Prevalence of Albuminuria in the U.S. Adult Population Over the age of 40: Results from the National Health and Nutrition Examination Survey (1999-2008)

J Reed III, N Kopyt

Introduction. Albuminuria, defined as either microalbuminuria with an Albumin to Creatinine Ratio (ACR) ratio of 30 – 300 or macroalbuminuria with an ACR ratio > 300, is accepted as a risk factor for the progression of chronic kidney disease and for cardiovascular disease. The purpose of this study was to examine the prevalence of albuminuria in the United States general population in total and by ethnicity over the age of 40 using the 1999-2008 National Health and Nutrition Examination Surveys. The relationship of hypertension, diabetes and metabolic syndrome to albuminuria with age will be reviewed. The effect of age on prevalence of albuminuria will also be demonstrated.

Results: Overall the prevalence of microalbuminuria in U.S. adults 40 years of age and older was 9.8% and the prevalence of macroalbuminuria was 1.7%. The prevalence of albuminuria is highest in patients with diabetes, a history of cardiovascular disease, obesity, and metabolic syndrome. While the prevalence of albuminuria does not differ by males or females in total, there is a difference with females > males in the fourth decade, males > females in the fifth and sixth decades, and then becoming equal with age > 70 years old. Albuminuria is higher in non Hispanic (NH) Black than either Hispanic or NH White.

Conclusion: The NHANES surveys provide a national estimate of the prevalence of albuminuria of nearly 7% in 40-49 year old US adults to 24% in 70+ year old US adults. As the US population ages, the implications of increased prevalence of obesity combined with increased proteinuria has profound implications for the healthcare system in the US - patients, providers, insurance companies, and policy makers. With greater implications is the increased risk of albuminuria across all age groups in the NH Black population. This seems to correlate with the increased cardiovascular risk in this population. The presence of metabolic syndrome seems to have a synergistic effect on increasing the prevalence of albuminuria. This data supports the need to promote increased utilization of albuminuria screening in these high risk populations.

INTRODUCTION

Chronic kidney disease (CKD) is rapidly evolving into a public health problem in the United States. The ever-increasing prevalence of obesity, hypertension and type 2 diabetes mellitus is influencing the rise of chronic kidney disease (CKD) in the United States. Markers of kidney damage typically used to evaluate CKD are a urine albumin-creatinine ratio or a decreased estimated Glomerular filtration rate (eGFR) and the assessment of albuminuria or proteinuria, a creatinine-normalized urinary ratio for albumin or total protein. Both albuminuria and decreased eGFR are linked to an increased risk of kidney failure and risk of fatal and nonfatal cardiovascular disease (1-7).

The goal of the present study was to examine the prevalence of proteinuria in the adult U.S. population over the age of 40 by gender, race/ethnicity, obesity, diabetes, hypertension, history of cardiovascular disease and the metabolic syndrome.

METHODS AND MATERIALS

The National Health and Nutrition Examination Survey (NHANES) is a nationally representative survey of the U.S. civilian non-institutionalized population conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention. Since 1999, NHANES has conducted continuous interviews and physical examinations. This study is based on ten years (1999-2008) of the continuous NHANES data.

NHANES participants are interviewed in their homes to obtain information on health history, health behaviors, and risk factors. Those participants then undergo a detailed physical examination, laboratory studies and additional
interviews were performed at a mobile examination center (MEC). The procedures followed to select the representative sample and conduct the interview and examinations are carefully outlined in the National Center for Health Statistics Analytic Guidelines and informed consent is obtained from all participants. During the MEC examination, a random untimed urine sample was obtained from each participant aged 6 years and older by using clean-catch techniques and sterile containers. Urine samples were placed on dry ice and shipped overnight to a central laboratory where they were stored at -20°C. Urine albumin concentration was measured by solid-phase fluorescent immunoassay on thawed urine specimens or those testing positive for hemoglobin using qualitative test strips. Urinary creatinine concentration was measured in milligrams per deciliter by the modified kinetic method of Jaffe by means of a Beckman Synchron AS/ASTRA analyzer. Venous blood samples were obtained during the physical examination. Serum creatinine was measured by the modified kinetic Jaffe reaction using a Hitachi 737 analyzer and is reported as milligrams per deciliter.

Two measures of urinary albumin excretion were used: UAC (in milligrams per liter) and urinary albumin-to-creatinine ratio (ACR) was computed and is reported in milligrams/gram. Microalbuminuria (MicroAlb) is defined as an ACR of 30 to 300 mg/g and macroalbuminuria (MacroAlb) is defined as an ACR ≥ 300 mg/g. These definitions are consistent for determining abnormal levels of albumin excretion in random spot urine collections (9-10).

Estimated glomerular filtration rate (eGFR), a measure of kidney filtration function, was estimated using the abbreviated Modification of Diet in Renal Disease (MDRD) Study formula based on serum creatinine, age, sex, and race. eGFR = 186.3 x (serum creatinine mg/dl) ^1.154 x age ^0.203 x (0.742 if (female) x (1.21 if black)). Before using the eGFR formula, 0.13 was added to the reported serum creatinine concentration for NHANES 1999-2000 participants. This serum creatinine correction factor is necessary to adjust the NHANES serum creatinine measure with the creatinine assays used in the development of the MDRD equation. eGFR was categorized based on the classification system established by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (New REf). Those categories are defined as follows: eGFR ≥ 90 mL/min/1.73 m², eGFR of 60 to 89 mL/min/1.73 m², eGFR of 30 to 59 mL/min/1.73 m², and eGFR of 15 to 29 mL/min/1.73 m². NHANES participants with an eGFR < 15 were excluded from this analysis.

Diabetes was defined from the NHANES questionnaire with a positive response to a self-report of diabetes or the use of medications to treat diabetes. Obesity was defined as a Body mass index (BMI) of 30 kg/m² or greater NHANES defines a history of CVD as self-reported history of coronary heart disease, angina/angina pectoris, heart attack, congestive heart failure or stroke.

The prevalence of the metabolic syndrome (MetS) as defined by National Cholesterol Education Program Adult Treatment Panel III (ATP-III) is the presence of any three of the following traits in the same individual: abdominal obesity: a waist circumference over 102 cm (40 in) in men and over 88 cm (35 in) in women, serum triglycerides 150 mg/dl or above, HDL cholesterol 40 mg/dl or lower in men and 50 mg/dl or lower in women, blood pressure of 130/85 or more and a fasting blood glucose of 110 mg/dl or above.

Demographic characteristics of participants were based on self-report. Age was defined as the participant’s age at the time of the household interview. Race/ethnicity was categorized as non-Hispanic white, non-Hispanic black, and Mexican American. Individuals who did not self-select into these categories were classified into an “other” race/ethnic group.

Hypertension was defined as present if either one of two criteria were satisfied: (1) an individual self-reported having both received a physician diagnosis of high blood pressure and was taking medication for control of blood pressure, or (2) the mean blood pressure reading was 140 mm Hg or greater systolic or 90 mm Hg or greater diastolic.

RESULTS

The prevalence of albuminuria in 14,585 NHANES by age in all participants, gender, race/ethnicity, obesity, hypertension, history of CVD and the MetS is shown in Table 1. The population albuminuria is a positively skewed variable with a dramatic increase in albuminuria prevalence in those aged 70 or more regardless of gender, race/ethnicity obesity, hypertension, history of CVD or the MetS with 23.7% of participants 70 years of age or older demonstrating proteinuria (microalbuminuria 20.5%, macroalbuminuria 3.2%).
Prevalence of Albuminuria in the U.S. Adult Population Over the age of 40: Results from the National Health and Nutrition Examination Survey (1999-2008)

Figure 1
Table 1. Prevalence of albuminuria by gender, race/ethnicity and selected risk factors by age.

<table>
<thead>
<tr>
<th>Total population</th>
<th>Microalbuminuria</th>
<th>Macroalbuminuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>50-69</td>
<td>&gt;70</td>
</tr>
<tr>
<td>Total</td>
<td>291 (6.9%)</td>
<td>51 (0.8%)</td>
</tr>
<tr>
<td>Female</td>
<td>184 (7.9%)</td>
<td>34 (1.4%)</td>
</tr>
<tr>
<td>Male</td>
<td>107 (5.0%)</td>
<td>17 (0.9%)</td>
</tr>
<tr>
<td>NH-Black</td>
<td>63 (6.0%)</td>
<td>14 (1.4%)</td>
</tr>
<tr>
<td>Mexican American</td>
<td>118 (8.0%)</td>
<td>34 (2.6%)</td>
</tr>
<tr>
<td>NH-White</td>
<td>73 (4.5%)</td>
<td>20 (1.3%)</td>
</tr>
<tr>
<td>Obesity</td>
<td>18 (10.5%)</td>
<td>3 (1.7%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>179 (9.0%)</td>
<td>32 (1.8%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>61 (21.3%)</td>
<td>20 (6.9%)</td>
</tr>
<tr>
<td>History of CVD</td>
<td>12 (12.0%)</td>
<td>3 (3.1%)</td>
</tr>
<tr>
<td>Metabolic Syndrome</td>
<td>20 (3.2%)</td>
<td>3 (1.5%)</td>
</tr>
</tbody>
</table>

The prevalence of diabetes in the U.S. Adult Population Over the age of 40 increased from 13.7% in the 1999-2000 NHANES survey to 17.0% in the 2007-2008 NHANES survey while the prevalence of hypertension and the metabolic syndrome remained relatively stable at 52.7% and 26.9% respectively.

Table 2 details the prevalence of albuminuria in all participants by diabetics, non-diabetic hypertensives, non-diabetic non-hypertensive, diabetic MetS, Diabetic non-MetS, non-diabetic MetS, and non-diabetic non-MetS populations. Nearly one-third (32.0%) of diabetics demonstrated albuminuria (microalbuminuria 24.2%, macroalbuminuria 7.8%), 13.4% of non-diabetic hypertensives demonstrated albuminuria (microalbuminuria 11.7%, macroalbuminuria 1.7%), and 5.5% of the non-diabetic non-hypertensives demonstrated albuminuria (microalbuminuria 5.0%, macroalbuminuria 0.5%). Over one-third (35.1%) of the diabetic MetS demonstrated albuminuria (microalbuminuria 26.5%, macroalbuminuria 8.6%), 28.6% of the diabetic non-MetS demonstrated albuminuria (microalbuminuria 21.7%, macroalbuminuria 6.9%), 13.1% of the non-diabetic MetS demonstrated albuminuria (microalbuminuria 11.6%, macroalbuminuria 1.5%), and 8.0% of the non-diabetic non-MetS demonstrated albuminuria (microalbuminuria 7.1%, macroalbuminuria 0.9%).

Figure 2
Table 2. Prevalence of albuminuria in study groups by age by diabetes status by hypertensive and metabolic syndrome status.

<table>
<thead>
<tr>
<th>Non-diabetic &amp; non-hypertensive population</th>
<th>Microalbuminuria</th>
<th>Macroalbuminuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>114 (4.2%)</td>
<td>9 (0.3%)</td>
</tr>
<tr>
<td>50-69</td>
<td>108 (4.2%)</td>
<td>8 (0.3%)</td>
</tr>
<tr>
<td>&gt;70</td>
<td>154 (5.4%)</td>
<td>11 (0.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>336 (3.9%)</td>
<td>16 (0.4%)</td>
</tr>
</tbody>
</table>

The prevalence of obesity in the U.S. Adult Population Over the age of 40 increased from 34.5% in the 1999-2000 NHANES survey to 37.5% in the 2007-2008 NHANES survey. Table 3 details the prevalence of albuminuria in all participants by obesity status by hypertensive and metabolic status. Overall, 14.3% of obese NHANES participants demonstrated albuminuria (microalbuminuria 12.0%, macroalbuminuria 2.3%), 15.2% of non-obese hypertensives demonstrated albuminuria (microalbuminuria 12.8%, macroalbuminuria 2.4%), and 5.8% of the non-obese non-hypertensives demonstrated albuminuria (microalbuminuria 5.2%, macroalbuminuria 0.6%). Nearly 20% (18.6%) of the obese MetS demonstrated albuminuria (microalbuminuria 15.6%, macroalbuminuria 3.0%), 10.9% of the obese non-MetS demonstrated albuminuria (microalbuminuria 9.2%,
macroalbuminuria 1.7%), 16.0% of the non-obese MetS demonstrated albuminuria (microalbuminuria 13.4%, macroalbuminuria 2.6%), and 8.7% of the non-obese non-MetS demonstrated albuminuria (microalbuminuria 7.6%, macroalbuminuria 1.1%).

**Figure 3**
Table 3. Prevalence of albuminuria in study groups by age by obesity status by hypertensive and metabolic syndrome status.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Non-obese Non-MetS</th>
<th>Non-obese MetS</th>
<th>Non-Hyper MetS</th>
<th>Obese Non-MetS</th>
<th>Obese MetS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microalbuminuria</td>
<td>63 (4.4%)</td>
<td>80 (4.0%)</td>
<td>46 (4.0%)</td>
<td>12 (5.0%)</td>
<td>17 (5.0%)</td>
</tr>
<tr>
<td>Macroalbuminuria</td>
<td>125 (8.9%)</td>
<td>145 (7.3%)</td>
<td>67 (5.6%)</td>
<td>20 (8.0%)</td>
<td>33 (10.5%)</td>
</tr>
</tbody>
</table>

The prevalence of albuminuria and renal insufficiency in all participants is shown in Table 4. As expected, the prevalence of albuminuria increases dramatically as eGFR decreases and as age increases.

**DISCUSSION**
Reportedly, 26 million Americans have CKD. Of these, nearly 50% have an eGFR of at least 60 mL/min/1.73 m² (kidney damage with normal of increased GFR and kidney damage with mildly reduced GFR) (11). Similarly, only 25% of Americans with albuminuria have reduced eGFR while a similar proportion of individuals with low eGFR have proteinuria (12). The presence of either albuminuria or low eGFR identifies an individual with a complex set of biologic conditions that take place in the presence of CKD increasing the risk of death, myocardial infarction and progression to kidney failure suggesting that eGFR and proteinuria could be used to jointly identify at risk individuals (2, 13).

The NHANES survey data provides a national snapshot of the prevalence of albuminuria in the United States. While the prevalence of albuminuria is higher in individuals with diabetes, hypertension, decreased eGFR, obesity, history of CVD, metabolic syndrome, older age and among non-Hispanic blacks, it is nearly equivalent between men and women and between Hispanic and non-Hispanic whites. This analysis mirrors the prevalence estimates in an analysis of NHANES III data (14). This analysis links albuminuria with older age, non-Hispanic black and Hispanic ethnicity, diabetes, hypertension and the MetS. Proteinuria is common among individuals without diabetes and/or hypertension and without MetS and is compounded by the occurrence of combinations of conditions.

As the US population ages, the implications of increased prevalence of obesity combined with increased albuminuria has acute implications to the US system of healthcare - patients, healthcare providers, insurance companies, and
policy makers. Even more so is the greater prevalence of albuminuria in NH Black population and especially in conjunction with metabolic syndrome (15). As we move into the era of electronic medical records and patient centered medical homes, these relationships will prove important in identifying high risk populations to screen early for cardiovascular and chronic kidney disease risk. Early implementation of cardiovascular risk factor reduction programs in these patients may help improve outcomes.

References
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