Prevalence of Kidney Damage in Australian Adults: The AusDiab Kidney Study

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Abstract. The incidence of ESRD is increasing dramatically. Progression to end-stage may be halted or slowed when kidney damage is detected at an early stage. Kidney damage is frequently asymptomatic but is indicated by the presence of proteinuria, hematuria, or reduced GFR. Population-based studies relating to the prevalence of kidney damage in the community are limited, particularly outside of the United States. Therefore, the prevalence of proteinuria, hematuria, and reduced GFR in the Australian adult population was determined using a cross-sectional study of 11,247 noninstitutionalized Australians aged 25 yr or over, randomly selected using a stratified, cluster method. Subjects were interviewed and tested for proteinuria—spot urine protein to creatinine ratio (abnormal: 0.20 mg/mg); hematuria—spot urine dipstick (abnormal: 1+ or greater) confirmed by urine microscopy (abnormal: >10,000 red blood cells per milliliter) or dipstick (abnormal: 1+ or greater) on midstream urine sample; and reduced GFR—Cockcroft-Gault estimated GFR (abnormal: <60 ml/min per 1.73 m²). The associations between age, gender, diabetes mellitus, and hypertension, and indicators of kidney damage were examined. Proteinuria was detected in 2.4% of cases (95% CI: 1.6%, 3.1%), hematuria in 4.6% (95% CI: 3.8%, 5.4%), and reduced GFR in 11.2% (95% CI: 8.6%, 13.8%). Approximately 16% had at least one indicator of kidney damage. Age, diabetes mellitus, and hypertension were independently associated with proteinuria; age, gender, and hypertension with hematuria; and age, gender, and hypertension with reduced GFR. Approximately 16% of the Australian adult population has either proteinuria, hematuria, and/or reduced GFR, indicating the presence of kidney damage. Identifying and targeting this section of the population may provide a means to reduce the burden of ESRD.

The health burden of renal disease is high for patients and health services worldwide. In Australia, renal disease currently consumes 5.7% of the health care budget, not including money spent in providing renal replacement therapy for those with ESRD (1). The incidence of ESRD is increasing, with a doubling in the number of patients treated for ESRD seen in Europe, the United States, and Australia over the past decade (2–4). Consistent with this trend, the burden of renal disease is likely to escalate as both the age of the population and the prevalence of diabetes are projected to increase dramatically (5).

ESRD is usually the result of slowly progressive kidney damage. Due to the asymptomatic nature of renal disease, kidney damage frequently remains undetected until late in the course, at which stage therapeutic interventions are often ineffective. In contrast, early detection and intervention may slow or halt the decline toward ESRD (6). The presence of kidney damage may be indicated by proteinuria, hematuria, or reduced GFR. Individuals with one or more of these indicators of renal disease are known to be at an increased risk of ESRD (7). However, the prevalence of indicators of kidney damage in the general population is not accurately known and the prevalence of early renal disease is probably underestimated. Such data are of vital importance in furthering our understanding of the evolution of renal disease, in planning health resource allocation, and in attempting to reduce the incidence of ESRD.

We therefore performed a population-based survey to define the prevalence of indicators of kidney damage in the general Australian population.

Participants and Methods

Subjects

The Australian Diabetes, Obesity and Lifestyle Study (AusDiab) was a national population-based cross-sectional survey undertaken to determine the prevalence of diabetes mellitus, obesity, and other cardiovascular disease risk factors in Australian adults. Data were also collected relating to indicators of kidney damage. The sample selection is described in detail elsewhere (8). In brief, a representative sample of the national population was drawn from 42 randomly selected urban and nonurban areas (census collector districts) across Australia, with six census-collector districts in each of the six states and the Northern Territory. The study was approved by the International Diabetes Institute ethics committee (Melbourne, Australia). Written informed consent was obtained from all individuals.
**Outcome Measures**

All subjects attended a local screening venue and completed a series of questionnaires, physical examinations, and specific laboratory tests examining diabetic status, cardiovascular risk factors, and kidney function. Blood specimens collected were centrifuged on-site and transported daily with urine samples to the central laboratory (HITECH Pathology).

**Proteinuria.** Urine protein and creatinine were measured on a morning spot urine sample. Urine protein was measured using pyrogallol red-molybdate by the Olympus AU600 auto- analyser; the coefficient of variation was <4.1%. Urine creatinine were measured by the modified kinetic Jaffe reaction using the Olympus AU600 auto-analyser and the coefficient of variation was <1.1%. Proteinuria was defined in terms of urine protein to creatinine ratio, and values of 0.20 mg/mg or greater (approximating 250 mg/24 h) were considered abnormal (9,10).

**Hematuria.** Dipstick testing of morning spot urine samples was performed. Subjects recording zero or trace positive for blood were considered normal, and those with 1+ or greater were asked to provide a midstream urine sample, which was transported to a central laboratory and examined by repeat dipstick and urine microscopy. Subjects with 10,000 or more red blood cells per milliliter by microscopy or with a repeat positive dipstick (1+ or greater) were considered abnormal.

**Estimated GFR.** Blood was collected by venipuncture after an overnight fast. Serum creatinine was measured by the modified kinetic Jaffe reaction using the Olympus AU600 auto-analyser and the coefficient of variation was <1.9%. The Cockcroft-Gault method was used to estimate creatinine clearance (11). Adjustment for body surface area was made using the formula: weight (0.425) × height (0.725) × 0.20247 m$^2$ (12). Cockcroft-Gault estimates of creatinine clearance, when corrected for body surface area, have been found to correlate well with gold-standard measures of GFR in studies examining a similar range of subjects to those studied in AusDiab, including those with type 2 diabetes mellitus, the obese, and the ambulatory elderly (13–16). Renal impairment was defined as estimated GFR less than 60 ml/min per 1.73 m$^2$.

**Diabetes Status.** All participants, except those with a known diagnosis of diabetes mellitus who were taking hypoglycemic medications, were given a standard 75-g oral glucose tolerance test after collection of a blood specimen after an overnight fast of at least 10 h. A second blood sample was taken after 2 h to determine plasma glucose. Standard World Health Organization criteria for the diagnosis of diabetes mellitus were used: fasting plasma glucose ≥7.0 mmol/L or 2-h plasma glucose ≥11.1 mmol/L (17). Plasma glucose levels were measured enzymatically with a glucose oxidase method using the Olympus AU600 auto-analyser.

**Hypertension Status.** Hypertension was defined as systolic BP greater than or equal to 140 mmHg or diastolic BP greater than or equal to 90 mmHg, or use of medication for hypertension irrespective of the BP. BP was measured in a seated position after the participant had rested for at least 5 min using an appropriately sized cuff. In one of the states, BP was measured using a standard mercury sphygmomanometer. Two readings were taken, with a third if the first two differed by more than 10 mmHg. In the remaining states, BP was measured using the Dinamap semiautomatic oscillometric recorder, where three readings were taken at 1-min intervals. To obtain the final measure of BP, the mean of the first two readings was calculated, unless the difference between these readings was greater than 10 mmHg, in which case the mean of the two closest of three measurements was used. Based on a comparison study of readings using the sphygmomanometer and the Dinamap, an adjustment was made to all diastolic BP readings recorded in the state using the sphygmomanometer.

**Statistical Analysis**

All analyses were conducted using Stata version 6.0 (Stata Corporation, College Station, TX, 1999) survey commands for analyzing complex survey data. The survey design included seven strata and 42 primary sampling units, and all prevalence estimates were weighted to represent the noninstitutionalized Australian population thereby accounting for nonresponse and producing nationally representative estimates.

The prevalence rates of hematuria, proteinuria, and reduced GFR were calculated stratified by age, gender, and risk factors for renal disease (diabetes mellitus and hypertension). Differences between subjects were tested by 2-tailed unpaired $t$ test for continuous data and $\chi^2$ test for categorical data. Age was modeled as a categorical variable (25 to 44 yr, 55 to 64 yr, 65 yr or older). The associations between age, gender, hypertension, and diabetes status, and indicators of kidney disease were determined by computing odds ratios and their respective 95% confidence intervals by logistic regression.

**Results**

Of the 19,215 households able to be contacted, 17,130 (89.1%) were eligible for inclusion in the study. Of these, 11,579 (67.0%) agreed to be interview. A total of 20,386 adults from these households were interviewed, and of these 11,247 (55.3%) presented for the physical examination. Information on indicators of kidney disease was available for 97.4% ($n = 10,949$) of participants examined. Subjects were predominantly Caucasian (92.9%), with a minority of Asian (5.7%), and Aboriginal and Torres Strait Islanders (0.8%).

**Prevalence of Indicators of Kidney Damage**

**Proteinuria.** Levels of urine protein to creatinine ratio of 0.2 mg/mg or greater were detected in 2.4% of participants (Table 1). The prevalence was similar in men and women, but increased with age from 0.8% in the 25 to 44 yr age group to 6.6% in those 65 yr of age and over ($P < 0.001$ for trend across age groups). The increase in prevalence of proteinuria with increasing age was seen in both men and women ($P < 0.001$ and $P = 0.013$, respectively, for trend across age groups). Levels of urine protein to creatinine ratio 0.80 mg/mg or greater (approximately 1 g/d urine protein excretion) were detected in 0.4% of participants, and were similar in men and women. The prevalence increased from 0.1% in the 25 to 44 yr age group to 1.0% in those 65 yr of age and over ($P = 0.010$ for trend across age groups). The increase in prevalence of proteinuria with increasing age was seen in both men and women ($P < 0.001$ and $P = 0.011$, respectively, for trend across age groups).

**Hematuria.** Hematuria (Table 2) was detected on initial dipstick testing in 5.2% (95% confidence interval [CI]: 4.3, 6.1). A confirmed finding of hematuria by microscopy or repeat dipstick testing on a midstream sample of urine was found in 4.6% of participants, and was more common in women than men ($P = 0.001$ for difference between genders). The increased risk of hematuria in women than in men was evident in the younger age groups ($P < 0.001$ for difference
between genders for 25 to 44 yr and 45 to 64 yr age groups), but not for those aged 65 yr or older. Given the likelihood that urinary tract infection or menstrual contamination contributed to the higher prevalence of hematuria in younger women, exclusion of cases of isolated hematuria in women under age 50 yr of age and hematuria in the setting of microbiologically confirmed urinary tract infection reduced the prevalence of hematuria to 2.5% (95% CI: 2.0, 2.9). After these exclusions, the risk of hematuria remained more common in women than men (P = 0.004 for difference between genders) and increased from 0.9% in the 25 to 44 yr age group to 5.0% in those 65 yr of age and over (P = 0.001 for trend across age groups). The risk of hematuria was greater in men than women for the 25 to 44 yr age group (P = 0.050 for difference between genders), but greater in women for the 45 to 64 yr age group (P = 0.001 for difference between genders). There was no difference between genders in those aged 65 yr and older.

Renal Impairment. An estimated GFR <60 ml/min per 1.73 m² was present in 11.2% of participants, including over half of those aged 65 yr or older (Table 3). The risk was greater in women (P = 0.002 for difference between genders), and it increased with age from 0.1% in the 25 to 44 yr age group to 54.8% in those 65 yr of age older (P = 0.001 for trend across age groups). The increase in prevalence of a GFR <60 ml/min per 1.73 m² with increasing age was seen in both men and women (P = 0.001 for trend across age groups), and was

Table 1. Prevalence of proteinuria according to age and gendera

<table>
<thead>
<tr>
<th></th>
<th>≥0.20 mg/mg</th>
<th>0.20 to 0.79 mg/mg</th>
<th>≥0.80 mg/mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>All men</td>
<td>2.3 (1.8, 2.9)</td>
<td>1.9 (1.3, 2.4)</td>
<td>0.4 (0.2, 0.7)</td>
</tr>
<tr>
<td>25 to 44 yr</td>
<td>0.5 (0.1, 0.9)</td>
<td>0.3 (0.0, 0.6)</td>
<td>0.2 (0.0, 0.4)</td>
</tr>
<tr>
<td>45 to 64 yr</td>
<td>2.4 (1.6, 3.2)</td>
<td>1.9 (1.1, 2.7)</td>
<td>0.5 (0.0, 1.1)</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>7.5 (5.3, 9.8)</td>
<td>6.4 (4.4, 8.5)</td>
<td>1.1 (0.0, 2.2)</td>
</tr>
<tr>
<td>All women</td>
<td>2.4 (1.2, 3.6)</td>
<td>2.0 (1.2, 2.8)</td>
<td>0.4 (0.0, 0.8)</td>
</tr>
<tr>
<td>25 to 44 yr</td>
<td>1.2 (0.5, 1.9)</td>
<td>1.1 (0.4, 1.8)</td>
<td>0.0 (0.0, 0.0)</td>
</tr>
<tr>
<td>45 to 64 yr</td>
<td>1.9 (0.8, 3.1)</td>
<td>1.4 (0.9, 2.0)</td>
<td>0.5 (0.0, 1.3)</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>5.8 (2.4, 9.2)</td>
<td>4.9 (2.3, 7.6)</td>
<td>0.9 (0.0, 1.8)</td>
</tr>
<tr>
<td>All subjects</td>
<td>2.4 (1.6, 3.1)</td>
<td>1.9 (1.4, 2.5)</td>
<td>0.4 (0.1, 0.7)</td>
</tr>
<tr>
<td>25 to 44 yr</td>
<td>0.8 (0.4, 1.3)</td>
<td>0.7 (0.3, 1.2)</td>
<td>0.1 (0.0, 0.2)</td>
</tr>
<tr>
<td>45 to 64 yr</td>
<td>2.2 (1.4, 3.0)</td>
<td>1.7 (1.3, 2.0)</td>
<td>0.5 (0.0, 1.2)</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>6.6 (4.6, 8.6)</td>
<td>5.6 (3.8, 7.4)</td>
<td>1.0 (0.4, 1.5)</td>
</tr>
</tbody>
</table>

a Data are percent prevalence (95% confidence interval). Proteinuria defined as urine protein to creatinine ratio, mg/mg.

Table 2. Prevalence of hematuria according to age and gendera

<table>
<thead>
<tr>
<th></th>
<th>All Casesb</th>
<th>Excluding UTIC</th>
<th>Excluding UTI and Possible Contaminationd</th>
</tr>
</thead>
<tbody>
<tr>
<td>All men</td>
<td>2.0 (1.4, 2.6)</td>
<td>2.0 (1.4, 2.6)</td>
<td>2.0 (1.4, 2.6)</td>
</tr>
<tr>
<td>25 to 44 yr</td>
<td>1.3 (0.6, 2.1)</td>
<td>1.3 (0.6, 2.1)</td>
<td>1.3 (0.6, 2.1)</td>
</tr>
<tr>
<td>45 to 64 yr</td>
<td>1.6 (0.8, 2.4)</td>
<td>1.6 (0.8, 2.4)</td>
<td>1.6 (0.6, 2.4)</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>4.7 (2.9, 6.5)</td>
<td>4.7 (2.9, 6.5)</td>
<td>4.7 (2.9, 6.5)</td>
</tr>
<tr>
<td>All women</td>
<td>7.2 (5.8, 8.5)</td>
<td>6.7 (5.4, 7.9)</td>
<td>3.0 (2.5, 3.4)</td>
</tr>
<tr>
<td>25 to 44 yr</td>
<td>7.3 (5.0, 9.5)</td>
<td>6.8 (4.6, 8.9)</td>
<td>0.5 (0.1, 0.8)</td>
</tr>
<tr>
<td>45 to 64 yr</td>
<td>8.2 (6.9, 9.4)</td>
<td>7.5 (5.1, 8.8)</td>
<td>5.1 (4.2, 6.1)</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>5.3 (3.4, 7.2)</td>
<td>5.2 (3.3, 7.1)</td>
<td>5.2 (3.3, 7.1)</td>
</tr>
<tr>
<td>All subjects</td>
<td>4.6 (3.8, 5.4)</td>
<td>4.4 (3.6, 5.1)</td>
<td>2.5 (2.0, 2.9)</td>
</tr>
<tr>
<td>25 to 44 yr</td>
<td>4.3 (3.1, 5.5)</td>
<td>4.1 (2.9, 5.2)</td>
<td>0.9 (0.5, 1.3)</td>
</tr>
<tr>
<td>45 to 64 yr</td>
<td>4.8 (4.0, 5.7)</td>
<td>4.5 (3.6, 5.4)</td>
<td>3.3 (2.6, 4.0)</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>5.0 (3.7, 6.4)</td>
<td>5.0 (3.6, 6.3)</td>
<td>5.0 (3.6, 6.3)</td>
</tr>
</tbody>
</table>

a Data are percent prevalence (95% confidence interval).
b “All cases” defined as ≥1+ hematuria on dipstick confirmed by urine microscopy of ≥ 10,000 red blood corpuscles mL or repeat ≥1+ hematuria on dipstick.
c “Excluding UTI” defined as hematuria excluding cases if hematuria was associated with a urinary tract infection without evidence of proteinuria or renal impairment.
d “Excluding UTI and possible contamination” defined as hematuria excluding cases if hematuria was associated with a urinary tract infection without evidence of proteinuria or renal impairment or was present in women under the age of 50 yr without evidence of proteinuria or renal impairment.
greater in women than in men in the 45 to 64 (P = 0.038) and over 65 (P = 0.061) yr age groups. The prevalence of an estimated GFR <30 ml/min per 1.73 m² was 0.3% (95% CI: 0.2%, 0.5%). The prevalence was similar in men and women, but increased with age from 0.0% in the 25 to 44 yr age group to 1.7% in those 65 yr of age and older (P = 0.001 for trend across age groups).

The Kidney Disease Outcomes Quality Initiative (K/DOQI) Work Party has proposed a staging system for chronic kidney disease (18). In adapting this classification to the AusDiab cohort we considered the presence of proteinuria and/or hematuria to indicate kidney damage. Thus, evidence of stage 1 kidney disease (proteinuria and/or hematuria with GFR ≥90 ml/min per 1.73 m²) was present in 0.9% (95% CI: 0.7%, 1.1%); stage 2 kidney disease (proteinuria and/or hematuria with GFR 60 to 89 ml/min per 1.73 m²) in 2.0% (95% CI: 1.6%, 2.5%); stage 3 kidney disease (GFR 30 to 59 ml/min per 1.73 m²) in 10.9% (95% CI: 8.4%, 13.3%); stage 4 kidney disease (GFR 15 to 29 ml/min per 1.73 m²) in 0.3% (95% CI: 0.2%, 0.5%); and stage 5 kidney disease (GFR <15 ml/min per 1.73 m²) in 0.003% (95% CI: 0.000%, 0.009%).

### Overlap between Indicators of Kidney Damage

The proportion of proteinuria found in the absence of either hematuria or reduced GFR <60 ml/min per 1.73 m² was 46.8%; 34.8% of participants with proteinuria also had a reduced GFR, 12.0% also had hematuria and 6.4% had both a reduced GFR and hematuria (Figure 1). The majority of hematuria occurred in the absence of other indicators of kidney damage; 12.1% of participants with hematuria also had a reduced GFR, 5.7% also had proteinuria, and 3.1% had both a reduced GFR and proteinuria. In participants with a reduced GFR, 86.6% occurred without either proteinuria or hematuria; 7.0% of participants also had proteinuria, 5.1% also had hematuria, and 1.3% had both proteinuria and hematuria.

### Predictors of the Presence of Kidney Damage

Older age (odds ratio: 5.0, 95% CI: 4.0, 6.3), diabetes mellitus (odds ratio: 5.0, 95% CI: 3.6, 6.9), and hypertension (odds ratio: 5.4, 95% CI: 4.3, 6.9) were strongly predictive of proteinuria on univariate analysis, and remained independently predictive of proteinuria on multivariate analysis (Table 4). Predictors of hematuria on univariate analysis included female gender (odds ratio: 3.8, 95% CI: 2.8, 5.2) and diabetes mellitus (odds ratio: 0.5, 95% CI: 0.3, 0.8). These variables remained independently predictive of hematuria on multivariate analysis. However, only age, gender, and hypertension status remained independently predictive on multivariate analysis. Age was by far the strongest independent predictor of renal impairment.

### Diabetes

The prevalence of proteinuria was fourfold higher in those with diabetes mellitus compared with those without (8.7%; 95% CI: 6.6%, 10.7% versus 1.9%; 95% CI: 1.2%, 2.5%; P < 0.001). The prevalence of hematuria in those with diabetes was half that seen in those without diabetes mellitus (2.5%; 95% CI: 1.2%, 3.8% versus 4.9%; 95% CI: 4.0%, 5.7%; P < 0.001). The prevalence of a reduced GFR <60 ml/min per 1.73 m² was threefold higher in those with diabetes mellitus compared with those without (27.6%; 95% CI: 22.0%, 33.1% versus 9.8%; 95% CI: 7.6%, 12.1%; P < 0.001).

### Hypertension

The prevalence of proteinuria was fivefold greater in hypertensive participants compared with those with normal BP (5.5%; 95% CI: 4.0%, 7.1% versus 1.1%; 95% CI: 0.7%, 1.5%; P < 0.001). The prevalence of hematuria was similar in those with and without hypertension (5.0%; 95% CI: 3.9%, 6.0% versus 4.5%; 95% CI: 3.6%, 5.4%; P = 0.44).

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**Table 3. Prevalence of renal impairment according to age and gender**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>GFR &lt;60 ml/min per 1.73 m²</th>
<th>GFR 30 to 59 ml/min per 1.73 m²</th>
<th>GFR &lt;30 ml/min per 1.73 m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>All men</td>
<td>9.3 (7.3, 11.4)</td>
<td>9.1 (7.0, 11.1)</td>
<td>0.3 (0.1, 0.4)</td>
</tr>
<tr>
<td>25 to 44 yr</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>45 to 64 yr</td>
<td>1.8 (1.0, 2.6)</td>
<td>1.8 (1.0, 2.6)</td>
<td>0.0 (0.0, 0.0)</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>51.8 (47.1, 56.5)</td>
<td>50.3 (45.6, 55.0)</td>
<td>1.5 (0.6, 2.3)</td>
</tr>
<tr>
<td>All women</td>
<td>13.0 (9.6, 16.4)</td>
<td>12.6 (9.4, 15.8)</td>
<td>0.4 (0.1, 0.7)</td>
</tr>
<tr>
<td>25 to 44 yr</td>
<td>0.0 (0.0, 1.0)</td>
<td>0.0 (0.0, 1.0)</td>
<td>–</td>
</tr>
<tr>
<td>45 to 64 yr</td>
<td>3.2 (1.9, 4.4)</td>
<td>3.2 (1.9, 4.4)</td>
<td>–</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>57.2 (51.4, 63.0)</td>
<td>55.3 (49.2, 61.4)</td>
<td>1.9 (0.7, 0.5)</td>
</tr>
<tr>
<td>All subjects</td>
<td>11.2 (8.6, 13.8)</td>
<td>10.9 (8.4, 13.3)</td>
<td>0.3 (0.2, 0.5)</td>
</tr>
<tr>
<td>25 to 44 yr</td>
<td>0.0 (0.0, 0.0)</td>
<td>0.0 (0.0, 0.0)</td>
<td>–</td>
</tr>
<tr>
<td>45 to 64 yr</td>
<td>2.5 (1.6, 3.3)</td>
<td>2.5 (1.6, 3.3)</td>
<td>0.0 (0.0, 0.0)</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>58.4 (50.2, 60.0)</td>
<td>53.1 (48.7, 57.5)</td>
<td>1.7 (1.1, 2.4)</td>
</tr>
</tbody>
</table>

* a Data are percent prevalence (95% confidence interval).
* b GFR defined as glomerular filtration rate calculated by the Cockcroft-Gault method and corrected for body surface area, ml/min per m².

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reduced GFR <60 ml/min per 1.73 m² was fivefold more prevalent in those with hypertension compared with those without (27.3%; 95% CI: 23.0%, 31.6% versus 4.7%; 95% CI: 3.5%, 6.0%; \( P < 0.001 \)).

**Discussion**

The AusDiab Kidney is the first nationwide, population-based, prevalence study to examine the three key indicators of kidney damage: proteinuria, hematuria, and low GFR. This study demonstrates that approximately 16% of Australian adults have one or more indicators of kidney damage. Our current knowledge of the natural history of such individuals suggests they are at increased long-term risk of ESRD. The implications of these data for the Australian adult population and, by inference, for communities throughout the developed world are significant.
Proteinuria was detected in 2.4% of participants by measuring the protein to creatinine ratio in a morning spot urine sample. Two previous population-based studies have examined the prevalence of proteinuria in adults. Iseki et al. detected proteinuria, as defined by a dipstick result of trace or greater, in 4.0 to 6.0% of men and 2.5 to 7.0% of women in a study of 107,192 Japanese volunteers (7). A similar prevalence, ranging from 1% in 35 to 44 yr olds to 6% in 55 to 64 yr men, was found in a study of US volunteers, which used the Quantitext to detect proteinuria (19). Given that dipstick detection of proteinuria has a low specificity and is likely to overestimate true prevalence (20), these data are consistent with the AusDiab results.

Proteinuria is the cardinal manifestation of overt diabetic nephropathy and hypertensive renal damage. Consistent with this, the prevalence of proteinuria was fourfold higher in diabetics and fivefold higher in those with hypertension. The presence of proteinuria indicates a significant risk of progressive kidney damage. In the general population, participants found to have proteinuria by dipstick on screening examination have been reported to incur a 14-fold relative risk of end-stage renal failure during 10 yr of follow-up (7). For those with established renal disease, proteinuria is an important predictor of the risk of progression (21) and mortality (19). Proteinuric renal disease is amenable to intervention with readily available therapies. Interventions including glycemic control (22), treatment of hypertension (23,24) and interruption of the renin-angiotensin system with converting enzyme inhibitors (25,26) or angiotensin II receptor antagonists (27–29) are known to be effective in retarding progression of diabetic nephropathy and other proteinuric renal diseases.

Hematuria was detected by dipstick in 5.2% of participants and confirmed in 4.6% by microscopy or repeat dipstick: 2.0% of men and 7.2% of women. Much of the higher prevalence in younger women is likely to be due to urinary sepsis and contamination from menstrual blood. Excluding cases of isolated hematuria in the setting of a confirmed urinary tract infection, the prevalence of hematuria was found to be 4.4 to 2.0% in men and 6.7% in women. The additional exclusion of cases of isolated hematuria in women under the age of 50 yr due to possible menstrual contamination results in a prevalence of hematuria of 2.5 to 2.0% in men and 3.0% in women. The prevalence reported in previous population-based studies has varied according to the definition of hematuria. One study based on dipstick results of 1+ or greater reported that 2.8% of men and 11.0% of women had hematuria (7). In contrast, the prevalence of hematuria based on microscopy results of more than ten red blood cells per high power field has been reported as only 0.6% in men and 1.4% in women (30).

On a population basis, hematuria is a less powerful predictor of progressive renal disease than is proteinuria. Participants with dipstick hematuria detected on screening were reported to incur a threefold relative risk of developing end-stage renal failure within 10 yr (7). This is likely because most causes of hematuria, with the exception of glomerulonephritis, are not recognized causes of renal failure: urinary tract infection, renal calculi, prostatic disease, urinary tract tumors, and thin base-membrane disease. Furthermore, the excess of hematuria seen in women of reproductive age also points to menstrual contamination as a likely contributor.

Renal function was assessed by estimated GFR and significant impairment of renal function was highly prevalent, particularly among the elderly and those with hypertension. The largest population-based studies of renal function have used serum creatinine as a measure of renal function (31,32). As in this study, renal impairment was strongly correlated with older age and the presence of hypertension. Elevated serum creatinine was detected in 3.0% of the adult population in NHANES III (31) and in 8.0 to 8.9% of participants in the Framingham cohort (32). However, serum creatinine is known to underestimate the prevalence of renal impairment (33). Prevalence of renal impairment based on GFR estimates was 6.3% in the adult population in NHANES III (34), although this study used serum creatinine cut-points as estimates of GFR <60 ml/min per 1.73 m² rather than Cockcroft-Gault estimated GFR calculated for each individual participant, which was performed in this study. The use of such serum creatinine cut-points has been shown to underestimate the prevalence of reduced GFR compared with the use of both the Cockcroft-Gault and Modification of Diet in Renal Diseases formulas (35). The prevalence of GFR <60 ml/min based on Cockcroft-Gault formula in nondiabetic adults from NHANES III was 14%, and although similar to the findings of this study was not adjusted by body surface area and therefore was not completely comparable (35).

Impairment of GFR has many implications for both the individual and the population, with even mild impairment of GFR having been associated with an increased cardiovascular risk (36–38) and increased mortality rate (32,39). Awareness of a reduced GFR is therefore important to enable targeting of cardiovascular risk factors and treatment of hypertension in particular, which is associated with a reduction in the progression of kidney damage. Reduced GFR also has significant implications for drug prescription and drug toxicities (40).

Proteinuria, microscopic hematuria, and reduced GFR are frequently asymptomatic. Data on the participant’s prior knowledge of renal impairment, proteinuria, or hematuria were not collected. However, knowledge of diabetes and hypertension was assessed and approximately half of those found to be hypertensive or have diabetes mellitus were previously unaware of their diagnosis. Thus, it is probable that many of the subjects were found to have one or more indicators of kidney damage for the first time. It is likely that most people in the community with indicators of kidney disease will remain unaware of their abnormality unless it is detected through screening.

The effect of intervention for those with indicators of kidney disease remains incompletely understood. However, it is clear that some forms of intervention are effective in either slowing or preventing progression toward ESRD. Individuals with hematuria may benefit from specific investigations to determine the etiology, as some processes, such as glomerulonephritis and cancer, may be amenable to therapy. Proteinuric nephropathies, and diabetic nephropathy in particular, may be respon-
sive to blockade of the renin-angiotensin system (25–29). Individuals with reduced renal function from any cause have been shown to benefit from frequent follow-up and monitoring (41). Those with hypertension are less likely to suffer renal failure when their hypertension is treated (23). Thus, individuals with one or more indicators of kidney damage may benefit from intervention. Effective interventions are widely available in Australia and in most developed countries. The major barrier to appropriate management therefore appears to be ignorance of the problem.

The AusDiab Kidney Study has documented a high prevalence of kidney damage in the general Australian adult population, and a similar prevalence is likely to exist in most developed countries. How kidney damage evolves over time and what should be done about it remain to be better defined. The effectiveness of screening for indicators of kidney damage similarly requires appropriate assessment. Given the increasing burden of ESRD worldwide, acquisition of this information should be a global priority.

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