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Myocardial Infarction in Young Ceylonese

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Abstract : Forty patients below the age of 40 years with myocardial infarction were studied with a view to finding the aetiological factors of the disease. The cholesterol values of the young patients with myocardial infarction were found to be significantly higher than those of the controls. The lipoprotein profile of young infarcts using nephelometry showed that the M fraction (= VLDL) in the patients was significantly higher than that of the controls. Hyperlipoproteinaemia occured in 45% of the young patients with myocardial infarction, W.H.O. type IV being the commonest. Another interesting feature was that arcus cornea occured in 50% of the young patients with myocardial infarction. 40% of the patients gave a family history of myocardial infarction in first degree relatives under the age of 60 years. Obesity, hypertension and diabetes mellitus are uncommon risk factors in our series. 90% of the patients had one or more of the risk factors for C.H.D. the major risk factors being smoking and abnormal lipoprotein patterns.

The cholesterol, triglycerides and "M" values (VLDL) of the relatives of the patients with myocardial infarction were significantly higher than those of the controls. Elevated VLDL appears to be a risk factor in the young patients with myocardial infarction.

1. Introduction

Coronary heart disease (C.H.D.) appears to have become a serious problem in Sri Lanka. For many years it was considered a disease of middle and old age; more recently there appears to be an increasing incidence in younger individuals.[14,17] This paper therefore focusses attention on the risk factors present in those individuals below the age of 40 years with a definite myocardial infarction.

2. Subjects, Methods and Terminology

The subjects comprised a group of 40 patients below the age of 40 years at the time of the first myocardial infarction, investigated in the Cardiology Unit, General Hospital, Colombo, between January and November 1974. Out of the 40 patients, 32 were admitted in the acute stage of the illness, while 8 patients had well documented myocardial infarction prior to January 1974. Those who failed to survive following the infarction were not included in this study.

All the patients were questioned with regard to (1) occupation and income, (2) any past history of ischaemic heart disease, hypertension, diabetes mellitus or cerebrovascular accidents, (3) smoking habits and (4) history of ischaemic heart disease, diabetes mellitus, cerebrovascular accidents or hypertension among the first degree relatives. In addition to the above, the females were questioned regarding the use of oral contraceptives.

The physical examination included : (1) a full examination of the cardiovascular system, (2) measurement of height and weight and (3) examination for clinical signs of hyperlipoproteinaemia such as arcus corneae, xanthomata, yellow deposits over palmar creases, yellow papules on skin and mucose, lipaemia retinalis and hepatosplenomegaly.

In every patient the following investigations were done routinely : (1) fasting blood sugar and if this is above 100 mg% or if there was a family history of diabetes mellitus in the first degree relatives, a glucose tolerance test 3 weeks following the ischaemic episode, (2) haemoglobin and packed cell volumes, (3) white blood count and differential count, (4) erythrocyte sedimentation rate, (5) plasma proteins, (4) serum cholesterol by Sackett's method, (7) serum triglyceride using method described by Laurell and Scan, after a 14 hour fast, (8) serial E.C.G's and (9) teleradiogram of the chest. The investigations (1)—(5) and (9) were done 2 weeks following the infarction. If the E.S.R. was persistently high, other laboratory tests to exclude collagenosis were performed.

Lipoprotein patterns of the young patients with myocardial infarction, their relatives, and controls were estimated by membrane filtration and nephelometry.[20,21] This is a simple and an inexpensive method of lipoprotein analysis. Blood was drawn after a 14 h fast at least 3 months after the attack of myocardial infarction. All the patients were advised to stop all the lipid lowering agents for at least one month prior to lipoprotein estimation. In this method L particles (chylomicrons, Sf $>$ 400), were separated from M particles (VLDL, Sf 20—400) by membrane filtration of diluted serum and the concentration of particles in each fraction quantified by measurement of light scattering intensity (LSI) using the nephelometer described by Thorp *et al.*[23] The concentrations of the three lipoprotein fractions S (beta fraction, Sf 0—20), M(prebeta, Sf 20—400) and L(chylomicrons, Sf $>$ 400), were calculated from the nephelometric measurements of LSI and the value of serum cholesterol, using the equation described by Stone *et al.*[22] These authors have shown a high degree of correlation between these estimated values and those obtained by analytical ultracentrifugation.

Twenty patients admitted to Cardiology Unit, suffering from noncardiac chest pain, congenital heart disease, chronic rheumatic heart disease and hypertrophic cardiomyopathy between ages of 20 and 40 years were used as a control group. Ten first degree relatives of the subjects were also studied.

Glucose tolerance was assessed by conventional criteria. Patients were considered overweight if their weight was 20% more than normal weight for the respective age, sex and height.[16]

The criteria for the diagnosis of myocardial infarction were the presence of 2 or more of the following : (1) characteristic clinical presentation (2) pathological Q waves, ST elevation or T wave inversion in the electrocardiogram with evolutional changes and (3) rise in serum aspartate aminotransferase (SGOT) and/or rise in total level of lactic acid dehydrogense (LDH) as well as a rise over 70% of the heat stable fraction of the LDH.

A person was considered to be suffering from hypertension when there was sustained diastolic pressure of more than 90 mmHg. In each set of cholesterol estimations made, the laboratory standards and I.C.I. reference standards were estimated as a check on accuracy. A person was considered to be hypercholesterolaemic if the serum cholesterol level was higher than 240% and hypertriglyceridaemic if the serum triglyceride level was higher than 140% respectively. The upper limit of normal for S fraction was taken as 47 mg% ; the upper limit of normal M fraction was taken as 470 mg%.

3. Results

3.1. Age

The age distribution of the patients with myocardial infarction is given in Table 1, which shows that myocardial infarction is rare before the age 30. The mean age of the group is 34.0 (± 4.89) years.

TABLE 1. Age distribution of young patients with myocardial infarction.

Age	No. of cases	Percentage
20 — 24	1	2.5
25 — 29	5	12.5
30 — 34	11	27.5
35 — 39	23	57.5
Mean age 34.0 (± 4.89)	40	100.0

3.2. Sex

There were only 4 females. Male : Female ratio in our group was 9 : 1.

3.3. Occupation

Table 2 shows that the majority of the patients with myocardial infarction belong to the middle and low income groups. The clerical staff was most commonly affected, followed by technicians.

TABLE 2. Occupations of young patients with myocardial infarction.

Occupation	No. of subjects
Doctors	4
Executives	3
Businessmen	4
Engineers	1
Planters	1
Army Personnel	2
Priests	1
Technical Staff	5
Clerical	10
Teachers	2
Stenographers	1
Housewives	2
Sailors	1
Rubber Tappers	1
Unemployed	2
	40

3.4. E.C.G. Appearances

Seventeen patients developed inferior transmural infarctions and 14 had anterior transmural infarctions. There was one patient who had two infarctions.

3.5. Risk Factors

3.5.1. *Hypercholesterolaemia and Hypertriglycerideamia*

Twelve patients had hypercholesterolaemia and 12 had hypertriglyceridaemia (Table 3). Of these, 5 patients had both hypercholesterolaemia and hypertriglyceridaemia. The cholesterol values of young patients with myocardial infarction were observed to be significantly higher than those of the controls (Table 4).

TABLE 3. Risk factors in young patients with myocardial infarction.

Risk factors	No. of patients	Percentage
Hypercholesterolaemia*	12	30.0
Hypertriglyceridaemia*	12	30.0
Hypertension	5	12.5
Smoking	27	67.5
Abnormal glucose tolerance	2	5.0
Obesity	9	22.5
F.H. of I.H.D.	16	40.0

*5 patients had both hypercholesterolaemia and hypertriglyceridaemia.

TABLE 4. Comparison of serum lipid values among patients with myocardial infarction and controls.

	Young Infarcts n = 40		Control n = 20		
	Mean	S. D.	Mean	S. D.	
Age	34.0	4.89	30.0	5.38	P > 0.1
B.P. Systolic	125.0	13.81	120.0	9.43	P > 0.1
B.P. Diastolic	78.0	4.58	78.0	7.35	P > 0.1
Serum Cholesterol	231.0	50.01	204.0	31.37	0.05 > P > 0.02
Serum Triglycerides	108.0	106.10	64.0	37.38	0.1 > P > 0.05

3.5.2. *Lipoprotein estimation*

Lipoprotein estimation showed that L(Sf > 400) and S(=Sf 0—20), values of patients showed no significant difference when compared to controls (Table 5); the M values (=Sf 20—400) of patients were significantly higher than those of the controls. In case of relatives of patients with myocardial infarction, cholesterol, triglyceride and M values were significantly higher than those of the controls (Table 6). Table 7 shows that out of 40 patients, 2 had type IIa pattern, 3 had IIb pattern, and 13 had type IV pattern indicating that 45% of the young patients with myocardial infarction had some type of hyperlipoproteinaemia.

TABLE 5. Comparison of serum lipoprotein values of patients and controls.

	Young Infarcts n = 40		Controls n = 20		
	Mean	S.D.	Mean	S.D.	
Age	34	4.89	30	5.38	p > 0.1
L(Sf over 400)	20	11.75	15	6.48	0.1 > P > 0.03
M(Sf 20 — 400)	450	246.12	306	81.01	0.02 > P > 0.01
S(Sf 0 — 20)	392	101.54	344	66.46	P > 0.1

3.5.3. *Hypertension*

The mean systolic blood pressure for the young infarcts (Table 4) was 125 mmHg (S.D. 13.81) and diastolic 78 mmHg (S.D.4.58) and there were 5 patients who had been treated for diastolic hypertension in our series. In three of them, blood pressure returned to normal following the infarction. In the remaining 2, persistent diastolic pressures of 95 to 100 mmHg and 105 to 110 mmHg respectively were recorded following the myocardial infarction.

TABLE 6. Comparison of serum lipid and lipoprotein values of relatives of patients and controls.

	Relatives of Young Infarcts n — 10		Controls n — 20		
	Mean	S.D.	Mean	S.D.	
Age	33.0	4.36	30.0	5.38	
B.P. Systolic	124.0	11.49	120.0	9.43	
B.P. Diastolic	84.0	5.91	78.0	7.35	
Serum Cholesterol	235.0	20.53	204.0	31.37	$0.05 > P > 0.02$
Serum Triglycerides	132.0	51.18	64.0	37.38	$0.001 > P$
L(Sf > 400)	18.0	10.72	15.0	6.48	$P > 0.1$
M(Sf 20 — 400)	550.0	29.43	307.0	81.07	$0.001 > P$
S(Sf 0 — 20)	374.0	54.55	344.0	66.46	$P > 0.1$

TABLE 7. Frequency distribution of different types of hyperlipoproteinaemia.

Type of Hyperlipoproteinaemia		Frequency distribution Young myocardial infarction	
Classification		Number	Percentage
SML	*WHO recommended*		
S	11a	2	5.0
SM + MS	11b	3	7.5
M + ML	IV	14	32.5
ML*	V	0	0

*ML patterns in which the large particles (Sf > 400) concentration exceeded 100mg/100ml.

3.5.4. *Cigarette Smoking*

There were 27 smokers and 13 non-smokers (Table 8). There were no patients who gave a history of cigar or pipe-smoking. Sixteen patients gave a past history of smoking less than 20 cigarettes a day and 7 had smoked over 3 packets (30 cigarettes) a day for several years.

3.5.5. *Diabetes Mellitus*

There were only 2 cases of diabetes mellitus confirmed by glucose tolerance test. Both were mild diabetics and were controlled on diet alone.

TABLE 8. Prevalence of cigarette smoking in young patients with myocardial infarction.

No. of cigarettes smoked per day.	No. of subjects
Less than 20	16
20 — 30	4
Over 30	7
	27

TABLE 9. Clustering of risk factors in patients with myocardial infarction.

No. of risk factors present	No. of subjects	Percentage
0	4	10.0
1	12	30.0
2	11	27.5
3	10	25.0
4	3	7.5

3.5.6. *Family History*

Sixteen patients gave a history of myocardial infarction in first degree relatives under the age of 60 years. Of these, 8 patients gave a history of myocardial infarction in 2 or more of their first degree relatives. Six patients gave a family history of diabetes mellitus among first degree relatives ; there were no cases with a family history of hypertension.

3.5.7. *Obesity*

Nine of the 40 patients had obesity.

3.5.8. *Haemotocrit, Sedimentation and Plasma Proteins*

Estimations of haemoglobin and packed cell volumes were done in all the cases. These values were found to be within normal limits. Erythrocyte sedimentation rate and plasma proteins were within normal limits.

3.5.9. *Arcus Cornea and Xanthomaia*

Twenty patients had arcus corneae and 5 patients had xanthelasma. Tuberous xanthomata were seen only in 3 patients. There were no patients with yellow papules over the skin or yellow palmer creases or with lipemia retinalis. Two patients had slight hepatomegaly but they gave a past history of alcohol consumption.

4. Discussion

It has been recognised for many years that ischaemic heart disease is an uncommon condition under the age of 40. A review of recent literature emphasies that more and more frequently coronary heart disease is diagnosed in young adults.[14,17,24]

In Sri Lanka myocardial infarction occurs on a background of atherosclerosis.[5] Table 3 shows that well known risk factors such as hypercholesterolaemia, hypertriglyceridaemia, hypertension, smoking, obesity, abnormal glucose tolerance and family history of ischaemic heart disease in first degree relatives were quite common in this group of young infarcts.

Table 9 shows that a majority of patients had more than one risk factor. In 4 patients there was no obvious risk factor and in 12 patients, only one risk factor was present.

Diabetes mellitus has often been suggested as an important explanation for the premature development of ischaemic heart disease.[7] In our series only 5% of the patients had evidence of abnormal glucose tolerance. In the series reported by Oliver,[12] only 4 out of 94 patients had abnormal glucose tolerance. In our series only 12.5% of patients gave a past history of hypertension. Thus hypertension and diabetes mellitus are uncommon risk factors in our series.

The effect of obesity on the incidence of coronary heart disease remains uncertain. French and Dock[6] analysing the clinical and pathological features of 80 fatal cases of young soldiers between 20 and 36 years revealed that the most striking presumable predisposing factor was overweight which was present in 91% of the cases and the basis of the coronary occlusion was found to be arteriosclerosis in all cases. Ancel Keys and his colleagues[8] suggested that neither relative weight nor obesity assessed by skinfold thickness had any significant effect on future coronary heart disease if the effects of increased age, serum cholesterol blood pressure and smoking were discarded. Authors of the Framingham study predict that for each 10% increase in weight, there is a 30% increase in the incidence of coronary heart disease. 9 (22.5%) in our series were obese and the incidence of obesity is higher than in an earlier series reported from Sri Lanka.[11]

In our series, 12 patients (30%) had hypercholesterolaemia and 12 (30%) had hypertriglyceridaemia (Table 3). Of these, 5 had both hyperchloesterolaemia and hypertriglyceridaemia. The cholesterol values of the young patients with myocardial infarction were observed to be significantly higher than those of the controls ($P<.05$) whereas comparison of the triglyceride levels of patients with controls showed no significant difference ($P>05$). Lewis and colleagues[10] too, found a similar incidence of hypercholesterolaemia and hypertriglyceridaemia in their coronary patients of the age group 26 to 39 years. There can be little doubt that an increase in cholesterol

and triglycerides levels predispose to overt and early appearance of clinical coronary disease.[10] There is evidence that in younger patients with I. H. D. hypercholesterolaemia is a commoner abnormality than in older patients.[13] A prospective study in Stockholm found that the occurrence of new events in coronary artery disease were linearly related to increased triglycerides, cholesterol and smoking and not to an increase in weight/height index.[1] Valentine *et al.*[24] investigated the angiographic appearances of coronary arteries in 40 patients below the age of 40 years with documented cardiac infarction and found an association between elevation of triglyceride levels with the more severe and more diffuse type of occlusive process. Raised triglyceride values were interpreted to be an independant risk factor for I.H.D. in 2 recent prospective surveys[1,15] but not in others.[2]

Estimation of the lipoprotein profile of young infarcts using nephelometry showed that the M fraction (VLDL, Sf 20—400) in the patients was significantly higher than that of the controls ($P < .02$) In the series reported by Lewis *et al.*[10] increase in the VLDL (M) fraction was the most pronounced abnormality detected in the young coronary patients and VLDL cholesterol contributed substantially in some patients to the total serum cholesterol. There is controversy regarding the changes in M fraction following an acute myocardial infarction. Smith[18] reported a rise in triglyceride rich prebeta (M) fraction reaching a maximum in 3 to 5 weeks after cardiac infarction. Dodds and Mills[3] confirmed these findings and showed that return to normal levels occured after the 8th week. The lipoprotein estimation in our cases was performed at least 3 months after the attack of cardiac infarction. The significantly high M(Sf 20—400) levels in our cases suggest that elevated M fraction may be a risk factor for coronary heart disease in young Ceylonese.

Another interesting feature in our series is that the triglyceride values and the M fraction of the relatives of the young infarcts were significantly higher than those of the controls, ($P < .001$) whereas the triglycerides of the patients were not significantly different from those of the controls (Tables 4 and 6). It is probable that the patients had modified their diet during the first 3 months following infarction to alter their triglyceride values from what prevailed before the infarct. If we assume that the dietary habits of the young patients with myocardial infarction and their relatives are similar, then the patients might have made drastic changes in their diet, since their "attack" to lower their triglyceride values in particular, whereas the relatives who had not been adequately motivated to alter their diet would show triglyceride values higher than those of the controls.

Table 7 shows that there is a very high prevalence of hyperlipoproteinaemia as assessed by membrane filtration and nephelometry.[20] Type IV hyperlipoproteinaemia appears to be the commonest type, and 45% of our patients showed some lipoprotein abnormality. Our series is similar to the series reported by Stone

and Dick[19] who using the same method of lipoprotein estimation found that 20% of his control group and 40% of the ischaemic heart disease patients had hyperlipoproteinaemia, type IV (W.H.O.) being the commonest. The method of membrane filtration and nephelometry has been shown to produce reproducible analysis in different laboratories.[21] The same authors have compared the results of analytical ultracentrifugation with those obtained by membrane filtration and nephelomtery and have demonstrated a high correlation ($r = 0.96$) between ultracentrifugation and nephelometric measurements. In the series reported by Lewis *et al.*[10], out of 15 patients under the age of 40 years 11 had hyperlipoproteinaemia, the commonest abnormality being type IV. The high incidence of hyperlipoproteinaemia in young infarcts has not been reported previously from Sri Lanka.

Paul and Siegel[14] in a study of 19 cases of myocardial infarcts below the age of 40 years found that 95% of the patients were cigarette smokers. Serum cholesterol was higher in the patients compared to the controls. The blood pressures were not very different although the diastolic pressures were higher in the coronary group. A family history of cardiovascular disease and diabetes occurring before the age of 65 years was found in approximately half the coronary group. Our group is similar to the series reported by Paul and Siegel[14] in that cigarette smoking, hypercholesterolaemia and positive family history are common findings in both series (Table 3).

Arcus corneas below the age of 40 years is associated with premature atherosclerosis. In our series 20 (50%) had arcus corneae. Three patients with type II hyperlipoproteinaemia had xanthomata in addition to arcus corneae.

The most striking feature in our series is that 90% of the patients had one or more of the risk factors for coronary artery disease. The major risk factors in our group were smoking and abnormal lipoprotein patterns.

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