and Malay and Chinese on the other (Danaraj et al., 1959; Toh et al., 1970; Barnes, 1972). Though genetic factors predisposing to myocardial infarction may be involved the fact that many investigations have attempted to implicate dietary difference as the main aetiological factor explaining susceptibility to myocardial infarction does suggest that this may be a factor in the Singapore situation (Keys and White, 1958).

Superficially there are similarities in the dietary patterns of Indians and Chinese in Singapore. Both are rice eaters and both use more or less the same basic ingredients of food. There is, however, a striking difference in the manner in which food is prepared by the Indian and Chinese communities; the former use mostly food fried in cooking oil such as coconut oil, ghee, etc., which are high in saturated fats, whereas the latter use mostly boiled or steamed food and such oil used (ground nut oil, soya bean oil, linseed oil, and lard) is high in polyunsaturated fats.
A substantial proportion of the Indian population in Singapore is still almost exclusively vegetarian, almost none of the protein in their diet coming from animal sources. Chong (1961/1962) quoted the percentage of calories derived from fat as 11·4% to 18·3% for Malay army and police personnel, 15·8% for Indian estate labourers, and 16·7% for Chinese labourers; these are very selective, low-income groups and do not represent the populations as a whole. However, we have recorded an intake of about 30% of calories from fat in medical students and police forces, mostly of Chinese origin, of both sexes and in pregnant and non-pregnant women during our study of energy metabolism in Singapore (Banerjee and Saha, 1970; Banerjee, Tan, and Saha, 1972). Wysham, Kohli, and Mulholland (1970) reported an intake of 29·5% of calories as fat in a Punjabi population; about 90% of which was saturated fat. In an early study of diet (by chemical analysis) in India a similar fat intake was observed (Banerjee, Lal, and Saha, 1965). Furthermore, Malmos and Wigand (1957) and Bronte-Stewart (1958) have reported the serum cholesterol raising effect of coconut oil in man when fed on fat levels of about 40% of total calories. It will be of interest to investigate further, in more detailed studies, the serum lipids in cases of myocardial infarction and in matched healthy controls from the three ethnic groups in Singapore. Such a study should include persons in all age groups and involve a simultaneous search for association of serum lipid levels with genetic markers.

The present study has failed to reveal any significant association between myocardial infarction and any of the genetic markers investigated, with the exception of the A factor of the ABO blood group system when this is considered together with AB group individuals among Indians. By itself a single significant association of this kind would not be noteworthy, since a large number of comparisons were carried out and it would be expected that some at least of these would show a significant difference at the 5% level. However it is of interest that the deviation between the myocardial infarction patients and controls is in the direction of an excess of group A among Indian patients as recorded in a number of other independent investigations (Mourant et al., 1971). It is possible that a larger series in Singapore would make the association between group A and myocardial infarction statistically significant, at least in Indians.

The authors are grateful to the Medical Superintendent of the General Hospital, Singapore for permission to carry out this study and to Dr R. L. Kirk and Professor H. M. Whyte for their help in the preparation of this manuscript. Thanks are also due to Miss E. Lowrie for secretarial assistance.

**REFERENCES**


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