Hypertension in a multi-ethnic Asian population of Singapore

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Abstract
The prevalence of hypertension varies by country and region, but it remains a leading yet modifiable risk factor of cardiovascular disease. There are many factors that contribute to the burden of hypertension in Asia, a region with diverse ethnicity. It has been shown that sociodemographic variability is related to ethnic differences, thereby emphasizing the importance of hypertension screening and educating at-risk or vulnerable groups. In this review, we describe the ethnic differences in genetic variants, dietary choice, and lifestyle habits, as well as its association with sociodemographic differences, hypertension awareness, and treatment control.

1 | INTRODUCTION
Hypertension is the leading preventable risk factor for cardiovascular disease.1 According to the World Health Organization (WHO), around 1.13 billion people have hypertension globally. Worldwide burden of hypertension has been estimated to exceed 1.5 billion people by 2025.2 Current antihypertensive therapies are effective and can reduce the risk of cardiovascular diseases and its complications, and lower the relative and absolute risk of cardiovascular mortality. Unfortunately, the levels of awareness, treatment, and control of hypertension vary between different...
countries and population groups. Asia is a diverse continent with diversities in hypertension prevalence, awareness, treatment, and control rates. 3, 4

Several factors contribute to the current hypertension burden in Asia, including modernization, urbanization, lifestyle changes (dietary high salt intake and obesity), and socioeconomic status. 5, 6 The impact of ethnic and socioeconomic disparities on hypertension outcomes has been well established in the Western countries. 7-9

Singapore is a rapidly aging, urbanized, and multi-ethnic Asian population (Chinese, Malays, and Indians). In this article, we review the ethnic difference in hypertension awareness and treatment control associated with the sociodemographic difference.

2 | EPIDEMIOLOGY OF RISK FACTORS AND CARDIOVASCULAR DISEASE

Singapore is a small city-state with a population of about 5.7 million (2019) of which about 4 million are residents. Majority of the population were Chinese (74.4%), followed by the Malays (13.4%) and Indians (9.0%). 3.2% were others. These proportions had been fairly constant for the past 10 over years. 10

In a Singapore National Health Survey 2010, resident Singapore population aged 18 to 79 years were surveyed from six locations including primary care clinics and community club that were well spread across the country. 11 Random sample selection was based on two-stage stratified design to select individuals within the vicinity of survey sites, and to yield a sample that was representative of national housing type, and demographics distribution. Oversampling was conducted for the Malay and Indian ethnicity groups to allow for reliable prevalence estimates for these groups. The prevalence of hypertension was 23.4%, 28%, and 19.3% in Chinese, Malay, and Indians, respectively. 11 Among the three major ethnic groups, Malays had the highest prevalence of hypertension, hyperlipidemia, obesity, and smoking and the highest age-standardized incidence rate of acute myocardial infarction (AMI) and stroke. (Tables 1 and 2) This was not unexpected based on the incidence of hypertension that was highest in the Malays who also had other associated risk factors. Indians had the highest prevalence of diabetes mellitus (DM), low high-density lipoprotein (HDL), and regular alcohol intake. (Tables 1 and 2).

From 2010 to 2017, the prevalence of hypertension stayed around just above 20%. 12 The prevalence of DM had remained stable around 8%, whereas obesity and smoking had fallen from 10.8% to 8.7% and 14.3% to 12%, respectively. However, the prevalence of hyperlipidemia had increased from 25.2% to 33.6%. (Table 3).

The incidence rate of AMI had also increased, whereas stroke had stabilized over the years. (13, 14) (Tables 2 and 3) The increase in AMI was observed in all ethnic groups. Similarly, stroke had seemed to be stable in all the 3 ethnic groups.

| TABLE 1 | Cardiovascular risk factors (prevalence by %) in Singapore |
|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| DM | Hyperlipidemia | Low HDL | Obesity | Abdominal fat | High BMI |
| Chinese | 9.7 | 17.1 | 5.6 | 7.9 | 15.5 | 19.4 |
| Malay | 16.6 | 22.6 | 12 | 24.0 | 18.9 | 38.0 |
| Indians | 17.2 | 12.6 | 23.2 | 16.9 | 26.1 | 32.8 |
| **Regular smoking** | **Regular alcohol** | **Regular exercise** |
| Chinese | 12.8 | 2.9 | 19.2 |
| Malay | 26.5 | 0.6 | 15.3 |
| Indians | 10.1 | 3.3 | 21.7 |

Abbreviations: BMI, body mass index; DM, diabetes mellitus; HDL, high-density lipoproteins.

| TABLE 2 | Age-standardized incidence rate in 2010 & 2017 (per 100 000 population) in Singapore |
|----------------------|----------------------|----------------------|----------------------|----------------------|
| AMI | Chinese | Malay | Indians |
| 2010 | 158.2 | 373.6 | 372.1 |
| 2017 | 187.4 | 453.4 | 447.0 |
| Stroke | Chinese | Malay | Indians |
| 2010 | 148.2 | 243.9 | 154.3 |
| 2017 | 144.4 | 243.8 | 160.3 |

Abbreviations: AMI, acute myocardial infarction; BMI, body mass index; DM, diabetes mellitus; HDL, high-density lipoproteins.

*Age-standardized incidence rate per 100 000 population.
3 | ETHNIC DIFFERENCES AND HYPERTENSION IN ASIA

In the United States (US) population, the age-adjusted prevalence of hypertension is highest in non-Hispanic blacks followed by non-Hispanic whites. The prevalence of hypertension, within the past 10 years, across various countries in Asia is described in Table 4, and this ranges between 23.5% to 60%. Of note, the methodologies that have been adopted by each survey or study may differ from one another, including the age range of target sample population, albeit the impact of other contributing factors like sodium intake or socioeconomic and culture differences on hypertension prevalence.

4 | GENETICS AND ETHNIC DIFFERENCES IN HYPERTENSION

There are several factors that contribute to the differences in prevalence of hypertension between countries, as well as ethnic groups. Kato et al conducted a genome-wide association study, which identified 12 genetic loci affecting blood pressure across three different ancestry groups. This study involved participants of East Asian (Japan, Korea, China, Philippines, Taiwan), South Asian (India, Singapore, Sri Lanka, Pakistan), and European ancestry, revealing common genetic variants at loci points genes involving vascular smooth muscle (IGFBP3, KCNK3, PDE3A, and PRDM6) and renal function (ARHGAP24, OSR1, SLC22A7, and TBX2). In addition, they demonstrated that DNA methylation played a possible role in linking these common genetic variants with various blood pressure phenotypes.

However, another study by Williams et al may offer an explanation to account for differences in hypertension among ethnic groups. They adopted a candidate gene approach to study how the central nervous system serotonin function is regulated by genetic factors. On chromosome 17, 5HTTLPR is a polymorphism in the promoter region of SLC6A4 that encodes for serotonin transporter. 5HTTLPR have long (L) and short (S) variants. The authors evaluated the association of 5HTTLPR alleles with prevalence of hypertension in two multi-ethnic populations from the United States and Singapore. L and L' alleles were found to be associated with hypertension prevalence in White Americans. In contrast, L' alleles were associated with lower hypertension prevalence in African/Native Americans as well as in Singaporean Chinese and combined Asian samples, while S' allele carriers were associated with higher diastolic blood pressure in these groups, thereby demonstrating a difference in effects of rs25531 genotype on blood pressure in various ethnic groups.

5 | SALT INTAKE AND SCREENING OF HYPERTENSION

A local National Nutrition Survey was conducted in 2010. Salt intake and urinary sodium excretion were evaluated. The mean urinary sodium excretion in adults was 142.2 mmol/24 hours, with an estimated average salt intake of 8.3 g/day. Men had a higher average salt intake of 9.6 g/day. Among the ethnic groups, there were no significant differences in salt intake.

As a worldwide comparison, Powles et al analyzed sodium intake in adults globally and showed a global average of sodium intake...
intake of 3.95 g/day. Between countries, highest intakes were observed in East Asia (4.80 g/day), Asia Pacific High Income (Japan and South Korean mainly, 5.0 g/day), and Central Asia (5.51 g/day), thereby emphasizing the need for sodium reduction and enhanced surveillance. In addition, based on Indonesia’s basic health research data (2018), a difference in hypertension prevalence was observed in each Indonesian province (25.9%-44.4%). This was related to cultural differences including high-fat and high-salt diets in several provinces. The prevalence of hypertension and age-standardized estimated sodium intakes by country are described in Table 4.

Lifestyle and dietary guidelines of hypertension, diabetes, and chronic kidney disease have recommended a daily dietary sodium intake of less than 100 mmol/day (<2.4 g/day). One method of estimating daily sodium intake is by measuring 24-hour urinary sodium excretion. Subramanian et al developed a 5-variable equation, including spot urine sodium to predict 24-hour urine sodium excretion in a multi-ethnic Singaporean cohort. The 24-hour urine sodium excretion measurements for those who were not on diuretics were as follows: 120.8 ± 73.1 mmol (Chinese), 112.5 ± 62.0 mmol (Malay), and 151.1 ± 68.1 mmol (Indians).

In addition to urinary sodium measurements, it would be important to screen for primary aldosteronism. A local study by Loh et al showed that prevalence of primary aldosteronism accounted for around 5% of the cause of hypertension in adults in Singapore. The study screened 350 patients by using random ambulatory plasma aldosterone concentration to plasma renin activity (PAC/PRA), followed by confirmatory studies including saline infusion suppression test, adrenal computed tomographic scan, and adrenal vein sampling. About half of patients with primary aldosteronism were due to unilateral aldosterone-producing adrenal adenoma.

### 6 | SMOKING AND ALCOHOL CONSUMPTION TRENDS

A cross-sectional study in 2016 compared smoking trends in 2016 with those of Singapore Mental Health Study in 2010. The prevalence of current smokers was similar to 2010 and remained around 16% in 2016, among which Malay ethnicity was associated with smoking. In the Singapore Mental Health Study 2016, among the current smokers, 63.7% were Chinese, 23.9% were Malays, and 9.8% were Indians. The study also observed Malay and Others’ ethnic groups were associated with current smoking prevalence. A similar trend was observed by another cross-sectional Malaysian study in which prevalence of smoking were higher in Malays and Bumiputras.

Based on the data from Singapore Mental Health Study 2010, another study assessed prevalence of heavy drinking which was based on the largest number of drinks in one single day, and was therefore defined as men having 5 or more drinks a day, and women having 4 or more drinks a day in the last 12 months. The definition of a drink was a can or bottle of beer, a glass of wine, a shot or jigger of liquor alone or mixed. The authors observed that Malays were less likely to engage in heavy drinking as compared to Chinese, which was possibly due to the impact of religious and cultural beliefs. In a National Health and Morbidity Survey 2011 in Malaysia, prevalence of alcohol use was higher in Chinese and Indian as compared to Malays. On the contrary, the practice of risky drinking was adopted more often by Malays than Chinese.

### TABLE 5 | Prevalence of smoking in Singapore, Malaysia, and Indonesia

| Country       | Prevalence of smoking (%) | Current smokers by ethnicity (%) |
|---------------|---------------------------|---------------------------------|
| Singapore     | 16%<sup>25,26</sup>       | Chinese: 63.7%<sup>25,26</sup>  |
| Malaysia      | 22.8%<sup>27</sup>        | Chinese and Indians: 7.8%<sup>27</sup> |
| Indonesia     | 31.9%<sup>28</sup>        | NR                              |

Abbreviation: NR, not reported.

### 7 | SOCIODEMOGRAPHIC AND ETHNIC DIFFERENCES IN HYPERTENSION AWARENESS AND CONTROL

In the National Health Survey 2010, 67.4% of all known hypertensives had good blood pressure control and 69.1% on treatment had good control.<sup>11</sup> Chinese had the highest proportion with good control (70%), followed by Indians (68.9%) and Malays (51.5%). 26.3% found to have hypertension was not previously diagnosed, of which Malays had the highest proportion (29.6%), followed by Chinese (26.0%) and Indian (23.8%).

A Singapore study conducted by Wu et al (2004-2007) revealed that working adults with higher levels of education and socioeconomic status were more likely to be undiagnosed but when treated, their blood pressures were better controlled.<sup>20</sup> The authors also emphasized the importance of screening and treating concomitant cardiovascular risk factors (diabetes mellitus, obesity, dyslipidemia, etc) by demonstrating association between presence of these factors with increased level of awareness and treatment of hypertension. However, hypertension remained uncontrolled albeit, a higher level of awareness of the diagnosis in this group of patients with concomitant risk factors.

In a later large cross-sectional multi-ethnic Asian study, Liew et al recruited participants (2004-2010) from three ethnic groups (Chinese, Malay, and Indian) to assess correlation between sociodemographic and hypertension, together with level of awareness, treatment, and control in Singapore.<sup>31</sup> Across the ethnic groups, the authors demonstrated that older age, lower education, and homemakers were related to higher odds of hypertension, and the relationship between sociodemographic factors and hypertension
varied. Comparing the ethnic groups, Malays and Indians had higher odds of hypertension with increasing age, while stronger association between gender and hypertension was observed among Chinese and Indians.

These two cross-sectional studies confirmed higher rate of hypertension in Malays than the Chinese and Indian.30,31 The Malays were also more likely to be unaware of hypertension and more likely to be uncontrolled.

Interestingly, the studies also noted that younger individuals with hypertension were more likely to be unaware of their diagnosis and also more likely to be untreated.30,31 Individuals who were unaware of hypertension were also more likely to be working adults, never married with higher levels of education and higher socioeconomic status.

On the other hand, those who were less likely to be unaware of the diagnosis of hypertension were individuals with older age, currently married or separated/divorced/widowed, lower educational level, and retired/unemployed status. In relation to lifestyle habits, smokers and alcohol consumers were more likely to be unaware of their hypertension status or were more likely to be untreated.

However, uncontrolled hypertension remained higher in those who were separated/divorced/widowed, or with higher education. Those with lower socioeconomic status were more likely to receive pharmacological treatment but tend to have poorer control.

The literature suggested that minority ethnic groups who were hypertensive were more likely to be aware of their hypertension.32 However, in the local studies, Malays had the higher rate of hypertension and unawareness.30,31 Conversely, Indians (lowest minority) were more aware of having hypertension than Chinese. The observed ethnic differences in hypertension awareness may be attributable to variations in lifestyle and cultural factors.

The ethnic differences in relation to hypertension were partly attributed to the differences in sociodemographic characteristics of each ethnic group. Educational level rather than household income was a more important consistent socioeconomic indicator associated with hypertension. Decreased educational level, homemaker, or retired/unemployed were associated with higher odds of hypertension. Educational level was related to hypertension independent of ethnicity. Lower education was consistently associated with higher odds of hypertension in all ethnic groups. Income-hypertension relationship was not found in Chinese and Malay ethnic groups, but Indians having lower income were significantly associated with hypertension.

In recent years, the Asia BP@Home study (2017-2018) was a multinational Asian specialty study evaluating home and clinic blood pressure control. Subanalysis of Singapore population revealed a different pattern of choice of drugs for hypertension from prior to 2010.33 The analysis showed the choice of anti-hypertensives used in decreasing order: CCB (74%), ARB (64%), beta-blockers (29%), and diuretics (22%).

9 | CONCLUSION
The awareness, treatment, and control rate of hypertension need to be improved in all ethnic groups in Singapore. The ethnic differences observed in hypertension were also associated with sociodemographic variability. Age, educational level, income, and lifestyles were important factors. More targeted strategies may be required, in particular, screening in younger, working adults with higher levels of education and higher economic status. Public health awareness through education and lifestyle changes such as stop smoking and drinking may help improved awareness and control of blood pressure.

Despite reductions in hypertension prevalence and improvements in control rates in recent years, almost one-third of all deaths in Singapore are still due to cardiovascular disease.33 Cardiovascular mortality rates in Singapore have remained virtually unchanged over recent years. In a multi-ethnic Asian population, controlling cardiovascular risk factors may need particularly important in certain ethnic groups with high cardiovascular events.

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AUTHOR CONTRIBUTIONS
Jam Chin Tay had the primary responsibility of writing this paper. Jam Chin Tay, Gek Cher Chan, and Boon Wee Teo wrote the essential

8 | PRESCRIBING PATTERN OF ANTI-HYPERTENSIVES IN SINGAPORE
Prior to 2010, the study by Wu et al observed that the commonest choice of drugs used was beta-blockers (62.1%).30 This was followed by calcium channel blocker (CCB, 35.3%), angiotensin-converting enzyme inhibitor/angiotensin receptor antagonist (ACE inhibitor/ARB, 30.5%), and diuretics (15%).
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