

RISK FACTORS IN STROKE PATIENTS

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SYNOPSIS

A Stroke Survey was conducted to study the clinical and social history of patients with stroke so as to identify the risk factors associated with stroke in Singapore. A questionnaire was devised to determine the symptoms of impending stroke and the past history of episodes of transient ischaemia. The result of the Survey shows that about 40% had, before the onset of stroke, experienced some form of transient ischaemic attacks mostly related to motor power deficiency. The patients were found also to be mildly hypertensive with a mean systolic pressure of 162 mm Hg and a mean diastolic pressure of 95 mm Hg. The plasma lipid value was in general high with mean plasma cholesterol of 215 mg/dl and triglyceride of 141 mg/dl, whilst high density lipoprotein cholesterol was low with a mean of 41 mg/dl.

INTRODUCTION

Stroke is one of the principle causes of death in Singapore (11% of total deaths in 1982) and also a major cause of disability. Multivariate etiologies predispose the patient to stroke and each etiology is significant in its contribution. Its consequence to the individual poses many problems in treatment, rehabilitation and social re-adjustment for the patient, his family and his community. Recognizing the importance of stroke in Singapore, a Stroke Committee was formed in February 1983 at the Ministry of Health with the objective of trying to identify the high risk factor levels that predispose patients to develop stroke.

MATERIALS AND METHOD

80 consecutive patients admitted to the Medical Units of Tan Tock Seng Hospital and Alexandra Hospital with established stroke, were included in the survey. A questionnaire to determine any symptoms indicative of previous transient ischaemic attacks (TIA) was completed for each patient at the time of admission. Other risk factors, such as history of hypertension, diabetes mellitus, cigarette smoking, were also included in this questionnaire. At physical examination, attention was paid to blood pressure level readings in both arms and to auscultation of the neck to detect carotid bruits.

The haematocrit value and platelet counts of all the patients were determined. Biochemical analysis of fasting blood samples were determined for levels of cholesterol, triglyceride, high density lipoprotein cholesterol and uric acid.

RESULTS

The age and ethnic distribution of the patients surveyed are shown in Table 1. There were 36 males and 44

TABLE 1 PROFILE OF PATIENTS

Age	Chinese		Malay		Indian		Others		Total	
	M	F	M	F	M	F	M	F	M	F
Below 50	2	5	1	2	-	-	-	-	3	7
50 - 59	8	9	1	-	2	3	-	-	11	12
60 - 69	10	6	1	-	3	-	1	-	12	9
70 - 79	5	11	2	1	1	-	-	1	8	13
80 & over	25	36	5	3	6	3	1	1	36	46

females with an ethnic distribution of 76% Chinese, 10% Malays and 11% Indians. The corresponding ethnic distribution in the general population were 76% Chinese, 15% Malays and 7% Indians. The Indians therefore appeared to show a higher tendency to stroke. The average age of the patients surveyed was 63 years. The types of TIA symptoms were determined through the completion of the questionnaire. The patients, or in the presence of coma or aphasia, their close relatives were asked for the specific symptoms sought by the questionnaire. Among the patients, 37 (46%) had previously experienced some form of TIA, mostly related to motor power deficiency, eg weakness (23), dropping of objects (10), slurred speech (10), clumsy gait (9) or numbness (8). 7 (9%) patients in addition experienced two symptoms and 14 (17%) patients experienced three symptoms of TIA. 5 patients said they had suffered from deterioration in memory.

Bruits in the neck were heard in 9 (11%) patients. 20 patients gave a history of being diabetic and 30 patients had a smoking history of 10 to 20 years and a smoking habit of between 10 to 20 cigarettes a day.

The blood pressure levels were higher in the females (systolic 136 ± 7 to 185 ± 12 , diastolic 87 ± 5 to 105 ± 6 mm Hg) than in males (systolic 130 ± 6 to

167 ± 9 , diastolic 89 ± 4 to 104 ± 5 mm Hg). However, no gross differences were seen in the blood pressure levels among various ethnic groups. The younger age group, under 60 years, showed higher blood pressure levels.

The mean serum cholesterol level was 250 ± 6 mg/dl with a range of 236 ± 18 to 267 ± 26 mg/dl. The serum cholesterol levels in the males (252 ± 10) was higher than that in the females (249 ± 7). The ethnic distribution of serum cholesterol levels showed that the Chinese have a higher mean level of 252 mg/dl compared to Malays (241) and Indians (250). A further examination also shows that the Chinese had consistently high levels of serum cholesterol in all the age groups, whereas the Malays showed a fall from 287 mg/dl to 218 mg/dl with rising age. The trend of the levels of cholesterol could not be determined for the Indians as insufficient number of patients were studied.

The mean serum triglyceride level was 141 ± 6 mg/dl with a range of 135 ± 26 to 155 ± 18 mg/dl. The triglyceride levels in the males (149 ± 9) was higher than in the females (135 ± 7).

The mean serum high density lipoprotein cholesterol (HDL-C) level was 41 ± 2 mg/dl with a range of 38 ± 4 to 46 ± 9 mg/dl. The serum HDL-C was lower in males than in females. Among the 3 ethnic groups, the Chinese showed the highest level of serum HDL-C with a mean level of 43 ± 2 against the mean level of 34 ± 3 for Malays and 35 ± 3 for the Indians. The total serum cholesterol-serum HDL-C ratio (atherogenesis ratio) was 6.1 with a higher ratio for males, 6.8 (range 5.1 to 8.5) than for females, 5.7 (range 5.1 to 6.4). A high ratio was also seen in the younger age groups in both males and females. Comparing the 3 ethnic groups, the atherogenic ratio was higher in the Indians and Malays (7.1) than the Chinese (5.9).

DISCUSSION

80 consecutive stroke patients admitted to the Medical Units of Tan Tock Seng Hospital and Alexandra Hospital were studied in an attempt to determine the profile of stroke patients and the levels of risk factors which predispose a patient to develop stroke. The natural cause of events for patients who have had a TIA is that one-third will develop a cerebral infarct within 5 years. Of these, more than 20% will have a stroke within one month of the first attack and about 50% within one year (1). The protocol was designed and tested for its usefulness to identify patients with TIA. It is realised that the protocol has its limitations. The results could be biased by the interviewer and the history from a witness, in the event of coma or aphasia of the patient, may not be as reliable. Nevertheless, it is hoped that the protocol will be used by medical practitioners or medically trained personnel to determine which patients have TIA so that treatment may be initiated early to prevent the on-set of a completed stroke.

Carotid bruits were heard in 9 patients. Any bruit in the carotid territory is suspicious and a well-defined diastolic bruit is strongly suggestive of a tight carotid stenosis (2). Thomson (3) has found that 27% of patients with a symptomatic bruit will have TIA and that 19% will have a sudden ischaemic stroke.

TABLE II BLOOD PRESSURE LEVELS

Age	Mean \pm SE (mm Hg)	
	Systolic	Diastolic
All Patients		
Below 50	151 \pm 9	100 \pm 5
50 - 59	171 \pm 7	102 \pm 3
60 - 69	154 \pm 8	92 \pm 4
70 - 79	170 \pm 9	90 \pm 3
80 & above	136 \pm 7	87 \pm 5
Total	162 \pm 4	95 \pm 2
M A L E		
Below 50	130 \pm 6	89 \pm 1
50 - 59	167 \pm 9	104 \pm 5
60 - 69	149 \pm 11	89 \pm 4
70 - 79	147 \pm 8	91 \pm 4
80 & above	-	-
Total	152 \pm 5	94 \pm 3
F E M A L E		
Below 50	167 \pm 11	105 \pm 6
50 - 59	174 \pm 10	101 \pm 4
60 - 69	164 \pm 10	97 \pm 7
70 - 79	185 \pm 12	90 \pm 4
80 & above	136 \pm 7	87 \pm 5
Total	170 \pm 5	96 \pm 2
C H I N E S E		
Below 50	150 \pm 6	98 \pm 5
50 - 59	175 \pm 8	104 \pm 3
60 - 69	157 \pm 10	95 \pm 4
70 - 79	173 \pm 10	91 \pm 4
80 & above	136 \pm 7	87 \pm 5
Total	164 \pm 5	96 \pm 2
M A L A Y		
Below 50	170 \pm 31	105 \pm 13
50 - 59*	150	90
60 - 69*	140	70
70 - 79	140 \pm 21	90 \pm 6
Total	153 \pm 13	93 \pm 6
I N D I A N		
50 - 59	160 \pm 14	98 \pm 6
60 - 69	158 \pm 4	92 \pm 7
70 - 79*	150	90
Total	158 \pm 8	95 \pm 4

*One case only

TABLE III SERUM CHOLESTEROL, TRIGLYCERIDE
AND HIGH DENSITY LIPOPROTEIN CHOLESTEROL

AGE	Mean \pm SE (mg/dl)			Cholesterol HDL
	Cholesterol	Triglyceride	HDL-Ch	
All Patients				
Below 50	267 \pm 26	155 \pm 18	38 \pm 4	7.0
50 - 59	247 \pm 8	149 \pm 10	41 \pm 3	6.0
60 - 69	254 \pm 12	148 \pm 11	38 \pm 3	6.7
70 - 79	246 \pm 12	124 \pm 10	45 \pm 3	5.5
80 & above	236 \pm 18	135 \pm 26	46 \pm 9	5.1
Total	250 \pm 6	141 \pm 6	41 \pm 2	6.1
M A L E				
Below 50	348 \pm 58	167 \pm 24	41 \pm 5	8.5
50 - 59	249 \pm 12	154 \pm 15	36 \pm 3	6.9
60 - 69	252 \pm 16	151 \pm 16	35 \pm 3	7.2
70 - 79	221 \pm 16	132 \pm 20	43 \pm 7	5.1
80 & above	-	-	-	-
Total	252 \pm 10	149 \pm 9	38 \pm 2	6.8
F E M A L E				
Below 50	232 \pm 17	150 \pm 25	36 \pm 5	6.4
50 - 59	244 \pm 10	142 \pm 12	47 \pm 4	5.2
60 - 69	258 \pm 19	141 \pm 8	46 \pm 6	5.6
70 - 79	261 \pm 15	119 \pm 11	46 \pm 3	5.7
80 & above	236 \pm 18	135 \pm 26	46 \pm 9	5.1
Total	249 \pm 7	135 \pm 7	44 \pm 2	5.7
C H I N E S E				
Below 50	259 \pm 37	135 \pm 19	41 \pm 5	6.3
50 - 59	253 \pm 8	153 \pm 13	42 \pm 3	6.0
60 - 69	251 \pm 12	152 \pm 13	41 \pm 3	6.1
70 - 79	254 \pm 14	122 \pm 10	47 \pm 4	5.4
80 & above	236 \pm 18	135 \pm 26	46 \pm 9	5.1
Total	252 \pm 7	141 \pm 6	43 \pm 2	5.9
M A L A Y				
Below 50	287 \pm 17	202 \pm 30	30 \pm 4	9.6
50 - 59*	190	130	28	6.8
60 - 69*	220	115	45	4.9
70 - 79	218 \pm 17	160 \pm 45	36 \pm 3	6.1
Total	241 \pm 16	166 \pm 21	34 \pm 3	7.1
I N D I A N				
50 - 59	238 \pm 22	136 \pm 9	39 \pm 4	6.1
60 - 69	300 \pm 80	108 \pm 18	28 \pm 0	10.7
70 - 79*	200	100	34	5.9
Total	250 \pm 25	123 \pm 9	35 \pm 3	7.1

*One case only

STROKE SURVEY QUESTIONNAIRE

HOSPITAL REGISTRATION NO. _____

NAME _____

Questionnaire is

- Self Administered
- Administered by Doctor/Nurse
- Administered by Relative/Friend

The questions below relate to sudden onset of experiences or sensations that you have had, or to difficulties in performing an action. These problems may be experienced by you or be noticed by your relatives/friends. They may have lasted only a short period of time (a few minutes) or have persisted with you.

(In case of doubt please consult your doctor)

1. Have you ever had any of the following problems:-

	If "Yes", please tick (✓) appropriate box(es) to indicate which part(s) of body					
	Fingers	Arm	Leg	Foot	One side of face	Eye
a) A sensation of "heaviness"						
b) Weakness of						
c) Uncontrolled movements (jerks or twitching)						
d) Numbness or tingling						

- | | Yes | No |
|--|--------------------------|--------------------------|
| e) Clumsiness of walk | <input type="checkbox"/> | <input type="checkbox"/> |
| f) Dropping of Objects from your hand | <input type="checkbox"/> | <input type="checkbox"/> |
| g) Blindness, blurring or double vision | <input type="checkbox"/> | <input type="checkbox"/> |
| h) Sudden unexpected loss of memory | <input type="checkbox"/> | <input type="checkbox"/> |
| i) Inability to speak/slurred speech/garbled speech | <input type="checkbox"/> | <input type="checkbox"/> |
| j) Sudden inability to continue to conversation | <input type="checkbox"/> | <input type="checkbox"/> |
| k) Sudden change in the subject of your conversation (e.g. a hallucination) | <input type="checkbox"/> | <input type="checkbox"/> |
| l) Vertigo – an experience of yourself or your environment turning around | <input type="checkbox"/> | <input type="checkbox"/> |
| m) An episode of inability to recognise your location (where you are), objects (e.g. cup, glass) or people (e.g. friend) | <input type="checkbox"/> | <input type="checkbox"/> |
| 2. Do you think that your memory or you ability to think is deteriorating more than expected for your age? | <input type="checkbox"/> | <input type="checkbox"/> |
| 3. Do you have diabetes mellitus or high blood sugar? | <input type="checkbox"/> | <input type="checkbox"/> |
| 4. Do you smoke? | <input type="checkbox"/> | <input type="checkbox"/> |
| If yes (a) for how long | | |
| <input type="checkbox"/> less than 10 years | | |
| <input type="checkbox"/> 10 – 20 years | | |
| <input type="checkbox"/> more than 20 years | | |
| (b) No. of cigarettes per day | | |
| <input type="checkbox"/> less than 10 | | |
| <input type="checkbox"/> 10 – 20 | | |
| <input type="checkbox"/> 20 and above | | |

In a population survey conducted in 1974 among persons 20 years and above, the prevalence of hypertension in Singapore was about 14% with the sex ratio of 1.2 male to 1 female (4). In the survey, the systolic blood pressure of 160 mm Hg and a diastolic of 95 mm Hg was defined as the upper limit of normality. With that definition, about 7% of those in the youngest age group of 20 to 29 years were hypertensive and the rate was much higher at 40% in the 60 to 69 age group. In the present survey of stroke victims, most of the patients were mildly hypertensive. As hypertension is itself an independent risk factor for stroke, it is therefore important to initiate treatment on diagnosis and to maintain the treatment. Kennedy (5) found that nearly one-sixth of the hypertensive strokes occurred after one month of stopping treatment. In this series, no records were made of hypertensive medication.

The ethnic distribution of serum cholesterol showed that the Chinese had a higher mean level compared to the Malays and Indians. The relationship of this to diet warrants further study. Jacob (6) had previously determined the reference range of serum cholesterol in the Singaporean population aged 50 to 59 years as 185 to 290 mg/dl. The mean serum total cholesterol level of 250 mg/dl found among the stroke patients therefore appear to fall within the reference range. The American Heart Association in 1973 (7), however, recommended that dietary treatment should be initiated when the plasma cholesterol is greater than 220 mg/dl and plasma triglyceride greater than 140 mg/dl. The levels recommended for the initiation of treatment is greatly below the age specific, 95 percentile value. The recommendation to treat serum cholesterol above these levels is to prevent the occurrence of atherosclerotic disease, since atherogenesis seldom occur with plasma cholesterol concentration below 180 mg/dl over the lifetime.

The mean serum triglyceride level was 141 ± 6 mg/dl with the range of 135 ± 26 to 155 ± 18 . Jacob (6) had previously determined the reference range of serum triglyceride for the local population of age 50 to 59 years to be 50 to 185 mg/dl. These levels are also within the limits above which the American Heart Association has recommended that treatment be initiated (140 mg to 200 mg/dl).

Plasma triglyceride and its close association with very low density lipoprotein (VLDL) has been found to be related to atherosclerotic disease in epidemiological and clinical studies. This is reflected in the inverse relationship between VLDL and HDL in atherosclerotic diseases associated with raised plasma triglyceride. However, the interdependence of VLDL, triglyceride levels and HDL and the metabolic interrelationship between these two protein classes make it difficult to dissociate the positive "risk" associated with triglyceride and VLDL from the negative "risk" associated with HDL.

The recognition that HDL (25% of plasma cholesterol transport) is a negative risk factor for premature cardiovascular disease has led to intense interest in the protective mechanism of HDL against cardiovascular disease. In the study group, the mean serum HDL level was 41 ± 2 mg/dl and with a lower level seen in male patients (38 ± 2) and a high level in female patients (44 ± 2). Nubiola (8) et al studied HDL

in patients over the age of 50 years who presented with stroke. The HDL cholesterol in stroke patients showed a mean of 41 ± 13 mg/dl compared with control subjects of 54 ± 16 . In our series, no study on control subjects was done but the low levels of HDL in our patients seem similar to the findings of Nubiola. The higher levels of HDL seen in females compared to males corresponded to the findings of Noma (9) who, in studies of Japanese subjects aged 20 to 80 years, found that females had a higher level than males and that the levels tended to decrease with age. In that study, the HDL for normal men 20 to 80 years, ranged from 47.4 ± 1.1 to 41.8 ± 1.3 mg/dl and normal women of similar age, ranged from 56.8 ± 0.8 to 52.5 ± 1.2 mg/dl. In cerebral infarction, however, he found the mean values for HDL in the males was 48.3 and in females 48.9 mg/dl. In the Singapore series of stroke patients, the mean values for HDL were much lower compared to Noma's findings in the Japanese population.

The cholesterol atherogenesis ratio (10) allows for better interpretation when the serum cholesterol is within the normal reference range. Uhl et al (10) in looking at 572 asymptomatic air crew found 14 to 16 men with coronary artery disease to have a ratio 6 or more whereas only 4 men with normal coronary artery had a ratio of 6. In the present series of stroke patients, the mean cholesterol atherogenesis ratio was 6.1 with a range of 5.1 to 7.0. It can be seen also that the higher ratios were seen in the younger aged group stroke victims. These findings are similar to those seen in patients with cerebral vascular disease in Nubiola's series.

20 patients gave a history of diabetes mellitus. Hyperlipidaemia is frequently associated with diabetes mellitus and as such, is a risk factor in itself in the aetiology of cerebral vascular disease.

30 patients had a cigarette smoking history of more than 10 years and had a rate of 10 to 20 cigarettes per day. Epidemiological studies have established cigarette smoking as a risk factor of coronary heart disease. The Lipid Research Clinics Programme Prevalence Study (11) showed 11% to 14% difference in HDL levels between smokers and non-smokers (40.6 to 55.6 mg/dl vs 46.2 to 65.0 mg/dl). The lower levels of HDL cholesterol associated with smoking 20 or more cigarettes per day was substantial. A dose response relationship was also suggested for the above study because subjects smoking 1 to 19 cigarettes per day had HDL cholesterol levels intermediate between non-smokers and subjects who smoked more than 20 cigarettes per day. Furthermore, experimental subjects acutely smoking 2 cigarettes immediately decrease their HDL cholesterol by an average of 6 mg/dl.

10% of the patients presented with a serum uric acid level of 8.3 mg/dl (Jacob's reference range 3.9 to 8.3). A high uric acid level itself is not a direct risk factor but is best termed an indicator which carries no therapeutic implication because the mechanism by which a high uric acid level is associated with atherosclerosis or hypertension remains to be shown (12).

Atherosclerosis and cerebral vascular disease have multi-variate aetiologies. This clinical and biochemical survey of patients presenting with stroke cannot point to any one single item of its findings as a

specific index of stroke prediction in an individual. A protocol has been devised to seek out patients with TIA who may benefit from surgical correction before the on-set of a completed stroke. Lipid studies as an index to atherosclerotic vascular degeneration are strongly advised and would be necessary to educate the individual and the population at large in the necessity of living healthy lifestyles.

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