

Prevalence of Anemia in Chronic Kidney Disease in the United States

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Abstract

Anemia is one of the many complications of chronic kidney disease (CKD). However, the current prevalence of anemia in CKD patients in the United States is not known. Data from the National Health and Nutrition Examination Survey (NHANES) in 2007–2008 and 2009–2010 were used to determine the prevalence of anemia in subjects with CKD. The analysis was limited to adults aged >18 who participated in both the interview and exam components of the survey. Three outcomes were assessed: the prevalence of CKD, the prevalence of anemia in subjects with CKD, and the self-reported treatment of anemia. CKD was classified into 5 stages based on the glomerular filtration rate and evidence of kidney damage, in accordance with the guidelines of the National Kidney Foundation. Anemia was defined as serum hemoglobin levels ≤ 12 g/dL in women and ≤ 13 g/dL in men. We found that an estimated 14.0% of the US adult population had CKD in 2007–2010. Anemia was twice as prevalent in people with CKD (15.4%) as in the general population (7.6%). The prevalence of anemia increased with stage of CKD, from 8.4% at stage 1 to 53.4% at stage 5. A total of 22.8% of CKD patients with anemia reported being treated for anemia within the previous 3 months—14.6% of patients at CKD stages 1–2 and 26.4% of patients at stages 3–4. These results update our knowledge of the prevalence and treatment of anemia in CKD in the United States.

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Introduction

The kidneys function as filters of the blood, removing waste products and controlling the balance of fluid and electrolytes. Filtration occurs via bundles of capillaries called glomeruli (singular, glomerulus). A reduction in the glomerular filtration rate (GFR) to <60 mL/min/1.73 m² indicates chronic kidney disease (CKD), as do structural or functional renal abnormalities, which may be present in people with normal GFR [1]. Cross-sectional estimates of the prevalence of CKD in the United States range from 1.5% to 15.6% [2].

One of the lesser known functions of the kidneys is the production of erythropoietin, a signaling molecule that stimulates red blood cell production, in response to decreased oxygen levels in the blood. Any disruption of this process, e.g., secondary to a functional abnormality due to CKD, has the potential to produce anemia, a condition in which the number of circulating red blood cells, and therefore the level of hemoglobin, is lower than normal [3].

Other possible causes of anemia in CKD include iron deficiency, inflammation, and the accumulation of uremic toxins [3,4]. Thus, the abnormal composition of blood or urine is an additional indicator of kidney damage.

Anemia in CKD is associated with cognitive impairment, sleep disturbances, CKD progression, cardiovascular comorbidities, and higher mortality [3,5–7]. Direct healthcare costs are higher in CKD patients with anemia than in those without [7], and quality

of life issues (e.g., fatigue, reduced productivity) are common [3,5]. The prevalence of anemia (with or without CKD) increases with age [8,9], which means that, as the US population ages, the number of people affected by anemia in CKD will also increase.

Available population-based determinations of the prevalence of anemia in CKD are becoming dated, with many studies referring back to the National Health and Nutrition Examination Survey (NHANES) III, which ended in 1994 [8,10–12]. The most recent studies include NHANES data up to 2006 [8,13], but one was limited to adults over age 64 with advanced CKD [13] and the other used a GFR classification not directly comparable to that of most other studies [8]. This analysis assessed the prevalence of anemia in CKD in the adult (>18 years of age) US population during 2007–2010 using the GFR categories specified by the National Kidney Foundation.

Methods

Study Design and Data Source

This was an analysis of cross-sectional data from the NHANES in 2007–2008 and 2009–2010. The NHANES is a biennial national survey that assesses the physical health of the non-institutionalized civilian population in the United States (www.cdc.gov/nchs/nhanes.htm). It is carried out and overseen by the National Center for Health Statistics, whose institutional review board approves each survey cycle.

Study Sample

The study sample comprised adult subjects aged >18 years who participated in both the interview and examination components of NHANES. Participants provided written informed consent at the time of the survey.

Study Variables

Glomerular filtration rate (GFR) was calculated using the formula $GFR = 175 \times (S_{Cr})^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})$, where S_{Cr} is serum creatinine in mg/dL and age is expressed in years [14]. GFR units are mL/min/1.73 m². CKD was classified into five stages defined by the GFR and/or evidence of kidney damage, as recommended by the National Kidney Foundation [14] and shown in Table 1. Evidence of kidney damage was derived from the presence of albuminuria, which is defined as a urinary albumin-to-creatinine ratio (ACR) ≥ 30 mg/g [14]. The NHANES 2009–2010 data set provided a variable for the urinary ACR (URDACT), but the 2007–2008 data set did not. Therefore, the urinary ACR was calculated for both survey periods from the variables for urinary albumin and creatinine as follows: $ACR \text{ (mg/g)} = \text{urinary albumin (mg/dL)} / \text{urinary creatinine (g/dL)}$. Stage of CKD was not calculated if data for either GFR or ACR were missing, except when GFR values alone indicated CKD of stages 3–5. Anemia was defined as serum hemoglobin levels ≤ 12 g/dL in women and ≤ 13 g/dL in men, as recommended by the National Anemia Action Council and the World Health Organization [15,16].

Statistical Analysis

All analyses were performed in Stata MP v. 12.1 (StataCorp, College Station, TX). Four-year sample weights were calculated for the combined survey cycles as described in the NHANES analytic guidelines [17]. The sample weights were applied to calculate the proportions of subjects with CKD, anemia, and treatment for anemia. Standard errors obtained by Taylor series linearization were used to obtain 95% confidence intervals. Each outcome was determined for all subjects and by stage of CKD. The ‘subpopulation’ option in Stata was used for analyses of subgroups. Subjects with no calculated stage of CKD (N=977; 8.1%) were classified as not having CKD. The prevalence of anemia was determined in all subjects and then separately in subjects with and without CKD. Treatment for anemia was assessed only in subjects with anemia (and CKD). Prevalence values were converted to projections of the respective numbers in the US population based on the 2000 US census.

Table 1. Classification of stage of chronic kidney disease.

Stage	Criteria
1	GFR ≥ 90 plus evidence of kidney damage
2	GFR 60–89 plus evidence of kidney damage
3	GFR 30–59
4	GFR 15–29
5	GFR <15

Stages of CKD were defined in accordance with the recommendations of the National Kidney Foundation. [14].

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Results

Participants

A total of 12,077 adults participated in the interview and examination components of the NHANES surveys in 2007–2008 and 2009–2010.

Prevalence of CKD

The prevalence of CKD was 14.0% (Table 2). This represents an estimated 31.4 million people in the US population. About half (48.4%) of the people with CKD were at stage 3. A similar proportion (46.9%) was in stages 1–2 combined. Only 4.7% were in stages 4–5.

Prevalence of Anemia in CKD

The prevalence of anemia in the combined survey population, regardless of CKD, was 7.6% (result not shown). The prevalence of anemia was 15.4% in people with CKD (Table 3). This represents an estimated 4.8 million people. The prevalence of anemia increased with stage of CKD, from 8.4% at stage 1 to 53.4% at stage 5. The prevalence of anemia in people without CKD was 6.3%.

Treatment of Anemia

A total of 22.8% of CKD patients with anemia reported being treated for it (Table 4). Treatment frequencies were similar at stages 1 and 2 (12.1% and 16.2%; $P=0.57$; weighted mean 14.6%) and stages 3 and 4 (26.5% and 20.7%; $P=0.76$; weighted mean 26.4%).

Discussion

In our analysis of NHANES data from 2007–2010, an estimated 14.0% of the US population had CKD. There are several indications that this value represents a slightly increasing prevalence of CKD in the United States. The first is a comparison with an analysis of the NHANES III (1988–1994), in which the prevalence of CKD was 11.0% [18]. Secondly, the unweighted prevalence of CKD in the NHANES 1999–2004 surveys was reported to be 16.8% [19], slightly lower than the unweighted prevalence in the current study (17.6%). Thirdly, Coresh et al. reported prevalence values of 9.4–13.1% for stages 1–4 of CKD in various analyses covering NHANES III through 2004 [20,21]. Our analysis of stages 1–4 in years 2007–2010 yielded an estimated prevalence of 13.9%. Finally, reports on the Kidney Early Evaluation Program (KEEP) cohort of patients at high risk for CKD indicate that 15.6% of the cohort had GFRs corresponding to CKD stages 3–5 in 2000–2001 [22], whereas 16.8% met this criterion over the period 2000–2009 [23].

In our analysis, anemia was estimated to be present in 15.4% of people with any stage of CKD. The prevalence of anemia increased with stage of CKD, from 8.4% at stage 1 to 53.4% at stage 5. A similar trend has been reported by several other authors [11,24,25], consistent with the known pathogenesis of CKD (i.e., that erythropoietin production decreases as kidney function worsens). Fishbane et al. found high rates of iron deficiency in adult men (57.8 to 58.8%) and women (69.9 to 72.8%) with CKD stages 3–5 in the NHANES III and 1999–2004 surveys [12], indicating that anemia in higher stage CKD may have multiple causes.

Other studies of the prevalence of anemia in CKD focused on older adults (>64 years of age). According to Stevens et al., 29.9% of KEEP 2000–08 participants and 19.9% of NHANES 1999–2006 subjects in CKD stages 3–5 and over age 64 had comorbid

Table 2. Prevalence of chronic kidney disease.

	N	Weighted percentage (95% CI)	95% CI	Projected number in US
With CKD	2,125	14.0	13.2–15.0	31.4×10 ⁶
Stage 1	507	3.1	2.7–3.6	6.8×10 ⁶
Stage 2	489	3.4	2.9–3.9	7.4×10 ⁶
Stage 3	1,028	7.0	6.2–7.9	16×10 ⁶
Stage 4	70	0.4	0.3–0.5	0.9×10 ⁶
Stage 5	31	0.1	0.1–0.2	0.3×10 ⁶
Without CKD	9,952	86.0	85.0–86.9	190×10 ⁶

Percentages reflect the prevalence of each stage of CKD, survey weighted to the US population. The analysis was limited to subjects aged >18 with data from both the exam and interview components of the survey (N = 12,077).
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anemia, defined as hemoglobin levels <13.5 g/dL for men and <12 g/dL for women [13]. For comparison, the prevalence of anemia in stage 3–5 CKD patients aged >64 in the 2007–2010 NHANES surveys was 24.4%. A higher prevalence of anemia (64.9%; defined as hemoglobin <13 g/dL for men, <12 g/dL for women) was observed in US nursing home residents aged >64 with CKD stages 3–5 [25].

Treatments for anemia include iron supplementation and erythropoietin stimulating agents. Reported treatment rates are typically low (10–15%), regardless of the source of data. In an analysis of the National Ambulatory Medical Care Survey (1996–2002), just 10% of outpatient visits for anemia management in CKD resulted in prescription of medication for anemia [26]. In an online survey conducted in 2006, just 15% of 376 family medicine and internal medicine trainees in the United States reported that they would initiate treatment for anemia in CKD at hemoglobin levels <11 g/dL [27]. In our analysis of NHANES 2007–2010, 22.8% of CKD patients with anemia reported being treated for anemia within the previous 3 months.

Insight into the usual timing and types of treatments received (at least among older men) can be gleaned from a study of the Veterans Health Administration database by Lawler et al. [28]. Among 89,000 patients with anemia and CKD (96.7% male, median age 77.5), 7.1% initiated erythropoietin stimulating agents within a year of diagnosis of anemia, while 30.8% initiated iron

therapy and 16.5% used blood transfusions in the same time span. The median time to erythropoietin stimulating agent initiation was 138 days.

CKD prevalence values can vary markedly depending on how GFR is estimated [23,29]. We chose to use the definitions of CKD and GFR established by the National Kidney Foundation to maximize the comparability of our results with previous NHANES and other studies that used these same definitions. We note that a new method for estimating GFR has been shown to be slightly more accurate in classifying patients by stage of CKD [23]. In addition, hemoglobin levels may vary not only by sex but also by age, pregnancy, altitude and smoking status [30]. We used the definitions of anemia given by the National Anemia Action Council and the World Health Organization for simplicity, but did not account for the variables listed above. Our analysis of treatment for anemia was limited by the fact that NHANES data on the various treatments for anemia (e.g., ESAs, iron) were sparse.

Several elements of the study design may have skewed our estimation of the prevalence of CKD. First, inclusion of subject with missing data on GFR and/or ACR likely resulted in underestimation of the full number of people with CKD. On the other hand, albuminuria was assessed with a single spot urine test in NHANES and may have been a temporary condition, resulting in overestimation of the number of subjects at CKD stages 1–2. Lastly, as described in other NHANES-based analyses of CKD, “nonparticipation rates caused by illness relating to having a very low GFR are expected to be particularly high in [stage 5], severely

Table 3. Prevalence of anemia.

	N	Weighted percentage	95% CI	Projected number in US
With CKD	410	15.4	13.1–18.2	4.8×10 ⁶
Stage 1	57	8.4	5.5–12.4	0.6×10 ⁶
Stage 2	68	12.2	9.2–16.0	0.9×10 ⁶
Stage 3	231	17.4	13.7–21.8	2.7×10 ⁶
Stage 4	37	50.3	37.2–63.4	0.5×10 ⁶
Stage 5	17	53.4	34.1–71.7	0.2×10 ⁶
Without CKD	729	6.3	5.3–7.4	11×10 ⁶

The percentages reflect the prevalence of anemia, survey weighted to the US population. The analysis by stage of CKD was limited to subjects with CKD as defined in the Methods section (N = 2,125); data for anemia were missing for a total of 7 CKD patients (<1%), all in stages 1–3. Prevalence of anemia in subjects without CKD was determined in 9,269 subjects with non-missing data on anemia status.

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Table 4. Self-reported treatment of anemia in chronic kidney disease.

Stage of CKD	N	Weighted percentage	95% CI
1	8	12.1	5.4–25.0
2	9	16.2	7.0–33.3
3	59	26.5	21.2–32.6
4	8	20.7	8.8–41.2
5	6	43.0	17.1–73.4
Total	90	22.8	18.5–27.7

The weighted percentages reflect the frequency of treatment of anemia among people within each stage of CKD, survey weighted to the US population. The analysis was limited to subjects with anemia (N = 410).

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downwardly biasing these prevalence estimates” [18].

In summary, CKD prevalence appears to be increasing in the US adult population. In 2007–2010, anemia was present in approximately 15% of CKD patients and was more frequent at higher stages of CKD. Relatively few CKD patients with anemia were being treated for anemia.

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Author Contributions

Conceived and designed the experiments: TF MS. Analyzed the data: MS. Wrote the paper: MS.