

EPIDEMIOLOGICAL ASPECTS OF MACROVASCULAR DISEASE IN DIABETES MELLITUS

M.M.S. Ahuja

Macrovascular disease in diabetes contributes to significant morbidity and mortality. There seems paucity of information on the exact causation and pathogenicity of the promotive factors for the vascular disease, especially in context of the differences observed in the different ethnic groups. During 1973-1978, W.H.O. conducted a multinational study on vascular disease, employing standardized methods of assessment, to compare its prevalence and if possible, relate these to the profile of population or the characteristics of diabetes. This presentation is a part of this study and the available data has been analysed with the objectives of :

- a) To determine the prevalence rate of macrovascular disease in some well defined diabetic populations with different ethnic and environmental characteristics.
- b) To seek relationship of profile of population, age at diagnosis, sex, adiposity, cigarette smoking, with macrovascular disease.
- c) To seek relationship of macrovascular disease with the characteristic of diabetes, duration, glycaemia, lipid profile, hypertension and mode of treatment.

Methodology

The diabetics screened for this study were from amongst the representative sample from the on going diabetic clinics in a country and being under treatment for control of diabetes for some time. Age groups included those between 35-54 years with the known duration of diabetes varying from 1 to 14 years. Patients were further stratified based on age and duration basis; each subset having a minimum of 28 patients.

For the cardiovascular evaluation, questionnaire of Rose and Blackburn (1968) was followed, 12 lead resting ECG read centrally by two experts, using established criteria (Minnesota code) for the interpretation.

Interpretation of the macrovascular disease was based on following parameters :

ECG Coronary probable (1.1, 1.2, 7.1) (Major Q wave abnormalities and LBBB)
Coronary possible (1.3, 4.1, 4.2, 4.3, 5.1, 5.2, 5.3)
Evidence of stroke
Amputation, gangrene, trophic ulcer.

Blood glucose were determined using true glucose method and were converted to plasma values centrally for uniformity (data is available for 9 populations for this). Serum

Head Dept. of Endocrinology, Metabolism and Diabetes All India Institute of Medical Sciences, New Delhi-29.

cholesterol determinations were standardized in a central laboratory USPHS Centre for Disease Control, Atlanta. Triglyceride determinations were performed locally and are available for 5 populations only.

Results

Data on 3583 diabetics; (1745 males and 1938 females), 34-56 years of age from 9 populations was made available for this analysis. These populations include U.K., Poland, East Germany, India, Japan, Cuba, American Indians Oklahoma, Arizona and Switzerland, Table-I shows the prevalence of the macrovascular disease in the different populations vrs. pooled data (W.H.O. 1979)

- (i) *Coronary artery disease* : End point being the major Q wave changes in ECG, this is maximal in Oklahoma Indians while least frequent in Japanese. In other centres, prevalence is as for the pooled data.
- (ii) *Peripheral vascular disease* : End point being the amputation, this is maximum in Arizona Pima Indians or Poland while it is again least prevalent amongst Japanese or Indians.
- (iii) *Cerebrovascular disease* : End point being stroke, this is maximal in Oklahoma Indians (Havana figures have some discrepancy), while it is least frequent in Japanese and Indians.

Characteristics of the population, i.e. age, body build, duration of diabetes, smoking, blood glucose, serum cholesterol, BP and mode of treatment (insulin) are indicated in Table-II. Age (range 45-47 years mean 46 years) and duration (range 6-15 years, mean 9 years) is comparable to all populations screened. Systolic blood pressure is 125-146 mm Hg range. In body build, Oklahoma and Arizona Pima Indians have maximum adiposity, while Japanese and Indians have least of it. Blood glucose values indicate less severe glycaemia in East Berliners, Indians and Cubans. Cholesterol values are lower amongst Japanese and Indians and Arizona Pima Indians.

Risk factors were analysed in respect with and without manifestations of macrovascular disease, and it becomes evident that risk factors vary for the different types of macrovascular disease (Table-III).

Difference in age does not relate to variation for the vascular disease. In sex male predominate for the leg vascular disease, other vascular disease are equal in both sexes. *Over-weightness* is significantly related only to coronary artery disease (major Q wave changes). *Smoking* has relationship with leg vascular disease, especially intermittent claudications. *Duration* is significant for leg vessel disease and stroke but not for the coronary artery disease. *Plasma glucose* is significant for leg vascular disease, but not for coronary artery disease or stroke. *Systolic* blood pressure is not significant for vascular disease except for intermittent claudication.

TABLE I
Percent with macrovascular disease by population

Population	Major ECG Q waves		Any major ECG abnormality		Leg vascular disease		Amputation		Intermittent Claudication		Stroke		n								
	M*	F*	T*	M	F	T	M	F	T	M	F	T	M	F	T						
London	0.9	4.9	2.6	15.7	14.6	15.3	5.6	1.2	3.6	2.8	1.2	2.1	3.7	0	2.1	0.9	2.4	1.6	108	85	193
Switzerland	6.2	4.5	5.4	16.3	14.0	15.2	5.2	0.9	3.1	4.8	0.5	2.7	0.4	0.5	0.4	2.2	1.8	2.0	229	221	450
Warsaw	5.5	1.5	3.5	16.5	13.8	15.1	7.7	3.8	5.7	6.3	2.4	4.3	1.4	1.4	1.4	1.4	3.3	2.4	208	212	420
Berlin (GDR)	2.9	9.5	6.0	16.5	21.8	18.9	1.8	2.7	2.2	1.2	0.7	0.9	0.6	2.0	1.3	1.2	2.0	1.6	171	147	318
New Delhi	6.5	3.0	4.8	20.6	17.3	19.0	2.7	0.4	1.6	1.1	0	0.6	1.5	0.4	1.0	1.5	1.3	1.4	262	237	499
Tokyo	1.9	1.8	1.9	10.6	11.7	11.1	0.5	0.6	0.5	0.5	0	0.3	0	0.6	0.3	1.4	1.2	1.4	209	165	374
Havana	5.0	3.4	4.2	12.0	9.9	10.9	6.5	2.1	4.2	5.5	0.9	3.0	1.5	1.3	1.4	6.5*	9.5*	8.1*	200	232	432
Oklahoma Indians	9.5	8.9	9.2	20.5	25.6	23.5	1.1	2.0	1.6	0.7	2.2	1.6	0	0	0	3.5	3.5	3.5	283	403	686
Arizona Pima Indians	4.0	1.5	2.4	24.3	13.5	17.4	4.0	5.1	4.7	4.0	5.1	4.7	0	0	0	2.7	2.2	2.4	75	136	211
Pooled Data	5.3	4.7	5.0	16.8	16.9	16.8	3.7	2.0	2.8	2.8	1.4	2.1	0.9	0.7	0.8	2.5	3.4	2.9	1745	1838	3583
Subject In Whom Glucose Not Measured	4.7	5.6	5.2	16.3	17.2	16.7	3.8	3.8	3.8	1.6	2.5	2.0	2.7	1.3	2.0	2.0	1.8	1.9	449	446	895

*Male, female, total.

*In Havana, the high rate of stroke was thought to be, in part, spurious, because of the way the standard stroke question was understood when translated into Spanish.

TABLE II

Characteristics by population and for pooled data

Characteristics	POPULATION										Pooled
	London	Switzer-land	Warsaw	Berlin	New Delhi	Tokyo	Havana	Oklahoma Indians	Arizona Pima Indians		
Mean age (yrs.)	47	45	47	47	46	47	45	46	47	46	46
Adiposity (% ideal wt.)	111	116	125	123	112	100	121	146	140	123	123
Mean duration diabetes (yrs.)	15.9	11.5	11.4	8.1	8.1	9.1	10.9	6.1	9.6	9.5	9.5
% smokers	42	32	35	36	17	44	52	42	30	37	37
Mean plasma glucose (mg/dl)	273	191	218	150	175	157	160	198	233	189	189
Mean serum cholesterol (mg/dl)	234	247	215	244	198	197	245	209	190	219	219
Mean systolic B.P. (mm Hg)	135	139	142	146	136	132	144	135	125	138	138
% who take insulin	69	55	59	10	23	31	27	20	35	39	39
Mean serum triglyceride (mg/dl)	103	176	161	188	—	—	—	231	—	191	191
n	193	450	420	318	499	374	432	686	211	3583	3583

TABLE III

Mean value for selected variables in those with and without manifestations of macrovascular disease

Abnormality	Age (year)	% Male	Mean Adiposity % ideal weight	Smokers	Duration Diab. (yrs.)	Plasma glucose (mg/dl)	Syst. B.P. (mm/Hg)	Serum Cholesterol (mg/dl)	Serum Triglyceride (mg/dl)
Major Q abnormality	Yes	51.4	131	37	10.0	185	144	228	259
	No	48.6	122	37	9.5	189	137	211	185
Any major ECG abnormality	Yes	48.7	127	34	9.7	191	145	221	227
	No	48.8	122	37	9.5	189	136	210	182
Leg vascular disease	Yes	63.4	120	40	15.0	209	145	209	190
	No	48.3	123	36	9.3	189	137	213	191
Amputation	Yes	65.3	124	36	15.2	222	142	209	205
	No	48.4	123	37	9.5	189	137	212	190
Intermittent claudication	Yes	57.1	115	50	13.5	177	151	209	148
	No	48.7	123	36	9.5	189	137	212	190
Stroke	Yes	41.8	124	37	11.4	196	147	215	230
	No	48.9	123	37	9.4	189	137	212	189
Any macrovascular disease	Yes	48.8	126	36	10.2	193	144	218	219
	No	48.7	122	37	9.3	188	136	211	182
Pooled data	46.4	48.7	123	37	9.5	189	138	212	191
	3538		3571		3583	3583	3582	3523	1911

Serum cholesterol is as well significantly correlated only to coronary artery disease (major Q wave) while serum triglycerides are significant in coronary artery disease and stroke but not for peripheral vessel disease.

DISCUSSION

There is enough evidence forthcoming from this study that the macrovascular disease has variation in its distribution i.e. involvement of coronary, cerebral or peripheral vessels amongst the different populations. There is no single population profile in which all three are significantly more, i.e. population with maximal coronary vessel disease does not have equivalent cerebral or peripheral vessel involvement indicating that etiological determinants for different vessel involvement may be different.

In the population profile, India have lower figures for overweightness, less number as smokers, less severe hyperglycaemia, lower cholesterol values yet coronary artery disease, i.e. major Q wave changes are equivalent to the figure as of pooled data. With similar background in Japanese (except smoking that is more frequent) macrovascular disease of all types is least frequent of all the populations studied. Similarly, break up of risk factors brings out that there is lack of uniformity of these for each vessel disease while for the pooled data, overweightness, serum triglycerides has correlation to coronary artery disease, duration of diabetes, smoking, blood pressure, hyperglycaemia, serum cholesterol are not significantly related. For cerebral vascular disease, duration of diabetes, blood pressure and serum triglyceride have positive relationship while this is independent of overweightness, smoking, hyperglycaemia and serum cholesterol. Lastly, in peripheral vessel disease the risk factor relationship is abundant and relates to male sex, duration, smoking, hypertension, hyperglycaemia and serum triglycerides (6 out of 8 factors), while it is not related to overweightness or serum cholesterol.

As regards relation of mode of treatment, though coronary artery involvement does not seem related, stroke and amputation are more common in insulin treated patients (stroke in insulin treated group is 5.3%, while in non-insulin treated, it is 2.6%, amputation in insulin treated group 4.3% while in non-insulin treated group it is 10%).

This study is indicative that macrovascular disease is not directly related to diabetes and there exist other factors in each population which influence the frequency and distribution of this complication.

SUMMARY

Pattern of macrovascular disease differs in various population groups.

Risk factors eluded so far are not consistently present in each type of manifestation of macrovascular disease.

Diabetes is not directly related to the type of presentations of macrovascular disease except for peripheral vascular disease.

There is need to study elaborately the contributory factors in each population to identify the causation for such variations in the manifest macrovascular disease.

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