The healthcare burden of hypertension in Asia

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ABSTRACT

As the leading global risk for mortality, hypertension (HT) is a common healthcare problem in the world. The total number of patients with HT is likely to grow in the next few decades as the population age and the prevalence of obesity and diabetes increase. HT, as a major modifiable risk factor for cardiovascular disease, results in more deaths than any other risk factors, including diabetes and cigarette smoking. High prevalence, inadequate awareness, suboptimal treatment and low rate of achieving guideline-recommended target blood pressure control are key factors leading to severe cardiovascular complications that impose a heavy socioeconomic burden, especially in developing countries. Asia is the world's largest and most populous continent with approximately 4.3 billion people, hosting 60% of the world's current human population, and has a high growth rate. Asia differs very widely from the West with regard to ethnic groups, cultures, environments, economics, historical ties and government systems. Therefore, the purpose of this review is to comprehensively summarise the epidemiology, treatment practice and the status of control of HT in different Asian countries in order to guide the future prevention and management in this part of the world.

INTRODUCTION

Cardiovascular diseases account for about 30% of all deaths worldwide, with about 80% of global cardiovascular deaths occurring in low-income to middle-income countries where cardiovascular death always occurs at a younger age, exerting a profound impact on families and the society manpower.[1 2] The high prevalence of hypertension (HT), particularly in Asia, has contributed to the present pandemic of cardiovascular disease and death.

HT and its complications pose great burdens to the healthcare systems worldwide. The prevalence of HT increases as the population ages. Individuals with normal blood pressure (BP) at 55 years of age have a 90% lifetime risk for developing HT.[3] HT occurs in the majority of the population older than 65 years of age. The rising incidence of obesity will also likely increase the number of hypertensive individuals. Highly populated developing Asian countries, such as India and China, have a large absolute number of individuals with HT, which is a silent killer. Up to now, the epidemiology of HT in the Western world is well studied, but there are less data concerning the scope of the problem of HT in Asian countries. Therefore, the purpose of this review is to summarise the current data on the prevalence of HT and the status of use of antihypertensive treatment in Asia.

DEFINITIONS OF HT AND TARGET BP

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) Guideline has defined HT in adults as systolic pressure ≥140 mm Hg and/or diastolic pressure ≥90 mm Hg.[4] According to JNC 7,[4] the target BP of good control for HT patients is <140/90 mm Hg; for hypertensive patients with diabetes mellitus or chronic kidney disease, the target BP is <130/80 mm Hg. According the National Institute of Health and Care Excellence guidance, for patients older than 80 years, the optimal BP is <150/90 mm Hg.[5] The Candesartan Antihypertensive Survival Evaluation in Japan (CASE-J) trial reported by the Japanese suggested a target BP of <150/85 mm Hg for patients of 75–84 years old.[6] The new 2013 European Hypertension Guidelines published recently do make exceptions for special populations, such as those with diabetes and the elderly. For those with diabetes, <85 mm Hg diastolic BP is recommended. In patients younger than 80 years old, the systolic BP target should be 140–150 mm Hg, but physicians can go lower than 140 mm Hg if the patient is fit and healthy. The same advice applies to octogenarians, although physicians should also factor in the patient's mental capacity in addition to physical heath if targeting to less than 140 mm Hg.[7]

PREVALENCE OF HT

WHO estimates that between 2000 and 2025, the number of patients diagnosed with HT will increase by about 60% to up to 1.56 billion and Asia will contribute to a large proportion of this patient population. HT is less common in Asian countries than some Western countries,[8] but the much larger base Asian population results in a considerably larger absolute number of individuals affected. In China and India, the total number of hypertensive patients is expected to increase to more than 500 million by 2025.[9] The absolute increments for India and China are 95.3 million and 117.6 million, respectively (table 1).[9] In China, the approximate number of hypertensive patients was 200 million at least when estimated at the year of 2010, and one in five persons had HT.[10] While these figures have probably underestimated the true problem because other HT-related risk factors and westernisation of lifestyle in Asia have not been considered.[11]

The prevalence of HT in childhood and adolescent is increasing as a result of increasing prevalence of obesity and unhealthy lifestyle.[12] One study found that in adolescence the prevalence of HT was 3.2% and that of pre-HT was 15.7%.[13] Meanwhile, target organ damages, including LV hypertrophy, thickening of the carotid vessel wall, retinal vascular changes and even subtle cognitive

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Table 1 Estimated number of individuals aged >20 years with BP>140/90 mm Hg in 2000 and predicted number of affected individuals in 2025[9]

Region	Prevalence in 2000 (millions)	Predicted prevalence in 2025 (millions)	Increase (millions)
Established market economies	239.5	309.7	70.2
China	181.6	299.2	117.6
India	118.2	213.5	95.3
Latin America and the Caribbean	114.3	200.6	86.3
Former socialist economies	93.1	103.7	10.6
Sub-Saharan Africa	79.8	150.7	70.9
Middle East Crescent	73.8	152.6	78.8
Other Asia and islands	71.4	129.4	58.0
Total	971.7	1559.4	587.7

BP, blood pressure.

changes, are detectable in children and adolescents with high BP.[14]

On the other end of the spectrum, HT is also very common among elderly in many Asian countries (table 2).[15–20] Singapore[15] and Korea[16] have the highest prevalence of HT in the elderly population (study population age: ≥60 years for Singapore and ≥65 years for Korea), 73.9% and 68.7%, respectively, indicating that more than two-thirds of elderly populations have to receive antihypertensive treatment in these two countries. Most of the cardiovascular health burden attributable to HT occurs in the developing world.[21] In populations living in rural areas, the prevalence of HT is two to three times lower than those living in urban areas in Asia.[11] However, with urbanisation and westernisation of lifestyles in many developing countries, the lower prevalence of HT in rural areas will be gradually replaced by a higher prevalence and an increase in the absolute number of hypertensive patients in the countries. HT and stroke occur at a relatively younger age in Asia and the risk of HT increases at lower body mass index of 23–25 kg/m^2.[11]

AWARENESS, TREATMENT AND CONTROL OF HT IN ASIA

The awareness to HT (defined as self-report of any prior diagnosis of HT by a healthcare professional), the antihypertensive drug treatment rate (defined as the use of at least one prescription medication for management of HT at the time of the interview) and control rate (defined as an average systolic BP <140 mm Hg and an average diastolic BP <90 mm Hg while on treatment) of HT in those being treated with medication in Asian countries are summarised in table 3.[15 16 19 22–27] Because of the diversity of the study population, the awareness rates differ from country to country. China and India, with a wider age range of the populations, showed the lowest awareness rates —only about 25%; while the awareness to HT is higher among elderly population in Singapore and Korea.[15 22] According to the latest report in China, approximately 130 million patients were unaware of their diagnosis of HT; among those receiving antihypertensive treatment, only about 25% patients reach the optimal BP control.[10] Low BP control rate is a common phenomenon in Asia countries. Japan showed the highest control rate but also less than 50%.[27] One study from Korea reported the BP control rate was considerably lower among all the hypertensive patients, although the antihypertensive drug treatment rate is as high as 91.7%.[22] Furthermore, many countries, such as China, Thailand and India are facing the challenge of a large number of hypertensive patients with very low awareness rate and BP control rate.

Table 2 Prevalence of hypertension in studies focusing on elderly population among Asian countries

Study	Country	N	Age (years)	Prevalence (%)
Malhotra *et al*[15]	Singapore	4441	≥60	73.9
Kim *et al*[16]	Korea	995	≥65	68.7
Hypertension Study Group[17]	India and Bangladesh	1230	≥60	65
Lu *et al*[18]	Taiwan	1435	≥65	60.4
Porapakkam *et al*[19]	Thailand	19 374	≥60	51.5
Gu *et al*[20]	China	129 824 000	≥65	48.8

Previous studies indicated that 87% to 92% of the patients have received one or two medications (table 4)[16 28–33] while the rate of BP control below 140/90 mm Hg for treated patients was low in many Asian countries, ranging from 10.6% to 41.4% (table 3), implying that a considerable number of patients with poor BP control may need more aggressive treatment. Nevertheless, in about half of all treated patients, changes in lifestyle and medications are far from adequate to control high BP. Uncontrolled HT patients may be secondary to poor adherence and/or an inadequate treatment regimen, as well as those with true treatment resistance. Patients with true treatment-resistant HT are called 'resistant hypertension', which means that their BP is above accepted levels despite the use of three or more antihypertensive drugs with one diuretic.[34] The prevalence of resistant HT is unknown in Asia. Some cross-sectional studies and HT outcome studies suggest, however, that it is not uncommon. Considering the higher prevalence of resistant HT in Western countries[35] and its strong association with increased risk of adverse cardiovascular events,[36] further study will be needed to investigate the precise incidence and prognosis in Asian countries.

FACTORS ASSOCIATED WITH INADEQUATE BP CONTROL

Inadequate BP control is multifactorial, including age, gender, ethnic, healthcare conditions and patients' adherence to treatment.[37] Data from China focusing on the urban adults, patients like white-collar workers or obesity were more likely to have lower BP control rate.[25] The National Health Examination Survey (NHES) III in Thailand showed that residence in rural areas, low income and educational levels, current employment and old age were intimately associated with lower BP control rate.[19] In Singapore, men aged ≥65 years with moderate/high body mass index and diabetes were more likely to have inadequate BP control.[15] The associations in education level with HT awareness, treatment and control are inconsistent. The NHES III Study showed that lower education level was associated with poor BP control.[19] On the contrary, the CHPSNE Study[25] and Scottish MONICA Survey,[38] have found lower control rates among those with higher education levels. Among all the other factors, obesity and diabetes may be the most important problems in Asia.

The prevalence of obesity is rapidly increasing in developing countries. Obesity is strongly associated with HT, where obesity is often regarded as a cause of HT—'obesity hypertension',

Table 3 Hypertension (HT) awareness, treatment rate and BP control rate in Asian countries

Study	Country	N	Age (years)	Awareness rate		Treatment rate (%)	Control rate	
							Among HT (%)	Among treatment (%)
Malhotra *et al*[15]	Singapore	4441	≥60	69.7		68	24.1	35.5
Lee *et al*[22]	Korea	6388	≥40	60.1		91.7	16.1	27.2
Wu *et al*[23]	China	141 892	≥18	24		78	–	19
Porapakkham *et al*[19]	Thailand	19 374	≥60	43.9		15.8	1.7	10.6
Kim *et al*[16]	Korea	13 184	≥65	–		66.1	16.4	24.8
Ma *et al*[24]	Southern China	13 889	≥20	Urban	42.8	37.9	13.5	–
				Rural	17.6	10.4	3.4	–
Tian *et al*[25]	Northern China	25 196	18–74	42.9		28.2	3.7	–
Kaur *et al*[26]	India	10 463	25–64	25.1		20	6.6	32.6
Konta *et al*[27]	Japan	250 130	63.6±8.7	–		29.6	23.7	41.4

BP, blood pressure.

which is characterised by increased renal sodium reabsorption and blood volume expansion.[39] The obesity–HT pandemic imposes a considerable economic burden on societies. Obesity contributes to the high prevalence of HT in Asia[40] and results in lowering the BP control rate in China[25] and Singapore.[15] A 5% increase in body weight (equivalent to a gain of 4 kg in an average man or 3 kg in a woman) was closely correlated with a 20–30% increased odds of being hypertensive on 4-year follow-up.[41] In China, data have shown that overweight and obese subjects have about twofold to fivefold risk of developing HT compared with non-obese subjects.[25] What's more, the presence of obesity was also associated with higher rates of high BP in children and adolescents.[42]

East and South Asian populations are subjected to a greater relative risk of developing HT than Caucasian populations at the same level of BMI.[40 43] In Asians, the risk of HT increases at a relatively low body mass index of 22–25 kg/m^2, which is lower than the WHO cut-off for overweight (≥25 kg/m^2).[11 44] The relative risk of having at least one risk factor for cardiovascular disease increased at a relatively low BMI in Asian countries.[44] Data from China indicated that the prevalence of HT, diabetes, dyslipidaemia and clustering of risk factors all increased with increasing BMIs even at indices below the current cut-off point for overweight (ie, 25 kg/m^2).[45] All the above evidences lead to the concern that application of the current WHO BMI cut-off points will underestimate obesity-related risks in these populations.

Diabetes, another major risk factor associated with HT, is common in Asia. Sri Lanka (11.5%) and Malaysia (10.9%) share the highest prevalence in Asia and also rank the top 10 in the world. India and China share the largest contribution in the absolute number of diabetic patients (50.768 million and 43.157 million, respectively). It is estimated that the world prevalence of diabetes will increase by 7.7% (up to 439 million adults) by 2030; the number will reach 87.036 million for India and 62.553 million for China by 2030.[46] Diabetes develops at a younger age in Asians than in Caucasians,[47] and the increase in the number of diabetic patients is expected for all age groups, with doubling of the number for population over 60 years of age.[46]

HT is strongly associated with diabetes. The NHES III in Thailand has shown that the age-adjusted prevalence of HT in diabetic patients was 8.1 for men and 10.3 for women.[19] The Cardiovascular Risk Factor Prevalence Study-2 found that 58% of patients with diabetes had raised BP.[48] Approximately 50% of patients with essential HT are considered to be insulin resistant.[49] Among patients with diabetes, increasing degrees of systolic HT correlated with increased mortality. Data from the MRFIT Study with an average of 12-year follow-up showed that in diabetes, age-adjusted cardiovascular death rates at any given level of systolic BP exceed the death rates in the non-diabetic population.[50] BP control is still largely unsatisfactory in patients with diabetes, who could benefit the most from effective BP control. Study from Korea[28] revealed that diabetes was the most significant independent factor related to poor BP control. Compared with total patients (51%) at the BP control goal <140/90 mm Hg, the BP control rate in patients with diabetes (21.6%) is much more lower at the BP control goal <130/80 mm Hg.[28]

CURRENT STATUS OF TREATMENT OF HT IN ASIA

Lifestyle modification

Considering that overweight, sedentary behaviour, alcohol consumption, higher social class, salt intake, diabetes mellitus and smoking are risk factors for HT in most of the countries in Asia,[11] treatments of HT should involve lifestyle modification in combination with antihypertensive drug therapy. In clinical trial settings, the impact of moderate sodium restriction is a fall in BP in hypertensive and normotensive individuals by 4.8/2.5 and 1.9/1.1 mm Hg, respectively.[51] The 2013 European Society of Hypertension recommends salt intake of approximately 5–6 g per day for general population, in contrast with a typical intake of 9–12 g per day. A reduction to 5 g per day can decrease systolic BP about 1–2 mm Hg in normotensive individuals and 4–5 mm Hg in hypertensive patients.[7] However, the dietary salt intake in many Asian populations severely exceeds these recommended thresholds. In many parts of China, the average salt intake per day is more than 12–15 g,[10] about two to three times higher than the guideline recommendations.[7] Decline in BP induced by weight reduction generally ranges from 0.5 to 2 mm Hg for every 1 kg lost.[52] Therefore, weight reduction is the cornerstone in the management of the obesity–HT syndrome in Asian countries. Anti-obesity strategies, such as diet, exercise, medications and a combination of these measures, should be adopted in obese and overweight hypertensive patients. Other lifestyle modifications, such as cessation of smoking, exercise, limited alcohol intake, comprehensive intervention and patient education, are also important.

Medications

Asians appear to respond well to calcium channel blockers (CCBs).[53] ACE inhibitors have BP-independent benefits for the

Table 4 Antihypertensive drug classes and numbers among Asian countries

Study	Country	N	Age (years)	BP control rate (%)	Drugs N	Drug types				Drugs (N)		
						CCBs (%)	ACE inhibitors/ARBs (%)	β Blockers (%)	Diuretics (%)	Single (%)	2 (%)	≥3 (%)
Kim *et al*[28]	Korea	13 184	≥18	51	–	62.5	60	20.3	13.8	52.5	38	8
KLoSHa *et al*[16]	Korea	995	≥60	24.8	–	64.2	41.2	22	31	54	33	13
Cheng *et al*[29]	China	1208	61.3±13.7	–	1.45±0.66	58	51.7	16.9	16.7	62.9	29.4	7.7
Wu *et al*[30]	Singapore	5022	–	27.1	1.46	35.3	30.5	62.1	15.6	64.0	27.8	8.2
Wu *et al*[31]	Taiwan	29 685	–	59.4	1.62	–	–	–	–	47.4	42.2	10.1
Wong *et al*[32]	Hong Kong	67 113	65	–	–	49.4	22.7	46.2	11.8	51.4	37.0	11.6
Kamijima *et al*[32]	Japan	7356	–	–	1.79	56.6	62.7	14.5	30.5	45.1	–	–

ARBs, angiotensin-receptor blockers; BP, blood pressure; CCBs, calcium channel blockers.

cardiovascular protection,[54] but are associated with a higher incidence (about 20%) of cough in Asian patients. Angiotensin-receptor blockers (ARBs), such as Valsartan, have been shown to prevent more cardiovascular adverse events when added to conventional treatment in Japanese hypertensive patients.[55] Diuretics, such as chlorthalidone, are very effective in combination with other drug classes in Asian patients.[56] Table 4 lists the four main classes of antihypertensive agents used among Asian countries. CCBs and ACE inhibitors/ARBs are still the most frequently used drugs in many Asian countries except Singapore, where the rate of utilisation for β blockers is higher (62.1%) than the other three classes.[30] β Blockers are not recommended as the first-line monotherapy in the absence of a specific indication according to the JNC 7.[4] The prevalence of using β blockers as monotherapy is 26.3% in Hong Kong,[57] yet the BP control rate is comparable with that associated with the use of ACE inhibitors/ARBs (38.0% for β blockers vs 35.5% for ACE inhibitors/ARBs) in China.[58] Another study inspecting the profiles of all-cause and cardiovascular mortality among users of different antihypertensive classes in a Chinese population reported that the crude proportions of all-cause mortality were highest in α blockers (6.2%) and CCBs (5.7%), but lowest in diuretics (3.2%) and β blockers (2.8%).[57]

Data from a Japan study have shown that when compared with 1999, the fraction of hypertensive patients using ARBs has dramatically increased from 1.5% to 55% in 2005 in patients with diabetes and from 1.5% to 40% in patients without diabetes; the use of ACE inhibitors has decreased from 52% to 32% for diabetics and from 35% to 23% for non-diabetics.[33] The rapid increase in the use of expensive ARBs and underuse of cheap thiazides diurectics may increase the medical expenses and aggravate the financial burden for Asian countries.

When selecting antihypertensive drugs clinicians should also consider age, race and gender. Younger patients respond best to ACE inhibitors or ARBs and β blockers, while elderly patients often respond best to a thiazide diuretic or long-acting CCBs.[59] However, many elderly hypertensive patients have a specific indication for an ACE inhibitor or ARB, including heart failure, prior myocardial infarction and chronic kidney disease.[59] ARBs, although more expensive, may be suitable for Asian patients in whom intractable cough is a common side effect of ACE inhibitors. In addition, study from China demonstrated that women have greater BP reduction in response to hydrochlorothiazide and atenolol.[58]

Hypertensive patients who are less than 20/10 mm Hg above goal can initially be treated with monotherapy.[4] Monotherapy is used in 45.1% to 64.0% of the hypertensive patients in Asia (table 4). Data from the Chinese rural population who are treatment naive indicated that CCBs and diuretics were the most effective in achieving good BP control (52.0% and 51.8%, respectively).[58] However, antihypertensive monotherapy is often inadequate for patients with baseline BP more than 20/10 mm Hg above the goal[4] and combination therapy may be needed. The high rate of monotherapy with low rate of optimal BP control in Asian countries suggested that some of these patients may be undertreated. In many Asian countries, the frequency of use of combination therapy is growing but is still lower than the West. Data from a Japanese study demonstrated that when compared with 1999, the rate of use of monotherapy reduced in 2005 from 57.5% to 45.1%, especially in HT patients with diabetes.[33]

Few studies have evaluated patient adherence to drug treatment in Asia. Wong *et al* reported the compliances of the three main drugs in Hong Kong.[60–62] For CCBs,[60] β blockers[61] and

ACE inhibitors,[62] the compliances are 85.0%, 81.3% and 88.0%, respectively. The risk factors for poor or no compliance include younger age, waived fee for medications and newly diagnosed HT.[60–62]

Novel treatment

There are little data with regard to the prevalence of resistant HT in Asia. Novel non-pharmacological treatments, such as baroreflex activation therapy[63] and renal sympathetic denervation[64] appear to be promising with good safety profile and confer to a substantial reduction in BP in patients with drug-resistant HT.

CONCLUSION

HT is a serious problem in Asia. The total number of patients is considerably larger and the prevalence is climbing up due to ageing of the population and the epidemics of obesity and diabetes in Asian countries, although its prevalence is not as high as in Western countries. The insufficient awareness, low treatment and BP control rates are the major problems faced by clinicians treating HT in many Asian developing countries. Prevention programme focusing on the younger population and earlier intervention should be emphasised due to increasing prevalence of high BP in children, particularly in those with obesity. More epidemiological data with regard to the prevalence of drug-resistant/refractory HT, patient adherence to treatment and the burden of cardiovascular complications associated with HT are needed.

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