Hypertension and Renal Dysfunction: NHANES III

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Abstract. The incidence rate of end-stage renal disease has increased in many countries in the past 20 yr, including the United States and Singapore. The increase in ESRD incidence in the United States is primarily attributable to diabetes and to hypertension. In Singapore the major cause of ESRD is diabetes, however the prevalence of hypertension in the Singapore population is rising rapidly, and renal complications of hypertension may become more common in the future. Information on the association of hypertension with renal dysfunction and ESRD in the United States may be useful in predicting future trends in the incidence of ESRD due to hypertension in Singapore. This paper describes published and unpublished data presented at a conference to assist in developing plans for a comprehensive renal disease prevention program in Singapore. It compares recent data on the reported prevalence of hypertension in the United States and Singapore; and presents information on the association of hypertension with serum creatinine, urinary albumin excretion, and ESRD in the United States.

The incidence rate of end-stage renal disease has increased in many countries in the past 20 yr, including the United States (1) and Singapore (2). In 1997, Singapore had one of the highest incidence rates of ESRD in the world (158 cases per million), a rate that was comparable to the United States (296 cases per million) and Japan (229 cases per million) (3). In the US population, the increase in ESRD incidence is primarily attributable to diabetes and to hypertension, whereas in Singapore the major cause of ESRD is diabetes.

Comparison of trends in prevalence of hypertension in the United States and Singapore can be mutually useful. The association of hypertension with renal dysfunction and ESRD in the United States may be useful to health planners in Singapore in predicting trends in the incidence of ESRD due to hypertension, and in planning a renal disease prevention program. Conversely, the periodic National Health and Nutrition Examination Surveys (NHANES) in the United States have not been designed to provide subgroup analyses for Asian ethnic subgroups, and data on the prevalence of hypertension in Singapore may provide insight into disease patterns among US residents who are of Chinese, Asian Indian, and other Asian ethnic descent.

This paper describes published and unpublished data presented at a conference to assist in developing plans for a comprehensive renal disease prevention program in Singapore. It compares the reported prevalence of hypertension in the United States and Singapore, and presents information on the association of hypertension with serum creatinine, urinary albumin excretion, and ESRD in the United States.

Materials and Methods

NHANES III is a cross-sectional examination survey of the US civilian noninstitutionalized population that was implemented in two nationally representative phases (phase 1 in 1988 to 1991, and phase 2 in 1992 to 1994) (4). Overall, more than 29,300 persons aged 6 mo and older participated in NHANES III. Participants were identified using a complex multistage probability sample survey design, and responses were statistically weighted to provide estimated prevalence of diseases and risk factors. Race/ethnicity (non-Hispanic white, non-Hispanic black, and Mexican American) was based on a participant’s self-reported race and parental countries of origin. Non-Hispanic blacks, Mexican Americans, children, and elderly individuals were oversampled to allow more precise estimates of prevalence of disease in these groups. A detailed health interview was conducted in the home, and an extensive examination was conducted in a mobile examination center within several weeks of the interview. BP was measured three times in the home, and three times in the mobile examination center, with the participant seated, and using an appropriate cuff size. All available measurements from an individual were averaged to obtain the BP value used in the analyses. Hypertension was defined as present if a participant reported both ever being told that she or he had high BP and current use of medications to treat high BP, or if the average measured BP was ≥140 mmHg systolic, or ≥90 mmHg diastolic. Serum creatinine was measured by the modified kinetic Jaffe reaction, with a coefficient of variation that ranged between 0.2 to 1.4% during the study (5). Urinary albumin excretion was measured by solid phase fluorescence immunoassay, and urinary creatinine by the modified kinetic Jaffe reaction (6). Albumin excretion was expressed as urinary albumin (mg) to urinary creatinine (g) ratio (ACR).

Incidence counts of new cases with ESRD attributed to hypertension (1) and the estimated numbers of persons in the United States with hypertension (7) for the years 1984 to 1996 were used to calculate the age-specific ratios of the number of incident cases of ESRD per 100,000 hypertensive individuals in the US population.

SAS Proc SURVEYMEANS was used to estimate prevalence of albuminuria (ACR ≥30 mg/g) by level of BP (8).
Prevalence and Treatment of Hypertension in the United States and Singapore

The prevalence of hypertension in the United States in 1988 to 1991 was reported for adults aged 18 yr and older, using data from NHANES III, phase 1 (9). Mean systolic BP increased with increasing age in both men and women, and in all three of the racial/ethnic subgroups that were analyzed in NHANES III (Figure 1). Mean diastolic BP rose with increasing decile of age until age 50 to 59, and declined with increasing age thereafter. Overall, 24% of the adults had hypertension, representing 43.2 million individuals. The age-adjusted prevalence of hypertension was higher in non-Hispanic blacks compared with non-Hispanic whites and Mexican Americans (Figure 2). Among all persons with hypertension in the United States, 69% were aware that they had the disease, and 53% were being treated with anti-hypertensive medications. However, only 45% of the persons treated with antihypertensive medications had BP controlled to <140/90 mmHg. This represents 24% of the total hypertensive population in 1988 to 1991.

Another study, which compared hypertensive persons aged 18 to 74 yr in NHANES II and NHANES III phase I, found that 32% versus 55% were controlled to BP levels <140/90 mmHg in 1976 to 1980 and 1988 to 1991, respectively (10). Note that the 1990 US adult noninstitutionalized population aged 18 to 74 yr was used to standardize the rates.

Singapore conducted a nationally representative National Health Survey in 1992 and in 1998 (11). BP was measured 2 to 3 times using a standardized protocol in persons aged 30 to 69 yr, and the average of the two closest readings was calculated. Hypertension was defined as an average measured systolic or diastolic BP ≥140 mmHg or ≥90 mmHg, respectively. In 1998, hypertension prevalence rates were 31.5% in the Malay ethnic group, compared with 26.9% and 24.6% in the Chinese and the Indian ethnic groups, respectively. Among all persons aged 30 to 69 yr with hypertension in Singapore, 47% were aware that they had the disease. Only 30% of persons with known hypertension had measured BP values <140/90 mmHg. This represents 14% of the total hypertensive population. Comparing data from the 1992 and 1998 surveys, the age standardized prevalence of hypertension among persons aged 30 to 69 yr rose significantly from 22.2% to 27.3% (Figure 2). Note that the 1990 Singapore resident population was used to standardize the rates.
Association of Hypertension with Indicators of Renal Disease Function in NHANES III

In NHANES III, among persons aged 17 yr or older, mean serum creatinine was 1.2 mg/dl in men and 1.0 mg/dl in women (5). Elevated serum creatinine was defined as a serum creatinine value ≥1.6 mg/dl in men and ≥1.4 mg/dl in women (based on serum creatinine cut points that were greater than the 99th percentile of serum creatinine for the subset of the US population aged 20 to 39 who did not have hypertension or diabetes). Three percent of persons aged 17 or more (5.6 million people) had elevated serum creatinine. Elevated serum creatinine was more common in persons with hypertension (9.1%) than in persons without hypertension (1.1%).

The Sixth Joint National Committee on Prevention, Detection, Evaluation and Treatment of High BP (JNC 6) defined six BP control categories ranging from optimal control (BP <120/80) and normal control (BP 120 to 129/80 to 84) to severe stage 3 hypertension (BP ≥180/110) (12). As the JNC 6 BP control category worsened, the prevalence of elevated serum creatinine increased in a dose response fashion (5) (Table 1).

In persons with hypertension and renal insufficiency, the JNC 6 currently recommends BP treatment goals of <130/85 and <125/75 mmHg based on whether urine protein excretion is <1 g/day or ≥1 g/day, respectively (12). In NHANES III, these recommendations were rarely met; only 27% of persons with hypertension (diagnosed and undiagnosed) and elevated serum creatinine had measured BP <140/90 mmHg, and only 11% had BP <130/85 mmHg (5).

This failure to achieve good control may be partially explained by lack of aggressive treatment of high BP in persons with hypertension, even in persons who also have renin insufficiency. In an unweighted analysis of NHANES III participants who had hypertension and elevated serum creatinine, 49% were receiving only one antihypertensive medication (mean BP 151/77 mmHg), and 37% were receiving only two antihypertensive medications (mean BP 148/77 mmHg) (5).

BP control can be achieved with aggressive therapy even in subgroups considered to be difficult to control. The African American Study of Kidney Disease and Hypertension (AASK) enrolled 1094 persons aged 18 to 70 yr with hypertension and renal insufficiency due to hypertensive nephrosclerosis (GFR, 20 to 65 ml/min per 1.73 m²) (13). Participants were randomized to one of two BP treatment goals, a mean arterial pressure (MAP) <92 mmHg (similar to a BP goal <120/70 mmHg) or a MAP between 102 to 107 mmHg; and to one of three blinded study medications; amlodipine, ramipril, or metoprolol. Furosemide, doxazosin, clonidine, hydralazine, and minoxidil were added in a stepped care fashion if the BP was not at the goal level. At baseline, only 20% of those assigned to the low MAP goal had BP <140/90 mmHg; however, 14 mo after randomization 79% had BP controlled to <140/90 mmHg and 48% had a MAP <92 mmHg, using a mean of 3.5 antihypertensive medications.

Albuminuria is a potential indicator of renal dysfunction and is associated with increased risk of renal and cardiovascular disease morbidity and mortality in persons with hypertension (14). In NHANES III among adults aged 20 yr and older, the median albumin to creatinine ratio (ACR) was 5.0 mg/g in men, and 7.0 mg/g in women (6), and the prevalence of microalbuminuria, defined as an ACR between 30 to 299 mg/g, was 7.8% (6.1% in men and 9.7% in women). The prevalence of albuminuria (defined as ACR ≥30 mg/g) was 9.3% (15).

Prevalence of albuminuria increased with increasing severity of the JNC 6 BP category in adult men and women in the United States (Figure 3). The association of albuminuria with BP was also studied in 189,117 adult participants in a screen-

### Table 1. Mean serum creatinine level and prevalence of elevated serum creatinine levels, by blood pressure status, NHANES IIIa

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
<th>Serum Creatinine (mg/dl, mean, (SEM))</th>
<th>Elevated Serum Creatinine, (%) (SEM)d</th>
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</thead>
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<tr>
<td><strong>Total</strong></td>
<td>16,589 100</td>
<td>1.07 (0.003)</td>
<td>3.0 (0.2)</td>
<td></td>
</tr>
<tr>
<td><strong>BP category (JNC-6)</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>optimal</td>
<td>6998 48.3</td>
<td>1.02 (0.004)</td>
<td>1.0 (0.2)</td>
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</tr>
<tr>
<td>normal</td>
<td>3273 20.9</td>
<td>1.10 (0.006)</td>
<td>1.8 (0.3)</td>
<td></td>
</tr>
<tr>
<td>high-normal</td>
<td>2435 13.3</td>
<td>1.11 (0.007)</td>
<td>4.4 (0.5)</td>
<td></td>
</tr>
<tr>
<td>stage 1 hypertension</td>
<td>2656 12.8</td>
<td>1.14 (0.008)</td>
<td>6.6 (0.5)</td>
<td></td>
</tr>
<tr>
<td>stage 2 hypertension</td>
<td>941 3.8</td>
<td>1.21 (0.024)</td>
<td>13.6 (2.0)</td>
<td></td>
</tr>
<tr>
<td>stage 3 hypertension</td>
<td>286 0.8</td>
<td>1.23 (0.028)</td>
<td>18.1 (3.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Hypertension status</strong>x</td>
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<tr>
<td>normotensive</td>
<td>11,672 77.2</td>
<td>1.05 (0.003)</td>
<td>1.1 (0.1)</td>
<td></td>
</tr>
<tr>
<td>hypertensive</td>
<td>4917 22.8</td>
<td>1.16 (0.007)</td>
<td>9.1 (0.5)</td>
<td></td>
</tr>
</tbody>
</table>

a Adapted from Coresh et al. 2001 [(5)].
b Crude number of NHANES III participants.
c Percentage of noninstitutionalized civilian population.
d Elevated serum creatinine defined as ≥1.6 mg/dl (141 μmol/L) in men and ≥1.4 mg/dl (124 μmol/L) in women.
x Hypertension is defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, or use of anti-hypertensive medications.
ing program in Singapore (16). BP was measured 2 to 3 times, and the average BP was calculated. Proteinuria was defined as a urine dipstick test for protein that was 1+ (approximately 30 mg/dl) or higher. Most (88%) participants were 50 yr old. In the screened population, 6.6% reported a history of hypertension, whereas 14.6% had systolic BP ≥140 mmHg and 11.4% had diastolic BP ≥90 mmHg; 1% had proteinuria. Risk of proteinuria increased with systolic and diastolic BP. Simultaneous statistical adjustment was done for gender, age, race, pre-existing history of diabetes or hypertension or renal disease, body mass index (BMI), diastolic and systolic BP, hematuria, glucosuria, and clustering of family histories of diabetes, hypertension, and/or renal disease. The adjusted odds ratios (OR) for proteinuria compared with a systolic BP <110 mmHg were 1.2, 1.4, 1.7, 2.3, 3.3, and 3.8 for systolic BP levels of 110 to 129, 130 to 139, 140 to 159, 160 to 179, 180 to 199, and 200+ mmHg, respectively. The adjusted OR for proteinuria compared with a diastolic BP <80 mmHg were 1.1, 1.5, 1.7, 1.8, and 4.5 for diastolic BP levels of 80 to 89, 90 to 99, 100 to 109, 110 to 119, and 120+ mmHg, respectively. All OR were statistically significant, except the OR for diastolic BP 80 to 89 mmHg.

ESRD Attributed to Hypertension

The age-, gender-, and race-adjusted incidence rates of treated ESRD in the total US population have increased from 89 per million in 1981 to 218 per million in 1991 and 314 per million in 1999 (17), mostly due to the increased incidence of ESRD attributed to diabetes and hypertension (1). Aging of the US population cannot fully explain the increased incidence of ESRD due to hypertension, because the age-specific incidence rates of ESRD attributed to hypertension per 100,000 persons with hypertension have also increased, especially in persons aged 65 yr and older (Figure 4). The increasing incidence rates of ESRD attributed to hypertension have occurred despite a decrease in the prevalence of hypertension from 1976 to 1980 and 1988 to 1994 (Figure 5) (10) and a shift to lower values of systolic and diastolic BP in the US population. In addition, despite the dramatic increase in obesity in the United States, a decrease in the mean systolic and diastolic BP has occurred in each quintile of BMI (based on the BMI distribution in 1976 to 1980), from 1976 to 1980 and 1988 to 1994 (Figure 6) (10).

Discussion

Incidence rates of ESRD attributed to hypertension are rising. Prevalence of hypertension has decreased in the United

Figure 3. Prevalence of albuminuria (albumin creatinine ratio [ACR] ≥30 mg/g) by increasing JNC 6 BP control category, in men and women, NHANES III.

Figure 4. Incidence ratio of ESRD attributed to hypertension per 100,000 persons with hypertension, by age group and calendar year from 1984 to 1996. Incidence ratios were determined using the United States Renal Data System (USRDS) counts of incident cases with ESRD attributed to hypertension in each calendar year as the numerator, and National Health Interview Survey estimates of the number of hypertensive persons in the US population for each year as the denominator.

States, but control of BP to optimal levels in persons with hypertension is still a concern even after more than two decades of an extensive BP education program. Less than optimal control of hypertension may be important, because increasing BP is associated with increased prevalence of elevated serum creatinine and urinary albumin concentrations, two markers for possible kidney disease. The magnitude of the effect of other factors that could affect ESRD incidence rates, such as changes in the rate of premature mortality due to other complications of hypertension, is unclear.

These observations may be relevant to Singapore, which is experiencing a rapidly rising burden of both diabetes and hypertension. In 1997, 41% of incident cases of ESRD in Singapore were attributed to diabetes (2). A prevention program is being developed to decrease the incidence of ESRD in Singapore by screening for undiagnosed hypertension and diabetes in the general population. Although this approach has the potential to affect the future incidence rates of ESRD, the screening must be accompanied by an effective campaign to control BP to optimal levels in persons with both newly diagnosed and previously diagnosed hypertension.

References
17. Private communication from USRDS Data Request Service, usrds@usrds.gov