Incidence of Ischaemic Heart Disease and Stroke in Chinese, Malays and Indians in Singapore: Singapore Cardiovascular Cohort Study

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Abstract

***Introduction**: This is the first prospective cohort study in Singapore to describe the incidence of ischaemic heart disease (IHD) and stroke among Chinese, Malays and Asian Indians. **Materials and Methods**: The Singapore Cardiovascular Cohort Study is a longitudinal follow-up study on a general population cohort of 5920 persons drawn from 3 previous cross-sectional surveys. Morbidity and mortality from IHD and stroke were ascertained by record linkage using a unique identification number with the death registry, Singapore Myocardial Infarct Registry and in-patient discharge databases. **Results**: There were 193 first IHD events and 97 first strokes during 52,806 person-years of observation. The overall incidence of IHD was 3.8/1000 person-years and that of stroke was 1.8/1000 person-years. In both males and females, Indians had the highest IHD incidence, followed by Malays and then Chinese. For males after adjusting for age, Indians were 2.78 times (95% CI 1.86, 4.17;* **P** *<0.0001) and 2.28 times (95% CI 1.34, 3.88;* **P** *= 0.002) more likely to get IHD than Chinese and Malays respectively. For females after adjusting for age, Indians were 1.97 times (95% CI 1.07, 3.63;* **P** *= 0.03) and 1.37 times (95% CI 0.67, 2.80;* **P** *= 0.39) more likely to get IHD than Chinese and Malays respectively. For stroke, male Chinese and Indians had higher incidence than Malays (though not statistically significant). However, in females, Malays had the highest incidence of stroke, being 2.57 times (95% CI 1.31, 5.05;* **P** *= 0.008) more likely to get stroke than Chinese after adjustment for age. **Conclusions**: This prospective study of both mortality and morbidity has confirmed the higher risk of IHD in Indians. It has also found that Malay females have a higher incidence of stroke, which deserves further study because of its potential public health importance.*

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Introduction

Comparisons of disease frequency in different ethnic groups help to unravel the contributions of nature and nurture in their aetiology and to identify environmental or lifestyle factors that may be involved. This is aided when the ethnic groups live in the same country, so that differences in completeness and accuracy of diagnostic information as well as medical care will not operate. Singapore has a population of 3.3 million people comprising of 76% Chinese, 14% Malays, 7% Indians, and 3% Others. Of the Indians, 80% originate from Southern India (Tamil Nadu and Kerala) and Sri Lanka. It is an ideal setting to study ethnic differences in cardiovascular diseases between the three main ethnic groups. This is particularly so as Indians or South Asians (i.e. persons from the Indian subcontinent) have been found in a number of countries to be particularly susceptible to coronary heart disease (CHD).[1] This is currently of much interest.[2]

Previous studies in Singapore have been of mortality data[3-5] from routine statistics or cross-sectional studies measuring prevalence. These are limited by the fact that they are dependent on the interplay between the incidence and survival of patients. There is a need for prospective cohort studies to more accurately measure the varying ethnic susceptibilities to cardiovascular diseases and to relate their incidences to baseline risk factors. This article

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describes the methodology and initial findings of such a study in Singapore.

Materials and Methods

Cohort

The Singapore Cardiovascular Cohort Study is composed of participants from 3 previous cross-sectional surveys, which used disproportionate stratified random sampling from the general population of Singapore. Detailed methodologies of these 3 surveys have been described: the Thyroid and Heart Study (1982-1984),[6] the National Health Survey (1992)[7] and the National University of Singapore (NUS) Heart Study (1993-1995).[8]

There were 3568 subjects in the National Health Survey, 2143 subjects in the Thyroid and Heart Study and 983 subjects in the NUS Heart Study. There was duplication of 473 subjects from later surveys who had previously participated in the Thyroid and Heart Study, principally because a subsample of subjects from the Thyroid and Heart Study was re-studied in the NUS Heart Study. These subjects were analysed using baseline data from the earliest study (Thyroid and Heart Study). The National Registration Identity Card (NRIC) number of 53 subjects was unavailable and 242 non-Singapore citizens were also excluded. A further 6 persons who were not ethnic Chinese, Malay or Indian were excluded. A longitudinal follow-up study was conducted in March 1999 on the remaining 5920 persons from this cohort by the use of national registry data.

Data Linkage

Baseline information on demographics, personal and medical history was standardised and made consistent among the 3 surveys prior to data linkage. Outcomes were obtained by linking individual records with several national registers: the Registry of Births and Deaths, the Central Claims Processing System (CCPS) and Hospital Inpatient Discharge System (HIDS) and the Singapore Myocardial Infarct Registry (SMIR).[9] The Registry of Births and Deaths is of a high quality with regard to both completeness and accuracy.[3] The CCPS and its predecessor system, the HIDS, are databases that capture inpatient discharge information (including diagnosis) from all hospitals in Singapore, both government and private. The SMIR is a population-based registry with comprehensive coverage of acute myocardial infarction (AMI) occurring in persons below 65 years of age in Singapore. Full details of the methodology have been described.[9] Briefly, events were identified from cardiac enzyme data from hospital laboratories, discharge diagnosis and death certification, and confirmed by retrospective review of data from case-notes by a panel of cardiologists in accordance with MONICA criteria (the method of cold pursuit).

Record linkage with these registries was made possible by using the NRIC number which is a unique national registration identification number issued to all Singaporeans. Further cross-checking was performed using gender, race and date of birth. For reasons of confidentiality however, the NRIC number of all individuals in the data-set have been replaced by a serial number after linkage, with the key held by the Singapore Ministry of Health (which does not have access to the linked data-set).

Outcome Measures

All outcome measures were obtained from registry databases in coded form using the 9th Revision of the International Classification of Diseases (ICD-9). Deaths and causes of death were ascertained from the National Death Registry. Occurrence of AMI and IHD (ICD 410-414) was ascertained using the SMIR and data on hospitalisation diagnoses from the CCPS/HIDS. Occurrence of stroke (ICD 431-434 and 436) was ascertained using data on hospitalisation diagnoses from the CCPS/HIDS. Thus, outcome information included cause specific mortality as well as stroke and ischaemic heart disease morbidity (hospital admissions). The first event of IHD or stroke was used for the respective analyses.

Analysis

The cohort's 5920 subjects were followed up for a total of 52,806 person-years of observation. Subjects were censored at 1 March 1999 or their date of death, whichever occurred first. The average length of follow-up was 8.9 years. For the analysis of IHD incidence, 117 subjects with pre-existing IHD were excluded. Similarly, 18 subjects with pre-existing stroke were excluded for the analysis of stroke incidence.

Analyses were performed using the STATA 5.0 statistical package. Incidence rates were calculated using the person-time method, in which each subject contributes to the appropriate denominator the amount of time he spent in each particular age group during the follow-up period.

For example, a subject followed up from his 72nd birthday for 6 years would contribute 3 person-years to the 65 to 74 age group and 3 person-years to the 75 to 84 age group. Age-standardised incidence rates for IHD in male Chinese and Indians were calculated by direct standardisation using the world standard population. Age-standardised rates were not calculated for other outcomes and sub-groups because the age-specific rates are likely to be unstable due to small numbers. Cox's proportional hazards regression analysis was used to assess ethnicity as a risk factor for each outcome and to adjust for age at baseline. Subjects were analysed separately by gender. For all model comparisons, the likelihood ratio test was used, with conventional statistical significance set at 0.05. For

tests of interaction, models containing interaction terms were compared with models without interaction terms using the likelihood ratio test.

Results

The demographic profile of the study cohort at baseline is shown in Table I. Males comprised 49.3% and females 50.7% of the cohort. The mean age at baseline was 38.8 years. There were 193 first IHD events and 97 first strokes occurring during the period of follow up.

Table II shows that the overall incidence of IHD was 3.8 per 1000 person-years. In both males and females, Indians had the highest IHD incidence, followed by Malays and then Chinese. The age-specific incidence of IHD in males by ethnic group is shown in Figure 1. It can be seen that IHD incidence increases with age in all ethnic groups, with Indians having the highest incidence in all age groups. To avoid confusion, the IHD incidence for Malays in the 75+ age group has been omitted from Figure 1, as there were no events due to a small sample size with only a total of 26.3 person-years of observation. The age-standardised rate of IHD in Chinese males aged 35 to 74 years was 6.3 /1000. The age-standardised rate of IHD in Indian males aged 35 to 74 years was 17.9 /1000.

After adjusting for age (Table III), male Indians were nearly 3 times more likely to get IHD compared with male Chinese (hazard ratio: 2.78; 95% CI 1.86, 4.17; $P<0.0001$). Similarly, female Indians were nearly 2 times more likely to get IHD compared with female Chinese (hazard ratio: 1.97; 95% CI 1.07, 3.63; $P = 0.03$) even after adjustment for age. Smaller differences were noted for Malay males and females compared with Chinese.

Table IV shows that the overall incidence of stroke was 1.8 per 1000 person-years. In males, Chinese and Indians had higher incidences than Malays. However, in females, Malays had the highest incidence of stroke; the observed incidence was even higher than male Chinese and Indians.

After adjusting for age (Table V), male Malays were about 25% less likely to get stroke compared with male

TABLE I: GENDER AND AGE DISTRIBUTION OF STUDY COHORT AT BASELINE

	Chinese (%)	Malay (%)	Indian (%)	Overall (%)
Gender				
Male	1818 (49.3)	592 (49.1)	510 (49.8)	2920 (49.3)
Female	1871 (50.7)	614 (50.9)	515 (50.2)	3000 (50.7)
Age (y)				
Mean	38.6	38.5	40.2	38.8
<25	666 (18.1)	239 (19.8)	156 (15.2)	1061 (17.9)
25-34	942 (25.5)	324 (26.9)	276 (26.9)	1542 (26.1)
35-44	978 (26.5)	284 (23.6)	247 (24.1)	1509 (25.5)
45-54	621 (16.8)	165 (13.7)	160 (15.6)	946 (16.0)
55-64	348 (9.4)	143 (11.9)	137 (13.4)	628 (10.6)
65-74	128 (3.5)	50 (4.2)	49 (4.8)	227 (3.8)
75+	6 (0.2)	1 (0.1)	0 (0)	7 (0.1)

TABLE II: INCIDENCE RATE OF ISCHAEMIC HEART DISEASE (IHD)† BY ETHNICITY

	Number of events	Person-years of follow-up	Crude rate per 1000 person-years (95% confidence interval)	
Male				
Chinese	64	16,283	3.9	(3.1, 5.0)
Malay	21	4945	4.2	(2.8, 6.5)
Indian	40	3758	10.6	(7.8, 14.5)
Female				
Chinese	37	16,983	2.2	(1.6, 3.0)
Malay	16	5309	3.0	(1.8, 4.9)
Indian	15	4009	3.7	(2.3, 6.2)
Total	193	51,286	3.8	(3.3, 4.3)

† IHD defined by ICD-9 codes 410-414

TABLE III: UNADJUSTED AND AGE-ADJUSTED HAZARD RATIO (HR) FOR ISCHAEMIC HEART DISEASE (IHD)† BY ETHNIC GROUP

	Unadjusted HR (95% CI)	*P* value	Adjusted HR‡ (95% CI)	*P* value
Male				
Chinese	Baseline		Baseline	
Malay	1.03 (0.63, 1.70)	0.88	1.22 (0.74, 2.00)	0.42
Indian	2.52 (1.68, 3.77)	<0.0001	2.78 (1.86, 4.17)	<0.0001
Indian vs Malay	2.42 (1.42, 4.11)	0.0008	2.28 (1.34, 3.88)	0.002
Female				
Chinese	Baseline		Baseline	
Malay	1.31 (0.73, 2.37)	0.48	1.36 (0.75, 2.45)	0.40
Indian	1.64 (0.89, 3.01)	0.11	1.97 (1.07, 3.63)	0.03
Indian vs Malay	1.23 (0.61, 2.50)	0.57	1.37 (0.67, 2.80)	0.39

† IHD defined by ICD-9 codes 410-414

‡ adjusted for age at baseline by Cox proportional hazards regression models

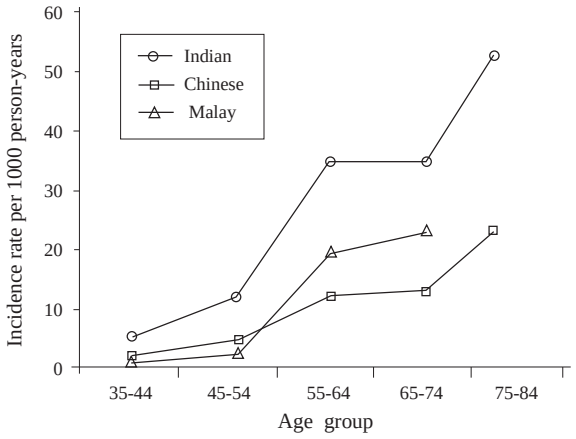

Fig. 1. Age-specific incidence rates of IHD for males by ethnic group.

TABLE IV: INCIDENCE RATE OF STROKE† BY ETHNICITY

	Number of events	Person-years of follow-up	Crude rate per 1000 person-years (95% confidence interval)	
Male				
Chinese	39	16,672	2.3	(1.7, 3.2)
Malay	8	5131	1.6	(0.8, 3.1)
Indian	9	4006	2.2	(1.2, 4.3)
Female				
Chinese	20	17,115	1.2	(0.8, 1.8)
Malay	15	5394	2.8	(1.7, 4.6)
Indian	6	4130	1.5	(0.7, 3.2)
Total	97	52,448	1.8	(1.5, 2.3)

† stroke defined by ICD-9 codes 431-434 and 436

Chinese (hazard ratio: 0.74; 95% CI 0.34, 1.58; $P = 0.4$). In contrast, female Malays were about 2.5 times more likely to get stroke compared with female Chinese (hazard ratio: 2.57; 95% CI 1.31, 5.05; $P = 0.008$) after adjustment for age. The test for interaction between gender and ethnicity was statistically significant ($P = 0.05$).

Discussion

This is the first community-based, longitudinal follow-up study of IHD and stroke morbidity in Chinese, Malays and Indians in Singapore. The cohort design of this study enables the calculation and comparison of incidence rates of IHD and stroke in the different ethnic groups. In contrast to studies based on routine mortality data, we were able to exclude subjects with symptomatic IHD and stroke at the start of the study, and able to include non-fatal events in the study as well as fatal events. IHD and stroke morbidity is an important end-point, as it is not influenced by case fatality, unlike mortality.

In this study, even after adjusting for age, male and female Indians were nearly 3 times and 2 times more likely to get IHD compared with male and female Chinese respectively. Smaller differences were noted for Malay males and females compared with Chinese.

The ranking of the ethnic groups is broadly in line with the findings of previous local studies. In Singapore, death registration data show that for both genders Indians have much higher mortality rates from IHD than Malays and Chinese, with Malays having higher rates from IHD than Chinese.[3]

In Malaysia, a study found a 1.5 times higher IHD proportionate mortality in Indians compared with Chinese and Malays.[10] A high incidence of IHD has also been found in Asian Indians in other parts of the world.[1,2]

The ethnic differences in incidence of IHD morbidity seen in this study and found in other local studies can only be partially attributed to differences in prevalence of risk

TABLE V: UNADJUSTED AND AGE-ADJUSTED HAZARD RATIO (HR) FOR STROKE† BY ETHNIC GROUP

	Unadjusted HR (95% CI)	*P* value	Adjusted HR‡ (95% CI)	*P* value
Male				
Chinese	Baseline		Baseline	
Malay	0.66 (0.31, 1.41)	0.27	0.74 (0.34, 1.58)	0.40
Indian	0.93 (0.45, 1.95)	0.89	0.91 (0.44, 1.90)	0.83
Indian vs Malay	1.47 (0.56, 3.82)	0.43	1.30 (0.50, 3.39)	0.59
Female				
Chinese	Baseline		Baseline	
Malay	2.37 (1.21,4.64)	0.02	2.57 (1.31, 5.05)	0.008
Indian	1.33 (0.53, 3.33)	0.50	1.74 (0.69, 4.38)	0.28
Indian vs Malay	0.56 (0.22, 1.45)	0.21	0.70 (0.27,1.85)	0.47

† stroke defined by ICD-9 codes 431-434 and 436

‡ adjusted for age at baseline by Cox proportional hazards regression models

factors in the different races.[7] Risk factor studies locally and elsewhere have identified a higher prevalence of diabetes mellitus, increased insulin resistance, central obesity and lower HDL levels as possible explanations for ethnic differences in IHD.[6-8,11-14] Further research is needed to explore the role of genetic factors and gene-environment interaction.

The issue of ethnic differences in stroke epidemiology has been less well studied locally. An earlier study[3] found little difference in males, but noted that Malay females appeared to have somewhat higher stroke mortality. In Singapore, Indians do not have the higher mortality from cerebrovascular disease[3] that has been reported from the UK.[15] It has also been reported from autopsy studies in Singapore that the only difference between Indians and Chinese for cardiovascular disease is in coronary disease.[16]

This study found that for males, there is virtually no difference between Chinese and Indians, with both having slightly higher risk for stroke than Malays, although the differences were not statistically significant. In contrast, for females, the risk of stroke was highest in Malays, followed by Indians and Chinese. Indeed, the rate of stroke observed in female Malays was even higher than male Chinese and Indians. This finding should be interpreted cautiously as the number of stroke events was small. However, this finding is supported by the previous study on stroke mortality in Singapore.[3] In Malaysia, it has been reported from clinical observation that Malay females have an apparent susceptibility to hypertension.[17] Further analysis of data from this study showed a high prevalence of hypertension in female Malays (12.4%) and female Indians (13.4%) compared with female Chinese (8.1%). The higher prevalence of hypertension may partially explain the higher risk of stroke in Malay females. The ethnic differences in incidence of stroke found in this study and in other local studies highlights a problem in Malay females that needs further study and research.

In longitudinal studies using registry follow-up, one has to consider the issues of completeness and accuracy of outcome ascertainment. As this study uses 3 different sources of information, the level of completeness in ascertaining outcomes is likely to be high. Hospital admissions prior to 1986 have not been recorded, but this only involves 2 to 3 years of early follow-up for the one study that commenced in 1982.

Since the morbidity data are based on hospital admissions, the outcomes of subject with non-fatal IHD or stroke who were not hospitalised would not have been captured. This may have resulted in underestimation of the IHD and stroke morbidity reported in this study, although most serious morbidity will have been captured. Also, such incompleteness is unlikely to differ systematically by ethnic group and to bias inter-ethnic comparisons. This is supported by a subsidiary analysis showing that inter-ethnic differences in IHD mortality (on which data is virtually complete, as death registration is a legal requirement) are similar to those found in the main analysis of this study.

With regard to outcome ascertainment, the linkage of individuals to the correct outcome can be considered to be accurate since cross-checking with gender, ethnic group and date of birth was performed. In Singapore, medical doctors fill the diagnosis on death certificates and discharge notification forms. Although doctors are not infallible, misclassification of outcome due to inaccurate diagnosis data would not bias the ethnic comparisons in this study unless such misclassification varies systematically by ethnic group, which is unlikely.

The Singapore Cardiovascular Cohort Study has confirmed the higher risk of IHD morbidity in Indians in a prospective observational fashion. It was also found that Malay females have a higher incidence of stroke and this observation deserves further study because of its potential public health importance.

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