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Original Research Article

Temporal trends and demographic disparities in mortality from chronic renal failure with cerebrovascular disease as a contributing cause – a retrospective, population-based observational study in the United States, 1999-2020

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ABSTRACT

Background: Chronic renal failure (CRF) is a major cause of mortality worldwide. However, most studies focus on CRF alone and overlook the contribution of coexisting conditions.
Methods: A retrospective population-based study was conducted using the CDC wonder multiple cause of death database from 1999-2020. Deaths among U.S adults aged ≥25 years with chronic renal failure (ICD-10: n18) as the underlying cause and cerebrovascular disease (ICD-10: i60-i69) as a contributing cause were identified. Mortality trends were analyzed by sex, race, urbanization status, and place of death. Age-adjusted mortality rates and annual percentage changes were calculated using joinpoint regression analysis.
Results: A total of 22,719 deaths were identified, corresponding to a crude mortality rate of 5.1 per million population. The age adjusted mortality rate (AAMR) increased significantly from 2013-2020 (annual percentage changes (APC) +2.9%). Females accounted for 52.1% of deaths and males for 47.9%. Most deaths occurred among whites (68.7%) and black individuals (27.0%). Metropolitan areas accounted for 81.7% of deaths, while inpatient facilities represented the most common place of death (52.3%). Mortality increased among black populations from 2005 (APC +2.6%) and among whites from 2012 (APC +3.1%).
Conclusions: Mortality associated with CRF and cardiovascular disease (CVD) increased after 2013, with substantial disparities across racial, sex, and urbanization groups.

Keywords: Chronic renal failure, Cerebrovascular diseases, Trends in mortality, Age-adjusted mortality rate, Retrospective study, CDC WONDER

INTRODUCTION

Chronic renal failure (CRF) is a growing global public health challenge with a 40% rise in the prevalence and incidence over the past couple of decades.[1] There can be multiple adverse health outcomes preceded by at least three months of abnormalities in kidney structure or function.[2] The majority of people affected are unaware of their diagnosis which leads to challenges to treatment.[3] Cerebrovascular disease (CVD) includes a variety of medical conditions that affect the cerebral circulation and decreased brain perfusion.[4] Chronic renal failure is very much associated with acute and chronic forms of cerebrovascular disease.[5] There are only limited number of studies that address reduction in eGFR is a risk factor for cerebrovascular diseases independent of traditional cardiovascular risk factors such as high blood pressure, smoking, high cholesterol, obesity, physical inactivity, diabetes.[6]

Multiple biological pathways plausibly connect chronic kidney dysfunction to cerebrovascular injury. The kidney and brain share small vessel vulnerability, promoting endothelial dysfunction and impaired auto-regulation. Chronic inflammation and pro thrombotic changes accelerate atherosclerosis, and chronic renal failure related mineral bone disorder together with ureic platelet dysfunction increases bleeding tendencies.[7] Although studies have explored the independent effects of chronic renal failure and cerebrovascular disease on mortality, only few have investigated how these conditions co-occur and influence over all death rates.[8]

Therefore, with the use of CDC multiple causes of death database (MCD), we hypothesis that mortality involving both Chronic renal failure and Cerebrovascular disease where cerebrovascular disease is a contributing cause from 1999 to 2020, has increased over time and is unevenly distributed across demographic and geographic groups such as age, race, sex and geographic location.[9]

Aim and objectives

The aim of the study was to examine temporal trends and demographic disparities in CRF-related mortality with CVD in the U.S. (1999-2020).

METHODS

A retrospective original research study was conducted using the Centers for disease control and prevention wide-ranging online data for epidemiological research (CDC WONDER) multiple cause of death database. The analysis drew upon publicly available mortality data derived from DE identified death certificates for all recorded deaths in the United States. Data were extracted on 01 August 2025. Because the dataset is publicly accessible and contains only DE identified information, the study was classified as non-human subjects research and was therefore exempt from institutional review board (IRB) approval.[10]

Mortality data were extracted from the CDC WONDER MCD database for the years 1999-2020. The study included individuals aged 25 years and above, chronic renal failure (CRF) (ICD-10: N18) was the underlying cause of death, while cerebrovascular disease (CVD) (ICD-10: I60-I69) was selected as the multiple cause of death to assess the co-occurrence of these conditions. Records meeting the age, study-period, and cause-of-death criteria were eligible for inclusion. Death records involving individuals younger than 25 years, records in which chronic renal failure was not identified as the underlying cause of death, and records in which cerebrovascular disease was not identified as a contributing or multiple cause of death were excluded from the analysis. Demographic variables such as gender (male and female) and race/ethnicity (American Indian or Alaska Native, Asian or Pacific Islander, Black or African American, White) were included to analyze disparities in mortality outcomes.

Geographic variables included urbanization based on the 2013 classification, categorizing metropolitan cities into large central metro, large fringe metro, medium metro, and small metro, and non- metropolitan cities into metropolitan and non-core rural areas. Additionally, the place of death was categorized as a medical facility, home, hospice, or nursing facility. Mortality rates were standardized using age-adjusted rates per 1,000,000 population, with adjustments based on the U.S. standard population from the year 2000 to allow for accurate comparisons over time.

Descriptive statistics, including absolute numbers and percentages, were used to summarize the demographic and geographic variables. Age-adjusted mortality rates were calculated for each subgroup using the CDC WONDER MCD database.

To evaluate temporal trends, join point regression analysis (join point software version 5.3.0.0, November 2024) was used to determine annual percentage changes (APC) in mortality with CRF, CVD as a contributing cause. Trends were assessed over the 1999-2020 study period to identify statistically significant changes in mortality patterns across different demographic and geographic groups.[12]

RESULTS

From 1999 to 2020, the CDC MCD database recorded 22,719 deaths in the United States among individuals aged 25 years and older. Among these, deaths were chronic renal failure (ICD-10: N18) was listed as the underlying cause of death and cerebrovascular diseases (ICD: 160-169) was recorded as a multiple cause of death were included in the study (n=22,719).

The crude mortality rate for chronic renal failure with cerebrovascular diseases as a contributing cause was 5.1 per 1,000,000 population. Deaths due to causes other than these criteria were excluded.

Demographic characteristics

Among total deaths analyzed, males accounted for (n=10,881, 47.90%) while females accounted for (n=11,838, 52.1%). The mortality rate for chronic renal failure with cerebrovascular diseases as a contributing cause was higher in females compared to males, indicating a potential demographic disparity. Regarding racial distribution, the highest proportion of deaths occurred among white individuals (n=15,605, 68.7%), followed by Black or African American individuals (n=6,126, 27%), Asian or pacific islander individuals (n=827, 3.60%), and American Indian or Alaska Native individuals (n=161, 0.70%). The mortality burden was highest among whites with, highlighting racial disparities in mortality trends related to chronic renal failure and cerebrovascular diseases (Table 1).

Geographic characteristics

A majority of deaths occurred in metropolitan areas (n=18,574, 81.70%) while non-metropolitan areas accounted for (n=4,145, 18.20%) of deaths. Regarding place of deaths most deaths occurred in medical facilities (n=12,658, 55.70%), followed by nursing home or long-term care facilities (n=5,410, 23.80%), decedents homes (n=2,943, 13.00%), and hospice facilities (n=1,032, 4.50%).

Overall temporal trends

From 1999 to 2020, the age adjusted mortality rate (AAMR) for chronic renal failure with cerebrovascular disease as a contributing cause initially showed a declining trend from 1999 to 2007 with an APC of -1.00% (Figure 1). However, from 2007 to 2013, the AAMR began increasing with an APC of +1.21%. A further steep incline was observed from 2013 to 2020, with an APC of +2.87% ($p<0.05$). The AAMR changed from 2.40 in1999 to 2.90 in 2020, with APC of +2.87% ($p<0.05$) (Figure 3). Significant inflection points were observed in, indicating changes in disease prevalence, treatment advances, and public health interventions.

Gender-specific trends

When stratified by gender, males had a higher AAMR (AAMR: 3.8) compared to females (AAMR: 2.3). However, both groups exhibited different trends, with APCs of +6.37% and -0.91%, respectively. Males showed a significant increase in mortality during 2001 to 2017, while the opposite trend was observed in 1999 to 2001. Females showed a significant increase in mortality during 2001 to 2017, while the opposite trend was observed in 1999 to 2001 (Figure 2).

Race-specific trends

Racial disparities were observed in mortality trends. Whites had the highest AAMR, followed by Blacks or African Americans. The APC for whites was +3.10%, while Black or African American showed a different APC of +2.55%. Trends for Asian or Pacific Islander and American Indian or Alaska Native were not displayed due to data suppression for counts <10, limiting reliable trend analysis.

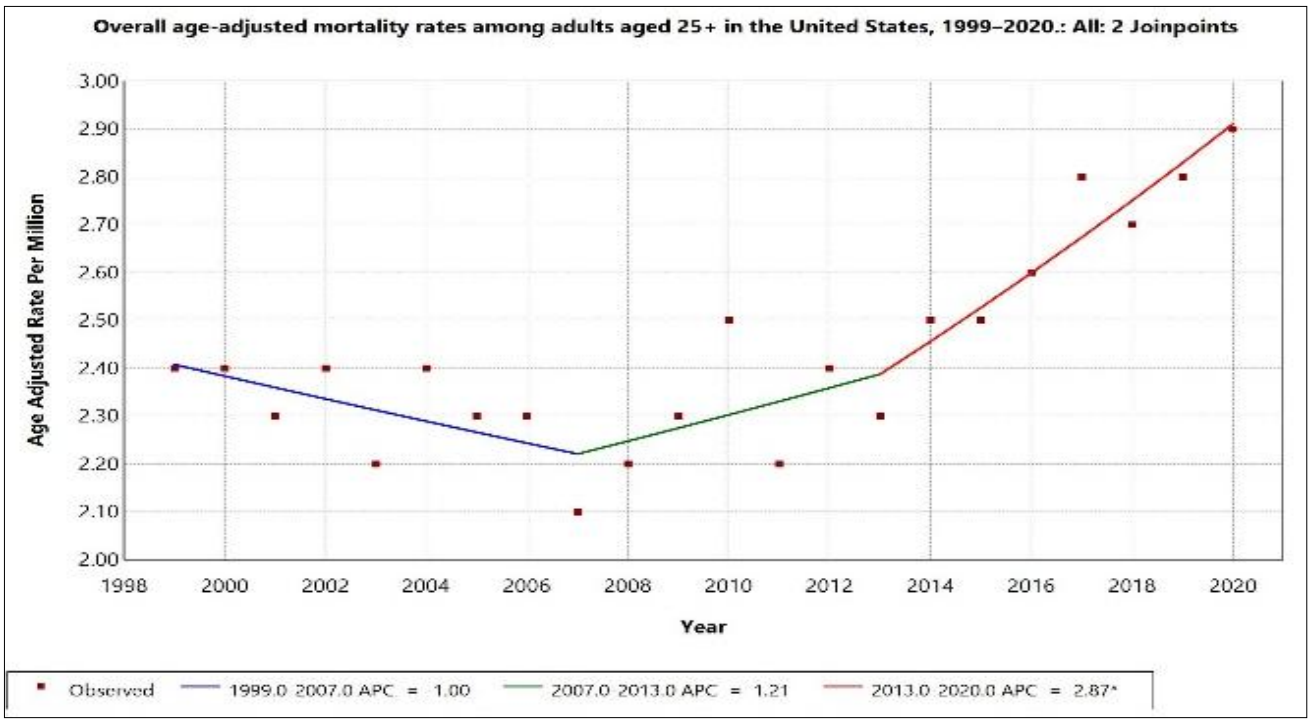

Figure 1: Overall age-adjusted mortality rates among adults aged 25+ in the United States, 1999-2020.
*Indicates that the APC is significantly different from zero at alpha=0.05 level

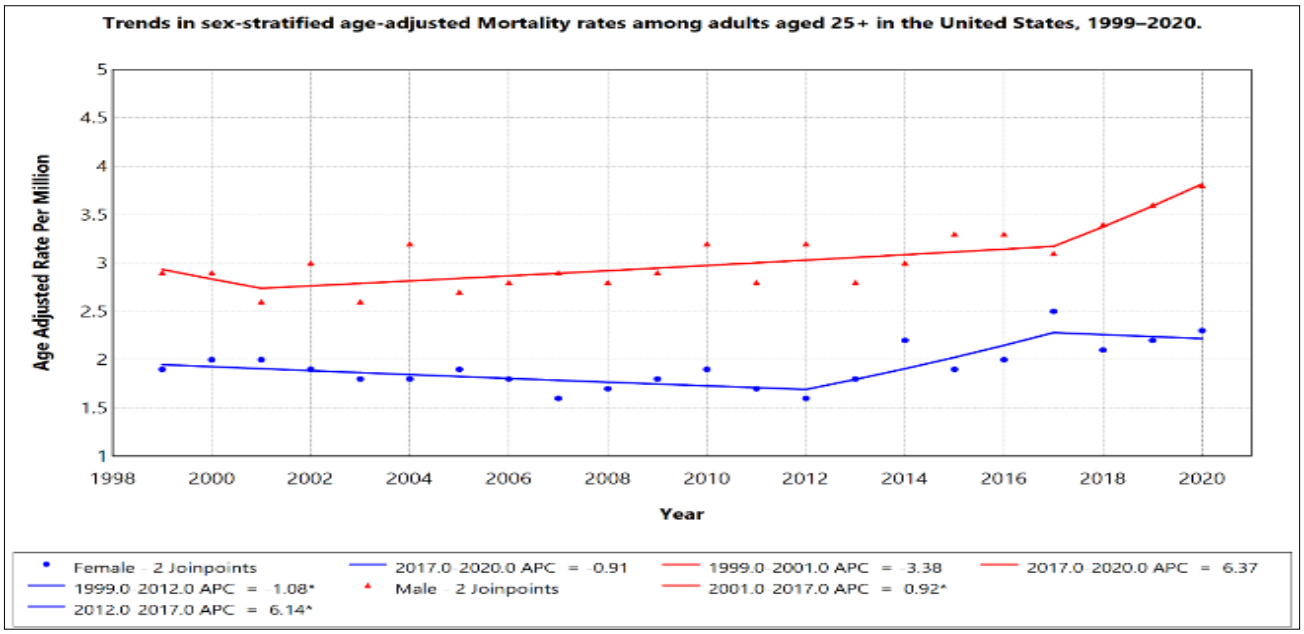

Figure 2: Trends in sex-stratified age-adjusted mortality rates among adults aged 25+ in the United States, 1999-2020.

*Indicates that the APC is significantly different from zero at alpha=0.05 level

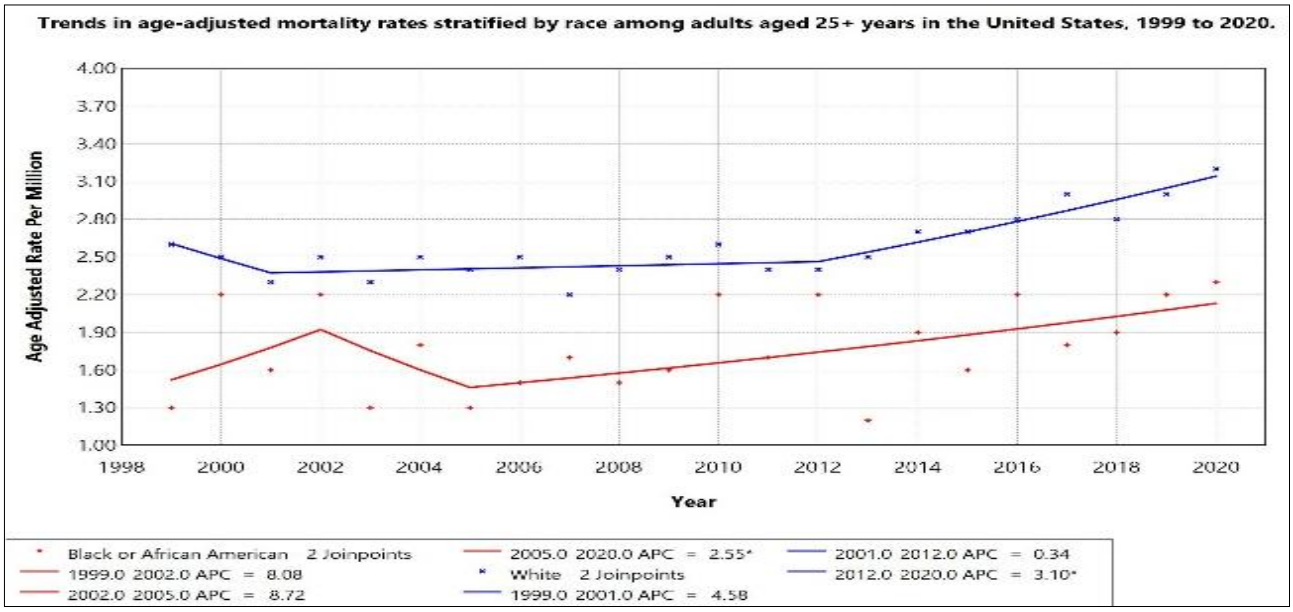

Figure 3: Trends in age-adjusted mortality rates stratified by race among adults aged 25+ years in the United States, 1999 to 2020.

*Indicates that the APC is significantly different from zero at alpha=0.05 level

Table 1: Distribution of deaths by urbanization, place of death, sex, and race.

Category	Number of deaths	Percentage
Urbanization		
Metropolitan area	18,574	81.70
Large central metro	6,483	28.50
Large fringe metro	5,020	22.10
Medium metro	4,749	20.90
Small metro	2,322	10.20

Continued.

Category	Number of deaths	Percentage
Non-metropolitan area	4,145	18.20
Micropolitan	2,279	10.00
Non-core	1,866	8.20
Place of death		
Medical facility	12,658	55.70
Decedent's home	2,943	13.00
Hospice facility	1,032	4.50
Nursing home/long-term care	5,410	23.80
Other	676	2.90
Sex		
Male	10,881	47.90
Female	11,838	52.10
Race		
American Indian or Alaska Native	161	0.70
Asian or Pacific Islander	827	3.60
Black or African American	6,126	27.00
White	15,605	68.70

Temporal trends for American Indian/Alaska Native and Asian or Pacific Islander are not displayed due to data suppression for counts <10, limiting reliable trend analysis.

DISCUSSION

A retrospective study using the CDC MCD database was conducted to assess mortality trends of (N18) (CRF) with cerebrovascular disease (I60-I79) (CVSD) as a contributing cause in the United States from 1999 to 2020 among individuals aged 25 years and older. In the study a total of 22719 deaths were identified where CRF was listed as the underlying cause and CVD was a contributing cause. Over the study period, the AAMR for CRF with CVD showed a declining trend from 1999 to 2007 (APC=-1.00) followed by an increasing trend from 2007 to 2013 (APC=1.21) and finally a significant increasing trend from 2013 to 2020 (APC=2.87). Most deaths occurred among females (52.1%), whites (68.7%), and in metropolitan areas (81.5%).

CRF also known as chronic kidney disease, is evidenced by a gradual loss of kidney function owing to progressive kidney damage. A relationship between renal function and brain structural alterations have been a topic of great interest in recent years. Studies have shown a relationship between CKD markers, CVSD burdens, and cortical thickness.[13,14] The relationship between Albuminuria and WMH burdens has been documented and explained by the shared pathophysiology between kidney and the brain.[14] Larger declines in eGFR were associated with increased MRI-detected infarcts and WMH volumes.[15] Both the organs are exposed to a high blood flow through each cardiac cycle which renders them susceptible to vascular abnormalities. Endothelial damage in the kidney can manifest as a decline in GFR whereas, in the brain it causes defects in the blood brain barrier integrity and development of cerebral infarcts, micro bleeds and white matter changes.[15,16]

This study shows that CRF with cerebrovascular disease has an overall AAMR of 2.4/million in 1999 to 2.95/million in 2020 with an APC of 2.87%. These findings are in line with prior research stating that every 10 ml/min/1.73 m^2 decline in GFR is associated with a 7% increased stroke risk.[17] Another study proves that reduced GFR (<60) is linked with 1.58× higher risk of major vascular events.[18]

This study shows that males had a higher AAMR than females, which is consistent with published articles stating that the female mortality is consistently 30% lower than that of males with the percentage change being less favorable among females than males in more than two-third of the 50 countries examined in the study.[19] Though males have had a slight rising trend ever since 2001 the major difference in trends is seen in the years 2017-2020 where males have had a rising trend compared to females having a downward trajectory. Despite having lower overall mortality women are found to face a higher risk of stroke and stroke related disabilities due to starting treatment for CRF late at lower eGFR and having poor dialysis adequacy.[20] Racial disparities were also observed, with white individuals experiencing the highest increase in AAMR (+3.10% APC from 2014 to 2020). This can be understood by prior research concluding that White people have a greater burden of cardiovascular risk as well as the differences in nutritional and inflammatory profile across races.[21]

This shows a significant difference in mortality between metropolitan and non-metropolitan regions. Several research articles conclude that rural residents have a higher risk of stroke incidence and other cardiovascular mortality when compared to the urban areas.[22,23] This is reflecting the difference in healthcare access, screening and

treatment continuity. Extreme remoteness and limited access to healthcare centers markedly elevates mortality risk- more so than simple rural classification.[24]

This study identified a decline in AAMR from 1999 to 2007 (-1.0) followed by a rise from 2007 to 2013 (APC=1.21) and a significant increase from 2013 to 2020 (APC=2.87). The initial decline can be attributed to early detection and enhanced treatment modalities. However, the inclining trend found post 2007 is probably due to the shifting disease dynamics and rising risk factor prevalence which began pushing mortality upwards in the mid-2000s. The burden was also found to be significantly higher in regions with poor healthcare access and quality (HAQ).[25]

The increasing mortality trends in CRF patients with cerebrovascular disease suggest the need for early detection and risk stratification of CKD. Routine screening for eGFR and albuminuria in high-risk populations.[26]

Aggressive cardiovascular and cerebrovascular risk. Management and improving access and quality of dialysis and stroke care. This can be provided by expanding tele-nephrology and mobile stroke units in rural areas, improving stroke rehabilitation resources and better transport.[19]

Limitations

This data is obtained from CDC WONDER, which relies on underlying and multiple causes of death information as recorded on death certificates. This source may contain inaccuracies or inconsistencies. It lacks data on CKD stage, GFR, albuminuria, and dialysis status. Since it uses cross-sectional mortality records, disease progression and treatment history cannot be tracked. Dependence on precise mortality data in a large dataset.

CONCLUSION

This study, based on CDC multiple cause of death data from 1999 to 2020, highlights a concerning rise in mortality from chronic renal failure when cerebrovascular disease was listed as a contributory cause. Although a decline in age-adjusted mortality was observed until 2007, subsequent years showed a steady and significant increase, particularly after 2013 (APC +2.87%). Mortality burden was greater among females, white and black populations, and in metropolitan areas, with the majority of deaths occurring in inpatient facilities. These findings underscore persistent disparities by gender, race, and geography, reflecting inequities in healthcare access, risk factor control, and continuity of care. The parallel burden of kidney and cerebrovascular disease emphasizes the shared pathophysiological pathways and the need for integrated management strategies. Targeted public health measures such as early screening for kidney dysfunction, aggressive control of cardiovascular and cerebrovascular risk factors, and improved access to dialysis and stroke care, especially in underserved communities are urgently needed. Addressing these gaps will be key to reversing the rising trend and improving survival in this high-risk population.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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