Research Article

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Trends in Mortality Related to Acute Renal Failure in the U.S. from 1999 to 2020: A Retrospective Analysis

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Abstract

Background: *Acute renal failure (ARF) indicates a sudden deterioration in renal function. This study analyzes mortality trends related to ARF in the U.S. from 1999 to 2020 to identify disparities.*

Methods: *We extracted the data from the Centers for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER). Age-adjusted mortality rates (AAMRs) per 100,000 population were calculated for variables: year, gender, race and geographic regions. Annual percent changes (APCs) were analyzed using Joinpoint regression software.*

Results: *From 1999 to 2020, 1,174,156 deaths were reported for ARF-related fatalities in the U.S. Overall AAMR increased from 1999 (17.55, 95% CI 17.36 to 17.75) to 2010 (28.34,95% CI 28.2 to 28.6) with an APC of 4.44 (95% CI 4.17 to 4.7) followed by a decrease from 2010 to 2018 (24.51, 95% CI 24.32 to 24.71) and then an increase till 2020 (30.84,95% CI 30.62 to 31.05) with an APC of 11.85 (95 % CI 7.9 to 14.87). AAMR remained higher in males (30.82) than in females (20.31). Blacks (33.68) had the highest mortality rates, while Asian/Pacific Islanders had lower (16.38). Upon stratification by geographical distribution, the highest AAMR was in the South (26.37). The highest AAMR was observed in Texas and Indiana, with mortality rates being twice as high as states at the lower end of the spectrum, including Alaska, Arizona, and Florida.*

Conclusion: *High ARF-related mortality rates warrant the need for targeted public health initiatives to address these issues and provide healthcare access that can influence ARF-related outcomes.*

Keywords: Acute Renal Failure, Mortality Trends, CDC-WONDER, Epidemiology

Abbreviations

ARF: Acute renal failure
AAMR: Age-adjusted mortality rate
APC: Annual percent change

1. Introduction

Acute renal failure, also known as acute kidney injury, indicates a sudden and usually reversible deterioration in renal function decline in glomerular filtration rate, increased creatinine concentration in serum and plasma, and changes in urine output [1]. The disease burden can be seen from a study conducted in pediatric ICU that indicates that the incidence of ARF was found to be 4.3% among 1145 admissions, and it was the leading cause of mortality, accounting for a 39.1% mortality rate among affected individuals [2].

The causes may be divided into pre-renal, intrinsic and post-renal. Pre-renal causes include hypoperfusion prerenal azotemia that may be due to hypovolemia or low effective arterial blood volume as in

heart failure and cirrhosis/hepatorenal syndrome [3]. The low renal perfusion leads to ischemia and necrosis of renal parenchyma and rapid decline of function. The reduced end arterial blood volume accounts for acute renal failure in hepatorenal syndrome, which is characterized by splanchnic vasodilation, leading to low kidney perfusion despite normal or even increased blood volume status [4]. Postrenal cause is urinary obstruction which may be due to stones, BPH, neoplasm or congenital anomalies [3]. All of these factors cause impaired flow of urine and thus lead to pooling of urine in areas proximal to the obstruction. This leads to a decrease in GFR and ultimately also causes a decrease in renal blood flow. These causes are usually reversible and must be treated promptly [5]. Intrinsic causes include acute tubular necrosis, glomerulonephritis and vasculitis [3]. Risk factors are chronic diseases such as heart failure, liver disease, and diabetes, age above 65 years, vascular diseases, drugs, electrolyte abnormalities, sepsis, etc [3].

Complications include electrolyte abnormalities hyperkalemia, acidosis, etc. and cardiovascular events, which include primarily arrhythmias influenced by these electrolyte abnormalities [6]. Other complications may be neurological, such as uremic encephalopathy, characterized by confusion, seizures, or even coma due to the accumulation of toxins in the blood [7]. Cardiopulmonary complications include pulmonary edema caused by fluid overload due to a decline in kidney function and partly due to fluid retention, and this may manifest as tachypnea and tachycardia [8].

The high load and mortality of the condition necessitated the evaluation of demographic mortality trends attributed to acute renal failure. Early diagnosis of this potentially fatal condition may improve clinical outcomes and prevent lifelong complications [9]. This study aims to identify mortality trends pertaining to acute renal failure from 1999 to 2020. The time zone signifies the advancements made in medical and surgical techniques in the two decades between 1999 and 2020. Clinicians will benefit from the findings of this study.

2. Materials and Methods

2.1. Study Design and Population

We extracted the data for this study from the Centers for Disease Control and Prevention's (CDC) Wide-Ranging Online Data for Epidemiologic Research (WONDER) database. We evaluated the mortality trends due to Acute renal failure in individuals aged 25 years and above in the United States from the year 1999 to 2020. The International Statistical Classification of Diseases and Related Health Problems (ICD-10), 10th Revision codes NI7.0, N17.1, N17.2, N17.8, and N17.9 were used to identify cases of acute renal failure with tubular, cortical, medullary necrosis and other unspecified causes. Prior studies have utilized similar codes for such analysis [10]. Our study focused on certificates of death within the Multiple Cause of Death Public Use dataset to retrieve the mortality data among patients aged ≥25 years with acute renal failure listed as the cause of death. There was no requirement for Institutional review board approval as the data utilized was retrieved from a government-provided, de-identified, publicly available dataset. This study follows the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for reporting.

2.2. Data Extraction

Data from 50 states of the U.S. was retrieved from 1999 to 2020. Extracted data was categorized according to the following variables: year, gender, race, census region and state. Different races included non-Hispanic (NH) White, NH Black or African American, Hispanic or Latino, NH American Indian or Alaskan Native, and NH Asian or Pacific Islander. Consensus regions were divided into four regions: Northeast, Midwest, South and West, as defined by the US Census Bureau [11]. The patients were distributed into 10-year intervals based on whether they were young adults (25–44 years), middle-aged adults (45–64 years), or older adults (65–85+ years).

2.3. Statistical Analyses

We calculated the crude and age-adjusted mortality rates (AAMR) per 100,000 individuals for acute renal failure. This enabled us to adequately analyze the mortality rates over the years. AAMR was standardized to the 2000 US population, a method that accounts for the differences in age distribution in the population [12]. While using the statistical software Joint Point Regression Program (Joinpoint V 5.3.0, National Cancer Institute), Annual percent change (APC) values with 95% CI in AAMR were calculated, and temporal trends were evaluated by fitting log-linear regression models to our raw data. The Grid Search method was used to assess all the join points within the data. Permutation test and parametric method were utilized to estimate the annual percent change (APC) and corresponding 95% CIs. Increasing or decreasing trends as indicated by the APC values were assessed by their statistical significance. APC values were considered significant if $P \leq 0.05$, according to 2-tailed t-tests.

3. Results

3.1. Annual Trends

A total of 1174156 deaths were recorded between 1999 and 2020 with an AAPC of 2.45 (95% CI 2.11 to 2.97) among adults above 25 years of age caused by acute renal failure. The overall age-adjusted mortality rate (AAMR) in 1999 was 17.55 (95% CI 17.36 to 17.75) which increased till 2010 to 28.34 (95% CI 28.2 to 28.6) with an APC of 4.44 (95% CI 4.17 to 4.7). Conversely, there was a decline in AAMR from 2010 to 2018 (24.51 95% CI 24.32 to 24.71) with an APC of -2.2 (95% CI -2.68 to -1.86) and then there was again an increase in AAMR till 2020 (30.84, 95% CI 30.62 to 31.05) with an APC of 11.85 (95 % CI 7.9 to 14.87) **(Figure 1)**.

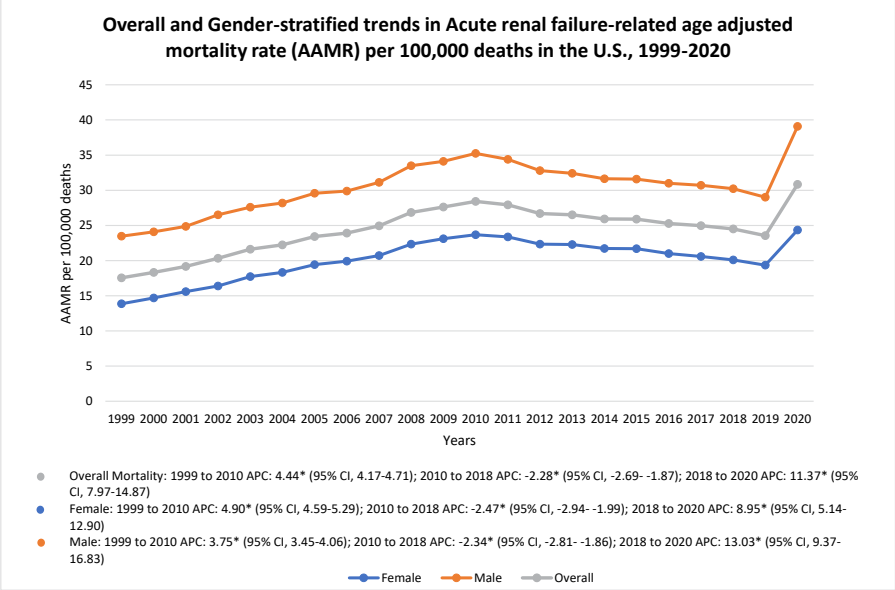

Figure 1: Overall and Gender-stratified Trends in Acute renal failure-related AAMR per 100,000 deaths in adults (> 25 years) in the United States, 1999 to 2020. [* Indicates that Annual Percent Change (APC) is significantly different from zero at $\alpha = 0.05$; AAMR = Age adjusted mortality rate]

3.2. Stratification by Gender

The age-adjusted mortality rate (AAMR) for acute renal failure stratified by gender revealed a higher rate in males (30.82, 95% CI 30.75 to 30.9) than in females (20.31, 95% CI 20.26 to 20.36) throughout the study period, although both reported similar trends in AAMR. In 1999, the AAMR for males was 23.47 (95% CI 23.1 to 23.85), which showed a significant increase to 35.24 (95% CI 34.84 to 35.64) till 2010 with an APC of 3.75 (95% CI 2.7 to 5.22) and then showed a decrease in AAMR to 30.23 (95% CI 29.9 to 30.56) till 2018 with an APC of (-2.33, 95% CI -7.5 to -1.10). A significant rise in AAMR was again reported from 2018 to 2020 (AAMR=39.08, 95% CI 38.71 to 39.44) with an APC of 13.03 (95% CI 3.24 to 18.63). In 1999, the AAMR for females was 13.86 (95% CI 13.64 to 14.09) which showed an increasing trend till 2010 to 23.68 (95% CI 23.41 to 23.95) with an APC of 4.89 (95% CI 4.07 to 5.89) and then a decreasing trend was reported till 2018 to 20.11 (95% CI 19.87 to 20.34) with an APC of -2.4 (95% CI -5.4 to -1.4). A significant rise in AAMR was again reported from 2018 to 2020 (AAMR=24.34, 95% CI 19.87 to 20.34) with an APC of 8.95 (95% CI 1.33 to 12.88) (Figure 1).

3.3. Stratification by Race

The age-adjusted mortality rate for acute renal failure stratified by race revealed highest AAMR in African American patients with a rate of 33.68 (95% CI 33.5 to 33.85), followed by American Indian patients (25.28, 95% CI 24.71 to 25.85), White patients (23.97, 95% CI 23.92 to 24.01), Hispanic/Latino patients (22.24, 95% CI 22.08 to 22.41). The lowest AAMR was recorded in Asian or Pacific Islander patients (16.38, 95 % CI 16.19 to 16.57).

In 1999, the AAMR in African American patients was 27.61 (95% CI 26.76 to 28.46) which increased till 2009 to 38.02 (95% CI 37.12 to 38.92) with an APC of 3.18 (95% CI 2.5 to 3.7) which then decreased till 2018 to 30.22 (95% CI 29.53 to 30.9) with an APC of -3.2 (95% CI -3.9 to -2.5) and then showed a significant increased till 2020 to 44.67 (95% CI 43.87 to 45.48) with an APC of 21.52 (95% CI 14.95 to 28.47). The White patients reported a similar trend in AAMR. In 1999, the AAMR was 16.62 (95% CI 16.41 to 16.82) which increased till 2010 to 27.65 (95% CI 27.41 to 27.89) with an APC of 4.71 (95% CI 4.44 to 4.99) which decreased till 2018 to 24.24 (95% CI 24.03 to 24.45) with an APC of -2.06 (95% CI -2.49 to -1.63) and then showed a significant increase till 2020 to 24.63 (95% CI 29.4 to 29.86) with an APC of 9.33 (95% CI 6.02 to 12.74) (Figure 2).

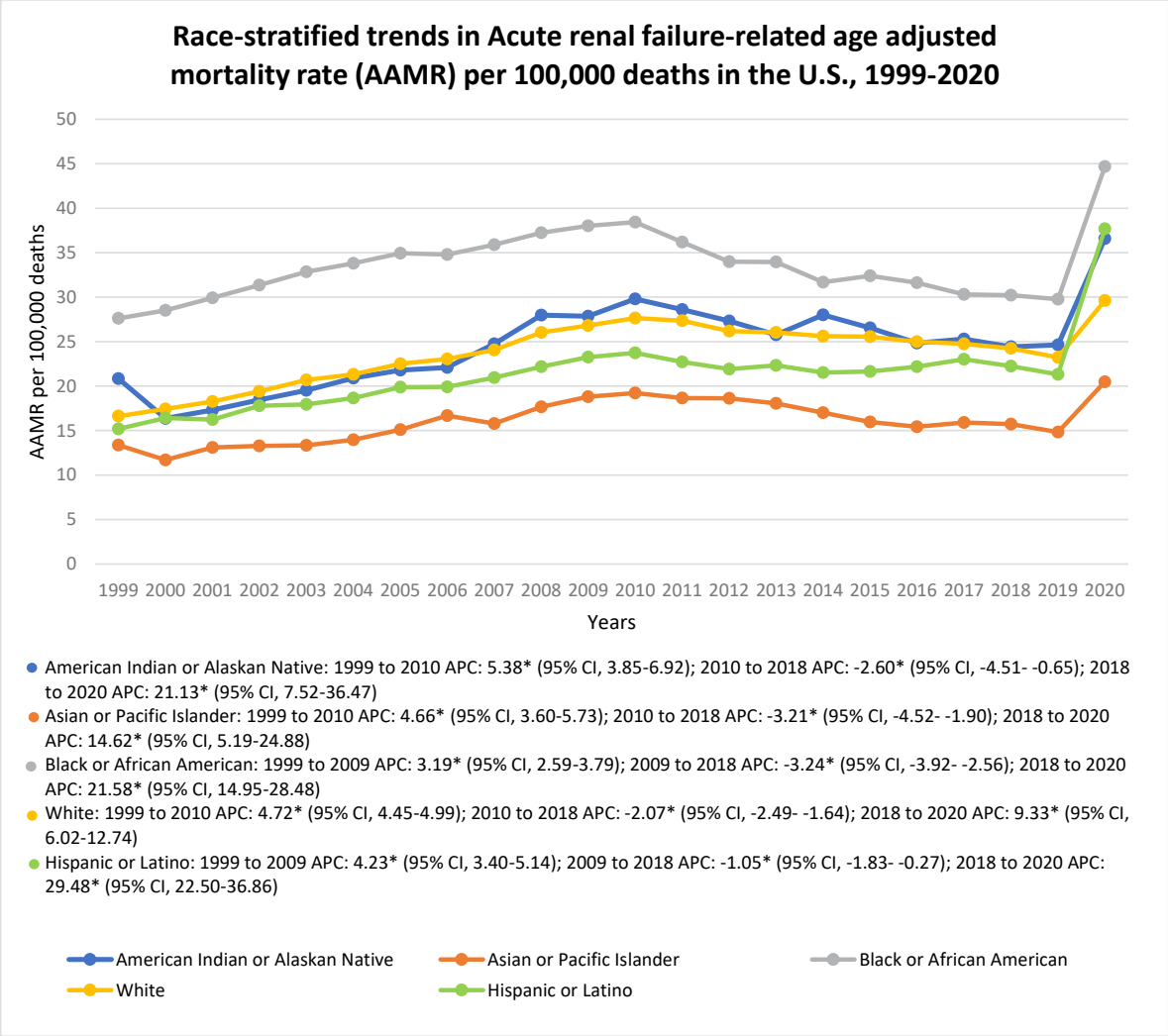

Figure 2: Race-stratified Trends in Acute renal failure-related AAMR per 100,000 deaths in adults (> 25 years) in the United States, 1999 to 2020. [* Indicates that Annual Percent Change (APC) is significantly different from zero at $\alpha = 0.05$; AAMR = Age adjusted mortality rate]

3.4. Stratification by Geographical Variations

The age-adjusted mortality rate for acute renal failure stratified by states revealed the highest AAMR in Texas that was 33.5 (95% CI 33.29 to 33.7), followed by Indiana (33.32, 95% CI 32.96 to 33.68) and the lowest was recorded in Florida with an AAMR of 16.18 (95% CI 16.05 to 16.31). Other states in which the upper 90th percentile of acute renal failure-related mortality were Delaware, Kentucky, South Carolina and West Virginia whereas the states in the lower 10th percentile were Alaska, Arizona, Colorado, Montana, and New York (Figure 3).

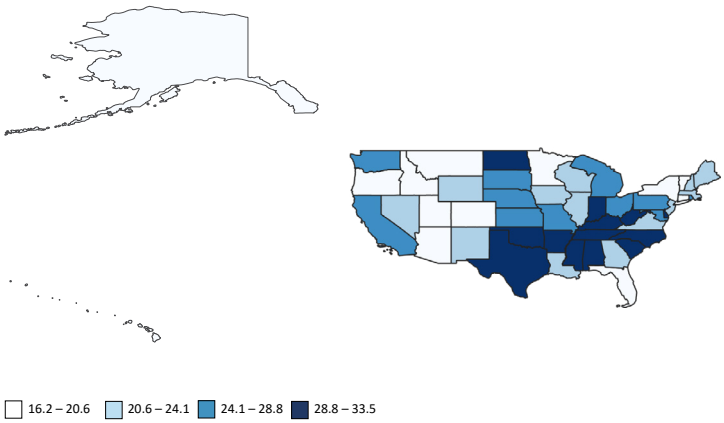

Figure 3: State-wise map showing states with highest and lowest mortality (arranged by state-wise age adjusted mortality rate per 100,000 deaths) in the United States, 1999 to 2020

Among all the regions in the US, the highest AAMR was recorded in the Southern region (26.37, 95% CI 26.29 to 26.44), followed by the Midwestern region (25.37, 95% CI 25.27 to 25.46) and the West (23.37, 95% CI 23.28 to 23.47). The lowest AAMR was recorded in the Northeast region (21.85,95% CI 21.75 to 21.94) (Figure 4).

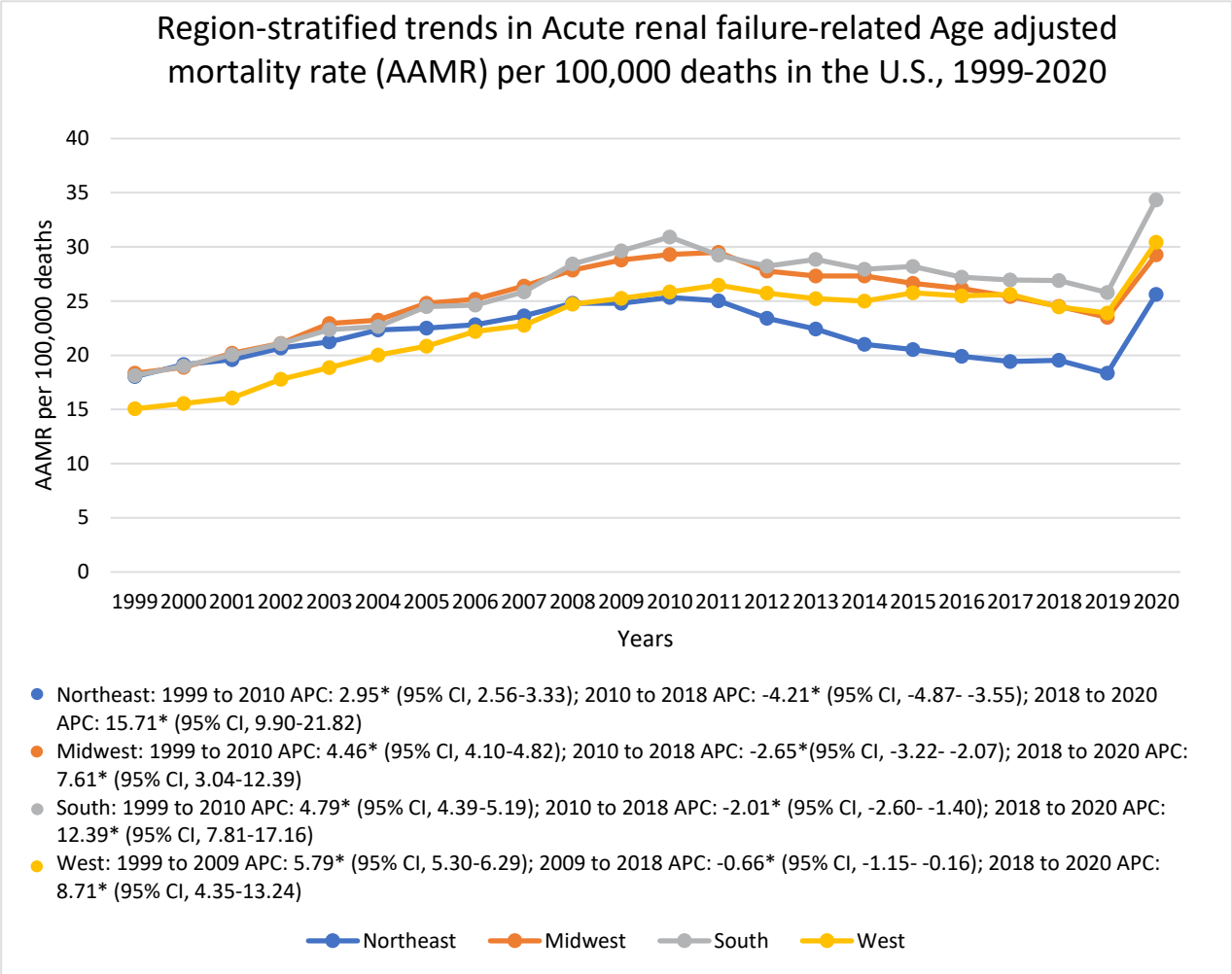

Figure 4: Region-stratified Trends in Acute renal failure-related AAMR per 100,000 deaths in adults (> 25 years) in the United States, 1999 to 2020. [* Indicates that Annual Percent Change (APC) is significantly different from zero at α = 0.05; AAMR = Age adjusted mortality rate]

4. Discussion

There has been an overall increase in mortality with the observed AAPC of 2.45 over the two decades, suggesting an exacerbating burden of acute renal failure with tubular necrosis. It is associated with three distinct phases: an initial rise from 1999 to 2010, a decline from 2010 to 2018 and a sharp increase from 2018 to 2020. Our study reveals that mortality rates are more consistent in males than in females, although both follow similar trends. Among the racial groups, African American patients have the highest AAMR followed by American Indians, White, Hispanic\Latino and Asian\Pacific islander patients. Geographical variations are also significant as the highest mortality rates are documented in Texas, Indiana and the Southern U.S. while the lowest are in Florida and the Northeast.

The initial increase in mortality is possibly due to the rising prevalence of diabetes and hypertension with advancing age. Diabetic ketoacidosis in type 1 diabetes increases the risk of developing acute renal failure [13]. Sepsis with urinary tract obstruction is a significant cause of acute renal failure in diabetics [14]. Disruption of the signaling pathways and increased vulnerability to hypoxia increases the risk of acute kidney damage [15]. Acute kidney injury is considered a major complication of diabetes and people with diabetes are more likely to develop it. Increased incidence of hypertension also elevates the likelihood of developing acute renal failure with oxidative stress as a key factor linking hypertension and acute renal failure [16]. A decline in the mortality trend from 2010 to 2018 is worth observing which can be contributed to improved clinical management and intervention. Improved treatment focusing on the underlying causes, optimizing hemodynamics and managing electrolyte disturbances can reduce mortality significantly [17]. Early initiation of renal replacement therapy can prolong survival [18].

The spike that is seen in the third phase from 2018 to 2020 can be attributed to disruptions in healthcare systems with the advent of COVID-19 which heavily burdened the ICUs.COVID-19 can cause acute kidney injury, posing challenges in the administration of renal replacement therapy [19]. Kidney is one of the major target organs of SARS-COV-2, directly affecting the renal tubules [20]. People with comorbidities and the elderly are more vulnerable to develop AKI due to COVID-19 which explains the sharp rise in mortality from 2018 to 2020 [21]. Hospital stays and the increased load of ICU patients during the pandemic might have contributed to the sharp rise in mortality in the third phase. The management of COVID-19 requires medicines that can put a load on the kidney [22]. Our study shows gender disparities, with males having higher mortality rates compared to females, although similar trends are followed by both. Males show greater renal impairment as compared to females which can be attributed to the protective role of female hormones and detrimental effects of male hormones. Estrogen is nephroprotective which plays a significant role in reducing oxidative stress as compared to testosterone which hastens kidney damage [23].

So, there is a complex interplay between gender and kidney injury susceptibility. Higher mortality in males can also be attributed to a higher prevalence of comorbidities like diabetes and hypertension in males more than females which can be seen across various ethnic groups like urban Bhutanese and western Nepal [24,25]. Another point worth discussing is the higher incidence of smoking and alcohol consumption in males which is a risk factor for acute kidney disease [26]. Men also tend to delay seeking healthcare due to masculinity norms which results in poorer outcomes and, hence, is one of the reasons for high rates of acute kidney injury in the male population [27].

Racial disparities in acute kidney injury are worth noting, with the black population facing greater risks compared to their White counterparts. This can be attributed to lower socioeconomic status, differences in health care delivery, and genetic factors. The disproportionate burden is greatest among African Americans and American Indians, which can be accredited to the presence of APOL1, a risk variant associated with faster progression to kidney disease [28]. Higher incidence of hypertension, diabetes and obesity in African Americans is another one of the risk factors for higher rates of acute kidney disease in this racial group [29]. Due to better access to healthcare and facilities and socioeconomic factors, the incidence is relatively lower among whites [30].

Geographical variations demonstrate the highest AAMR in Texas and the Southern U.S. and the lowest in the Northeast region. Better healthcare access and dialysis-requiring management in the Northeast region mitigates the burden of acute kidney injury [31]. The incidence of comorbidities like diabetes, hypertension and obesity in the Southern and Midwest US is far greater than in the Northeast owing to the highest AAMR in these areas [32]. Southern U.S. states like Texas and Indiana have a warmer climate compared to the Northeast states which predisposes the population to dehydration and hyperosmolality, heightening the risk of acute kidney injury [33].

Our study encompasses a nationally representative cohort of the U.S. population with detailed stratification like higher mortality rates in males, in the Southern and Midwest states and specific racial groups. It also covers 21 years from 1999 to 2020 with the identification of three major trend phases. It also uses indicators AAMR and APC which reduce the bias and highlight the statistically significant shifts. This allows comprehensive analysis of the data which then guides the targeted interventions in the high-risk groups and regions.

There are some limitations in our study. First, it is retrospective which increases the potential for bias and unreliability. Second, there is a lack of clinical history, treatment plan and lifestyle factors which limits the appropriate analysis of our findings. Third, the results cannot be generalized and the findings are limited by reporting bias and regional differences in healthcare access. Fourth, the death certificates and ICD coding in our study produce misclassification errors, which can lead to data discrepancies and, hence, affect the interpretation of our results.

In conclusion, this study shines light on the disparities in mortality due to acute renal failure. Following a period of decline, there has been a steep rise in mortality in the last decade which indicates the need for expanding the screening programs for early detection, improving healthcare access in vulnerable communities, and establishing climate-related and gender-specific health policies to reduce mortality.

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Total number of Acute renal failure-related deaths and Age adjusted mortality rate stratified by sex and race, among adults (> 25 years) in the United States, 1999 to 2020				
	Total Deaths	Overall AAMR per 100,000 deaths	95% Confidence Interval	
			Lower	Upper
Total	1174156	24.66	24.62	24.71
Gender				
Female	571751	20.31	20.26	20.36
Male	602405	30.82	30.75	30.9
Race				
American Indian or Alaska Native	8641	25.28	24.71	25.85
Asian or Pacific Islander	28951	16.38	16.19	16.57
Black or African American	149131	33.68	33.5	33.85
White	987433	23.97	23.92	24.01
Hispanic or Latino	79433	22.24	22.08	22.41
Region				
Northeast	208343	21.85	21.75	21.94
Midwest	274301	25.37	25.27	25.46
South	453350	26.37	26.29	26.44
West	238162	23.37	23.28	23.47
Abbreviations: AAMR, Age adjusted mortality rate.				

Supplementary Table S1: Total number of Acute renal failure-related deaths and Age adjusted mortality rate stratified by sex, race and region, among adults (> 25 years) in the United States, 1999 to 2020.

Acute renal failure-related age adjusted mortality rates per 100,000 deaths stratified by state in adults (> 25 years) in the United States, 1999 to 2020					
State	Deaths	Age Adjusted Mortality Rate per 100,000 deaths	95% Confidence Interval		% of Total Deaths
			Lower	Upper	
California	130725	25.25	25.11	25.39	11.13%
Texas	103607	33.5	33.29	33.7	8.82%
Pennsylvania	61994	26.06	25.86	26.27	5.28%
Florida	60413	16.18	16.05	16.31	5.15%
New York	55509	17.42	17.27	17.56	4.73%
Ohio	52698	27.5	27.27	27.74	4.49%
Illinois	43451	22.29	22.08	22.5	3.70%
North Carolina	42005	29.95	29.66	30.23	3.58%
Michigan	38834	24.22	23.98	24.46	3.31%
New Jersey	33667	23.36	23.11	23.62	2.87%
Indiana	33002	33.32	32.96	33.68	2.81%
Tennessee	29564	30.82	30.47	31.18	2.52%
Missouri	28133	28.78	28.44	29.12	2.40%
Massachusetts	27291	24.15	23.86	24.43	2.32%
Washington	26988	27.16	26.84	27.49	2.30%
Virginia	26302	23.14	22.86	23.42	2.24%
Georgia	26115	21.74	21.48	22.01	2.22%
South Carolina	23361	33.09	32.66	33.52	1.99%
Maryland	22081	26.05	25.7	26.39	1.88%
Kentucky	21836	33.21	32.76	33.65	1.86%

Wisconsin	21883	23.17	22.86	23.48	1.86%
Alabama	21561	29.15	28.76	29.54	1.84%
Arizona	19339	19.58	19.3	19.86	1.65%
Minnesota	16948	20.11	19.8	20.41	1.44%
Oklahoma	16606	28.83	28.39	29.27	1.41%
Louisiana	15465	23.71	23.33	24.08	1.32%
Arkansas	14344	30.48	29.98	30.98	1.22%
Mississippi	13021	29.86	29.35	30.38	1.11%
Oregon	13073	20.62	20.26	20.97	1.11%
Iowa	12706	22.73	22.33	23.14	1.08%
Colorado	12342	18.78	18.44	19.11	1.05%
Connecticut	12046	19.07	18.73	19.42	1.03%
Kansas	11631	25.1	24.64	25.56	0.99%
West Virginia	10382	31.27	30.66	31.87	0.88%
Nevada	7922	22.02	21.53	22.51	0.67%
Nebraska	7587	24.96	24.39	25.53	0.65%
New Mexico	6278	20.65	20.14	21.17	0.53%
Utah	5982	20.58	20.06	21.11	0.51%
Maine	5528	22.38	21.79	22.98	0.47%
Rhode Island	5336	27.56	26.81	28.31	0.45%
New Hampshire	4834	22.66	22.02	23.3	0.41%
Hawaii	4691	20.04	19.46	20.62	0.40%
Idaho	4587	20.54	19.94	21.13	0.39%
Delaware	4467	30.75	29.84	31.65	0.38%
South Dakota	3753	26.15	25.3	27	0.32%
North Dakota	3675	30.08	29.09	31.07	0.31%
Montana	3283	19.39	18.72	20.06	0.28%
District of Columbia	2220	25.93	24.84	27.02	0.19%
Vermont	2138	19.89	19.04	20.74	0.18%
Wyoming	1768	21.78	20.75	22.8	0.15%
Alaska	1184	18.27	17.16	19.38	0.10%
Abbreviations: AAMR, Age adjusted mortality rate					

Supplementary Table S2: Acute renal failure-related age adjusted mortality rates per 100,000 deaths stratified by state (arranged by states with highest to lowest % of total deaths) in adults (> 25 years) in the United States, 1999 to 2020.

Gender stratified Acute renal failure-related age adjusted mortality rate per 100,000 deaths in adults (> 25 years) in the United States, 1999 to 2020						
	Female			**Male**		
Year	**AAMR per 100,000**	**Lower 95% Confidence Interval**	**Upper 95% Confidence Interval**	**AAMR per 100,000**	**Lower 95% Confidence Interval**	**Upper 95% Confidence Interval**
1999	13.86	13.64	14.09	23.47	23.10	23.85
2000	14.70	14.47	14.93	24.09	23.71	24.46
2001	15.59	15.36	15.82	24.86	24.48	25.23
2002	16.40	16.16	16.64	26.51	26.13	26.90
2003	17.72	17.48	17.97	27.60	27.21	27.98
2004	18.32	18.07	18.57	28.20	27.81	28.59
2005	19.42	19.17	19.67	29.57	29.18	29.96

2006	19.91	19.66	20.17	29.88	29.50	30.27
2007	20.71	20.45	20.97	31.13	30.74	31.52
2008	22.33	22.07	22.60	33.49	33.09	33.89
2009	23.11	22.84	23.38	34.12	33.72	34.52
2010	23.68	23.41	23.95	35.24	34.84	35.64
2011	23.36	23.09	23.62	34.39	34.00	34.78
2012	22.33	22.07	22.59	32.79	32.41	33.16
2013	22.29	22.03	22.55	32.40	32.03	32.76
2014	21.73	21.47	21.98	31.64	31.28	32.00
2015	21.70	21.45	21.95	31.59	31.24	31.94
2016	20.99	20.75	21.23	30.99	30.65	31.34
2017	20.60	20.36	20.84	30.71	30.37	31.04
2018	20.11	19.87	20.34	30.23	29.90	30.56
2019	19.36	19.13	19.59	29.01	28.69	29.33
2020	24.34	24.08	24.59	39.08	38.71	39.44

Supplementary Table S3: Gender stratified Acute renal failure-related age adjusted mortality rate per 100,000 deaths in adults (> 25 years) in the United States, 1999 to 2020.

Race stratified Acute renal failure-related age adjusted mortality rate per 100,000 deaths in adults (> 25 years) in the United States, 1999 to 2020															
Year	American Indian or Alaska Native			Asian or Pacific Islander			Black or African American			White			Hispanic or Latino		
	AAMR per 100,000	95% Confidence Interval		AAMR per 100,000	95% Confidence Interval		AAMR per 100,000	95% Confidence Interval		AAMR per 100,000	95% Confidence Interval		AAMR per 100,000	95% Confidence Interval	
		Lower	Upper		Lower	Upper		Lower	Upper		Lower	Upper		Lower	Upper
1999	20.83	17.31	24.34	13.36	12.14	14.58	27.61	26.76	28.46	16.62	16.41	16.82	15.19	14.31	16.06
2000	16.37	13.54	19.2	11.7	10.62	12.78	28.53	27.68	29.39	17.42	17.21	17.62	16.41	15.52	17.29
2001	17.32	14.47	20.17	13.11	11.99	14.22	29.92	29.05	30.79	18.26	18.05	18.47	16.24	15.39	17.1
2002	18.46	15.56	21.37	13.28	12.2	14.37	31.35	30.46	32.23	19.4	19.19	19.62	17.79	16.92	18.65
2003	19.51	16.58	22.45	13.34	12.29	14.39	32.85	31.95	33.75	20.69	20.47	20.91	17.93	17.08	18.77
2004	20.89	17.86	23.91	13.97	12.92	15.02	33.8	32.9	34.71	21.31	21.09	21.53	18.67	17.82	19.52
2005	21.8	18.83	24.77	15.09	14.04	16.14	34.95	34.04	35.86	22.51	22.28	22.73	19.89	19.05	20.74
2006	22.08	19.21	24.96	16.7	15.63	17.77	34.8	33.9	35.7	23.04	22.82	23.27	19.91	19.09	20.73
2007	24.76	21.8	27.72	15.78	14.77	16.79	35.89	34.98	36.79	24.07	23.84	24.3	20.95	20.12	21.78
2008	27.98	24.88	31.08	17.68	16.64	18.72	37.23	36.33	38.14	26.03	25.8	26.27	22.19	21.37	23.02
2009	27.85	24.86	30.84	18.8	17.76	19.84	38.02	37.12	38.92	26.8	26.56	27.04	23.26	22.45	24.08
2010	29.79	26.74	32.84	19.22	18.19	20.25	38.43	37.54	39.33	27.65	27.41	27.89	23.73	22.92	24.55
2011	28.6	25.73	31.47	18.65	17.68	19.62	36.2	35.35	37.05	27.34	27.1	27.58	22.73	21.97	23.49
2012	27.31	24.57	30.05	18.64	17.7	19.57	33.98	33.17	34.79	26.18	25.95	26.41	21.92	21.2	22.65
2013	25.78	23.21	28.34	18.06	17.17	18.94	33.94	33.15	34.74	26.04	25.81	26.27	22.33	21.62	23.04
2014	28.01	25.41	30.61	17.01	16.19	17.84	31.67	30.91	32.42	25.61	25.39	25.83	21.54	20.87	22.22
2015	26.55	24.14	28.97	15.98	15.21	16.75	32.41	31.66	33.16	25.57	25.35	25.79	21.64	20.98	22.3
2016	24.83	22.58	27.08	15.42	14.68	16.16	31.61	30.88	32.34	25	24.78	25.22	22.17	21.52	22.82
2017	25.29	23.06	27.53	15.9	15.18	16.63	30.31	29.61	31.01	24.76	24.55	24.98	23.02	22.38	23.67
2018	24.43	22.31	26.54	15.73	15.02	16.43	30.22	29.53	30.9	24.24	24.03	24.45	22.23	21.62	22.84
2019	24.63	22.55	26.72	14.84	14.18	15.51	29.78	29.11	30.45	23.23	23.03	23.44	21.32	20.74	21.91
2020	36.58	34.14	39.03	20.49	19.73	21.25	44.67	43.87	45.48	29.63	29.4	29.86	37.69	36.94	38.45
Abbreviations: AAMR, Age adjusted mortality rate															

Supplementary Table S4: Race stratified Acute renal failure-related age adjusted mortality rate per 100,000 deaths in adults (> 25 years) in the United States, 1999 to 2020

Region stratified Acute renal failure-related age adjusted mortality rate per 100,000 deaths in adults (> 25 years) in the United States, 1999 to 2020												
Year	Northeast			Midwest			South			West		
	AAMR per 100,000	95% Confidence Interval		AAMR per 100,000	95% Confidence Interval		AAMR per 100,000	95% Confidence Interval		AAMR per 100,000	95% Confidence Interval	
		Lower	Upper		Lower	Upper		Lower	Upper		Lower	Upper
1999	18.03	17.6	18.46	18.34	17.93	18.75	18.13	17.8	18.47	15.06	14.65	15.46
2000	19.13	18.69	19.57	18.89	18.47	19.3	18.99	18.65	19.33	15.54	15.13	15.95
2001	19.6	19.16	20.05	20.18	19.75	20.6	20.04	19.7	20.39	16.06	15.64	16.47
2002	20.66	20.21	21.11	21.09	20.66	21.52	21.06	20.7	21.41	17.78	17.35	18.21
2003	21.24	20.78	21.7	22.93	22.49	23.38	22.37	22.01	22.73	18.86	18.43	19.3
2004	22.35	21.89	22.82	23.25	22.8	23.69	22.65	22.29	23.01	20.03	19.58	20.47
2005	22.5	22.03	22.96	24.81	24.35	25.27	24.5	24.13	24.87	20.83	20.38	21.27
2006	22.82	22.36	23.29	25.18	24.72	25.64	24.62	24.26	24.99	22.19	21.74	22.65
2007	23.63	23.16	24.1	26.39	25.92	26.85	25.84	25.47	26.22	22.75	22.3	23.21
2008	24.79	24.31	25.26	27.86	27.39	28.34	28.42	28.03	28.81	24.71	24.24	25.18
2009	24.8	24.33	25.28	28.8	28.32	29.29	29.63	29.24	30.02	25.26	24.79	25.73
2010	25.34	24.86	25.82	29.31	28.83	29.79	30.92	30.53	31.32	25.85	25.38	26.32
2011	25.02	24.55	25.49	29.5	29.02	29.98	29.24	28.87	29.62	26.47	26.00	26.94
2012	23.40	22.95	23.86	27.76	27.3	28.22	28.22	27.85	28.59	25.73	25.27	26.19
2013	22.41	21.97	22.85	27.31	26.85	27.77	28.85	28.49	29.22	25.21	24.76	25.65
2014	21.01	20.59	21.44	27.33	26.88	27.79	27.95	27.59	28.3	25.01	24.57	25.44
2015	20.54	20.12	20.96	26.65	26.2	27.1	28.19	27.83	28.54	25.75	25.31	26.18
2016	19.91	19.5	20.32	26.15	25.71	26.59	27.19	26.85	27.54	25.48	25.05	25.91
2017	19.41	19.01	19.81	25.42	24.99	25.85	26.95	26.61	27.29	25.62	25.2	26.05
2018	19.55	19.15	19.95	24.53	24.11	24.95	26.89	26.55	27.22	24.46	24.05	24.87
2019	18.35	17.97	18.74	23.49	23.09	23.9	25.8	25.48	26.13	23.89	23.49	24.29
2020	25.61	25.16	26.06	29.26	28.81	29.71	34.34	33.97	34.71	30.42	29.98	30.87
Abbreviations: AAMR, Age adjusted mortality rate												

Supplementary Table S5: Region stratified Acute renal failure-related age adjusted mortality rate per 100,000 deaths in adults (> 25 years) in the United States, 1999 to 2020.