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DISPARITIES IN MORTALITY TRENDS IN ACUTE MYOCARDIAL INFARCTION WITH METABOLIC SYNDROME IN THE U.S. POPULATION: A TWO-DECADE ANALYSIS FROM CDC WONDER DATABASE (1999–2020)

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Abstract

Background: Cardiovascular diseases (CVDs) remain the leading cause of death globally. In the U.S., approximately 1.5 million acute myocardial infarctions (AMI) occur annually, with metabolic syndrome (MetS) present in 40–50% of cases

Research Question: How have AMI mortality trends evolved among patients with MetS, and what disparities persist across different populations?

Aim: To analyze AMI-related mortality trends in patients with MetS, highlighting demographic and geographic disparities.

Methodology: CDC WONDER data for AMI (ICD-10: I21) deaths with metabolic disorders (ICD-10: E70–E89) as contributing causes were analyzed. Adults ≥ 45 years were stratified by gender, race, origin, region, and urbanization. Age-adjusted mortality rates (AAMRs) and annual percentage changes (APCs) were calculated using Joinpoint regression ($p<0.05$).

Results: From 1999-2020, 141,111 deaths were recorded (AAMR: 5.4, 95% CI: 5.4–5.4). Males (1999-2004) and females (1999-2008) had rising trends (APC: 5.0%, 1.05%). Hispanics (1999-2008, 2018-2020) and non-Hispanics (1999-2003, 2018-2020) showed mortality spikes. African Americans (APC: 12.68%, 2018-2020) and Whites (APC: 6.43%) had significant increases. Small Metro areas saw an 8.48% rise. The South had the highest burden, particularly in Mississippi and Alabama. Medium Metro areas also had a significant mortality increase (APC: 7.08%, 95% CI: 2.56–9.68, p=0.000).

Conclusion: AMI mortality in patients with MetS surged from 2018-2020, disproportionately affecting racial minorities and specific regions, highlighting the need for targeted interventions

INTRODUCTION

Cardiovascular diseases (CVDs) are the leading cause of death worldwide. In 2019, they were responsible for around 17.9 million deaths, making up 32% of all global fatalities. Out of these, acute myocardial infarction (AMI), commonly known as heart attack, and strokes accounted for nearly 85% of the cases.[1]

Metabolic syndrome Mts is a cluster of health issues, such as abdominal obesity, high triglycerides, low HDL cholesterol, elevated blood pressure, and increased fasting blood sugar. Together, these factors significantly heighten the risk of heart disease and type 2 diabetes.[2] Individuals with MetS have a higher risk of developing endothelial dysfunction, pro-inflammatory conditions, and atherosclerosis all of which contribute to cardiovascular mortality.[3-5] MetS is commonly found in the general American population[6,7] and frequently observed in patients suffering from acute myocardial infarction (AMI).[8]

The association of MetS and AMI-related mortality presents a serious public health challenge in the U.S., where approximately 1.5 million AMI cases occur each year, and MetS is identified in 40–50% of these patients.[9,10] Although advancements in AMI treatment have improved survival rates, discrepancy in outcomes remains prevalent. The association between metabolic syndrome (MetS) and the risk of cardiovascular disease leading to mortality differs based on factors such as race, ethnicity, age, geographic location, and access to healthcare. For instance, Hispanic and non-Hispanic Black populations exhibit a higher prevalence of MetS compared to non-Hispanic White populations. Additionally, women with MetS appear to have a greater relative risk of AMI-related mortality than men.[11-13] Similarly, Geographic variations also play a role, with rural regions reporting 15–20% higher AMI mortality rates among MetS patients than urban areas, likely due to reduced availability of specialized cardiac care.[14]

Many marginalized communities face barriers such as inadequate access to preventive healthcare, limited availability of nutritious food, and insufficient resources for managing chronic conditions. These factors collectively contribute to poorer cardiovascular outcomes and higher mortality rates among affected populations.[15]

By examining variations across sex, age, race, geographical distribution and access to healthcare within the entire U.S. population, our research aims to provide valuable insights for policymakers, enabling them to develop more effective health policies that address these trends.

METHODOLOGY

We conducted a retrospective analysis to retrieve data from CDC WONDER's (Wide-ranging Online Data for Epidemiological Research) database for multiple cause of death. This openly accessible registry has compiled data of mortality of US residents which is derived from death certificates throughout the United States. Each death certificate consists of one major underlying cause of death, up to twenty additional contributing causes, and demographic information.[16] This study included adults aged 45 years and older with acute myocardial infarction (AMI) as an underlying cause of death and Metabolic Disorders (Diabetes Mellitus, Hyperlipidemia, Lactose Intolerance, Glycogen Storage Disorders, Lipid-purine-Protein Metabolism Disorders etc.) as a contributing cause. These causes were selected using International Classification of Disease- 10th Revision (ICD-10) for Acute Myocardial Infarction (I-21) and Metabolic disorders (E-70 to E-89).[17] This study was not liable to Institutional Review Board (IRB) approval, as the CDC WONDER database contains publicly available data.

Geographical and demographic data were stratified including gender, race, Hispanic Origin, census region and 2013-Urbanization framework. Census regions were categorized into Northeast, Midwest, South, and West according to the Census Bureau definitions.[18] As described by National Center for Health Statistics (NCHS) urban-rural classification scheme, all US counties are divided into six areas: Large central metro and large fringe metro with population more than 1 million, medium metro within a range of 250,000-999,999 and small metro areas with population less than 250,000. Additionally, Micropolitan and non-core metro areas have a population range of 10,000-50,000.[19] Place of death include inpatient settings and nursing home/long term care.

Crude and Age-adjusted mortality rates (AAMR) were calculated per 100,000 population. We assessed variations in annual mortality trends over the study period across different categories like gender, Hispanic origin, race, census region and 2013 urbanization framework using the Joinpoint Regression (JPR) program (version-5.3.0, November 2024) developed by Surveillance Research Program at the National Cancer Institute. Annual percentage changes (APC) with 95% confidence interval were calculated for AAMR using Monte-Carlo permutation test in JPR to analyze unusual trends in mortality rate. A p-value of 0.05 was considered as a threshold of statistical significance.

RESULTS

In total, there were 141,111 recorded deaths, with an Age-Adjusted Mortality Rate (AAMR) of 5.4 (95% CI: 5.4–5.4) between 1999-2020 due to Acute Myocardial Infarction and metabolic disorders as contributing factors. Males represented 57.68% of the deaths, while females accounted for 42.32%, indicating a higher mortality rate among men. Among the ethnicities, Hispanic individuals made up 5.3% of the fatalities, with non-Hispanic individuals comprising 94.5%, highlighting significant demographic disparities. In terms of age distribution, 6.25% of deaths occurred in the 45-54 age group, while individuals aged 85 and older had the highest share, contributing to 24% of total fatalities. We found that most deaths (54.3%) occurred within hospital settings, encompassing both inpatient and outpatient facilities. Meanwhile, 40.76% of deaths took place in non-hospital environments, such as nursing homes, private residences, or hospice care. Further information according to different demographic and regional stratification is described in Table 1.

Table 1: Age-adjusted Mortality Rate (AAMR) by Sociodemographic and Regional Factors

Variable	Total Deaths	Population	Crude rate* (95% CI)	AAMR** (95% CI)
Age				
45-54 years	8,808	927,576,220	0.9(0.9-1.0)	Not available
55-64 years	23,204	766,424,847	3.0(3.0-3.1)	Not available
65-74 Years	34,313	510,458,341	6.7(6.7-6.8)	Not available
75-84 Years	40,893	298,504,433	13.7(13.6-13.8)	Not available
85+ Years	33,893	119,513,891	28.4(28.1-28.7)	Not available

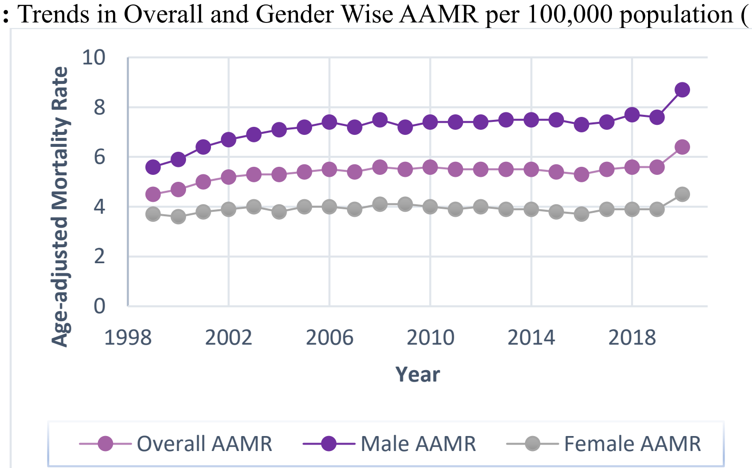
Demography				
Males	81,386	1,226,819,075	6.6(6.6-6.7)	7.3(7.3-7.4)
Females	59,725	1,395,658,687	4.3(4.2-4.3)	4.0(3.9-4.0)
Hispanic Origin	7,520	252,811,993	3.0(2.9-3.0)	4.0(3.9-4.1)
Non-Hispanics	133,324	2,369,665,739	5.6(5.6-5.7)	5.5(5.5-5.5)
Race				
American Indian or Alaska Native	788	24,165,862	3.3(3.0-3.5)	4.4(4.1-4.7)
Asian or Pacific Islander	3,946	121,193,424	3.3(3.2-3.4)	4.0(3.9-4.2)
Black or African American	13,348	286,475,812	4.7(4.6-4.7)	5.5(5.4-5.6)
White	123,029	2,190,642,634	5.6(5.6-5.6)	5.5(5.5-5.5)
Region				
CENS-R1	24,625	497,982,485	4.9(4.9-5.0)	4.8(4.7-4.9)
CENS-R2	35,293	580,373,620	6.1(6.0-6.1)	6.0(5.9-6.1)
CENS-R3	48,350	966,355,890	5.0(5.0-5.0)	5.1(5.1-5.2)
CENS-R4	32,843	577,765,737	5.7(5.6-5.7)	5.9(5.9-6.0)

Abbreviations: CENS-R1: Census Region 1 (Northeast), CENS-R2: Census Region 2 (Midwest), CENS-R3: Census Region 3 (South), CENS-R4: Census Region 4 (West)
*Crude Rate Per 100,000
**Age-Adjusted Rate Per 100,000

Annual Mortality Trends: Two surges were prominent in annual mortality trends, one from 1999-2003 with a mean APC of 4.73 (95%CI: 2.9 to 7.6, p=0.00) followed by a non-significant upward shift from 2003-2018. Additionally, a significant upward inflection was observed from 2018-2020 with an APC of 7.01 (95% CI: 3.43 to 8.94, p= 0.00). (Fig.1)

Demographic Stratification: Both Male from 1999-2004 and female from 1999-2008 displayed upward inflections in mortality rates with APCs of 5.0 (95% CI: 3.5 to 7.4, p=0.0004) and 1.05 (95%CI: 0.4 to 2.7, p=0.002), respectively. Moreover, females displayed a significant decline in mortality from 2008 to 2018 with a mean APC of -0.76 (95%CI: -9.34 to - 0.24, p= 0.0051) while a slightly upward but non-significant trend was observed in male fatalities during this period. (Fig.1)

Fig 1: Trends in Overall and Gender Wise AAMR per 100,000 population (1999-2020)

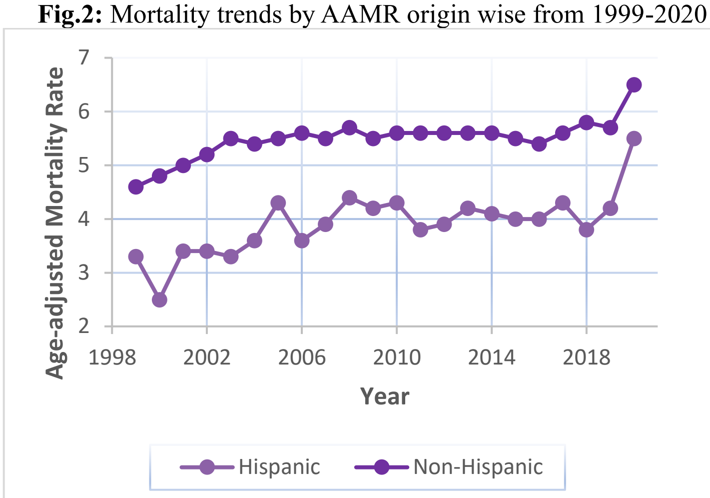


Additionally, Hispanics displayed a significant rise in mortality trends from 1999-2008 with an APC of 4.2 (95%CI: 2.2 to 10.3, p=0.0012) followed by a non-significant decline till 2018. Second upward surge in fatalities was experienced from 2018 to 2020 exhibiting mean APC of 16.6 (95%CI: 5.13 to 24.22, p= 0.0004). (Fig.2)

Two upward inflections in mortality rates were observed in non-Hispanics; one from 1999-2003, with an APC of 4.71 (95%CI: 2.94 to 7.7, p=0.00), and second from 2018 to 2020 with APC of 6.73 (95%CI: 3.23 to 8.74, p=0.00). The period from 2003 to 2018 remained non-significant with a slight upward shift in mortality trends. (Fig.2)

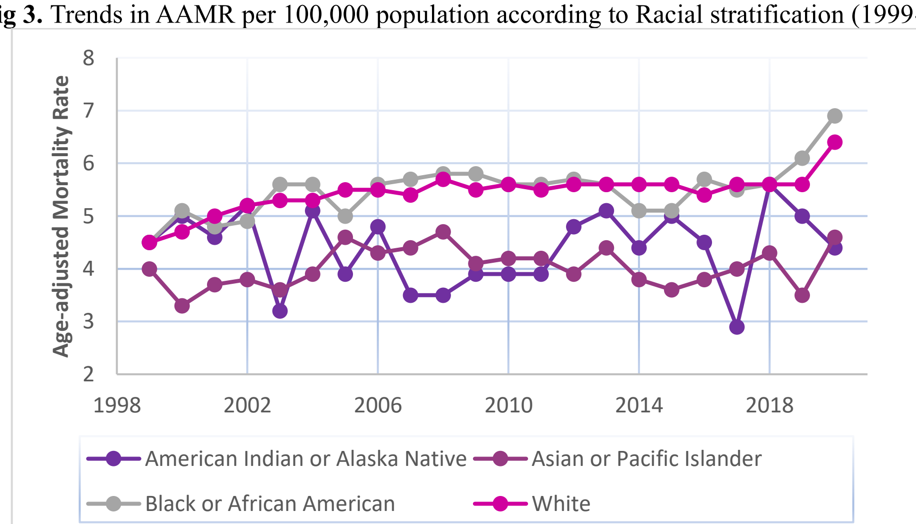
Among Hispanics, male showed significant upward inflection in mortality during the whole study period with APC of 1.77 (95%CI: 0.93 to 2.90, p=0.04). However, female displayed non-significant trends from 1999-2018 followed by an upward surge till 2020 with an APC of 18.1 (95%CI: 6.3 to 24.7, p=0.0000).
Between 2008 and 2016, non-Hispanic female exhibited significant decline in mortality trends accounting an APC of -1.12 (95%CI: -3.67 to -0.43, p=0.0012) while males of this origin showed no significant trend during described period. Additionally non-Hispanic male post 2018 and non- Hispanics female post 2016 displayed notable upward shifts in mortality trends with APCs of 6.87 (95%CI: 2.09 to 9.07, p= 0.00) and 3.33 (95%CI: 1.46 to7.43, p=0.0000), respectively.

Fig.2: Mortality trends by AAMR origin wise from 1999-2020 in the US population



Racial Stratification: Black or African Americans from 1999-2007 while whites from 1999-2005 displayed a significant upward inflection in mortality rates with an annual percentage change (APC) of 2.68 (95% CI: 1.41 to 6.01, p=0.000) and 3.13 (95% CI: 1.88 to 5.24, p=0.002), respectively. However, from 2005 to 2018, whites exhibited a relatively stable trend with a non-significant mean APC of -0.02 (95% CI: -1.21 to 0.31, p=0.706). (Fig.3)
Additionally, from 2018 to 2020, both Black or African Americans and whites showed significant upward inflection in death rates with a mean APC of 12.68 (95% CI: 5.19 to 17.10, p=0.0000) and 6.43 (95% CI: 1.55 to 8.77, p=0.000), respectively. In contrast, no significant trend in mortality was observed in American Indian/Alaska Native and Asian or Pacific Islanders. (Fig.3)

Fig 3. Trends in AAMR per 100,000 population according to Racial stratification (1999-2020)

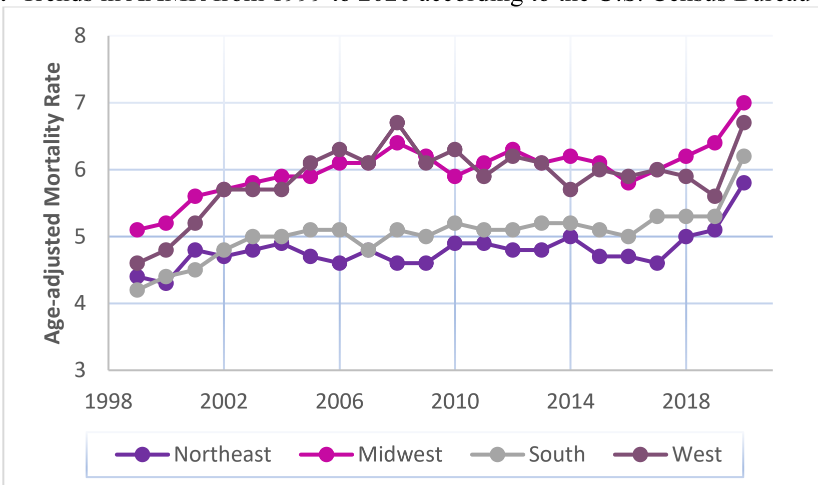


Regional Stratification: Mortality trends in CENS-R2: Midwest and CENS-R4: West showed a significant increase from 1999 to 2006, with an APC of 2.67 (CI 95%: 1.52 to 4.49, p=0.001) and 4.33 (CI 95%: 1.65 to 10.27, p=0.013) respectively. However, from 2006 to 2017, CENS-R2: Midwest displayed non-significant trends in mortality rates, and CENS-R4: West showed a slightly declining curve until 2018. In CENS-R2: Midwest, a significant increase in mortality rates was observed from 2017 to 2020 with an APC of 4.17 (CI 95%: 1.31 to 8.24, p=0.0004). Similarly, from 2018 to 2020, CENS-R4: West showed a significant increase in mortality with a mean APC of 6.03 (CI 95%: 0.41 to 9.31, p=0.027).

In CENS-R1: Northeast, a significant rising trend was seen from 1999 to 2014 with an APC of 0.66 (CI 95%: 0.38 to 2.05, p=0.009), followed by a non-significant decline in mortality rates from 2014 to 2017 with an APC of -2.42 (CI 95%: -4.31 to 0.08, p=0.07). However, a significant increase in mortality rates was observed from 2017 to 2020 with an APC of 7.72 (CI 95%: 4.94 to 12.42, p=0.000).

In CNS-R3: South, a significant increase in mortality rates was observed from 1999 to 2003 with an APC of 4.52 (CI 95%: 2.58 to 8.12, p=0.000), followed by non-significant trends until 2018. From 2018 to 2020, a significant increase in mortality rates was seen with an APC of 8.16 (CI 95%: 3.93 to 10.38, p=0.000). (Fig.4)

Fig 4. Trends in AAMR from 1999 to 2020 according to the U.S. Census Bureau Classification



2013-Urbanization Framework: From 1999 to 2002, Micropolitan and non-core areas experienced a significant increase in mortality rates, with a mean annual percentage change (APC) of 7.15 (95% CI: 2.05 to 17.41, p = 0.0004) and 8.91 (95% CI: 3.97 to 16.28, p = 0.000), respectively. However, both areas did not show statistically significant trends in mortality rates from 2002 to 2018. Between 2018 and 2020, both Micropolitan and non-core areas saw a significant rise in mortality rates, with an APC of 10.22 (95% CI: 2.38 to 14.61, p = 0.000) and 7.04 (95% CI: 1.99 to 10.90, p = 0.000), respectively.

From 1999 to 2004, Medium Metro and Small Metro areas exhibited significant increases in mortality rates, with mean APCs of 3.39 (95% CI: 0.84 to 11.94, p = 0.0004) and 5.81 (95% CI: 2.43 to 14.44, p = 0.007), respectively. From 2004 to 2018, Medium Metro showed relatively stable trends in mortality rates, while Small Metro displayed a non-significant rising curve. However, both areas experienced a significant increase in mortality rates from 2018 to 2020, with APCs of 7.08 (95% CI: 2.56 to 9.68, p = 0.000) and 8.48 (95% CI: 1.99 to 12.51, p = 0.0004), respectively.

For large fringe metro areas, a slight but significant increase in mortality trend was observed from 1999 to 2001, with a mean APC of 6.31 (95% CI: 1.67 to 10.06, p = 0.000). From 2001 to 2011, a relatively stable but non-significant trend was observed, followed by a significant decrease in mortality rates from 2011 to 2015, with an APC of -3.58 (95% CI: -5.85 to -1.36, p = 0.026). However, from 2015 to 2020, a significant increase in mortality rates was observed, with an APC of 2.97 (95% CI: 1.57 to 5.75, p = 0.005).

In large central metro areas, there were slightly rising and non-significant trends in mortality rates from 1999 to 2007 and from 2018 to 2020. However, from 2007 to 2018, a statistically non-significant decline in mortality trend was observed.

Geographical Stratification: Nevada had the lowest Age-adjusted mortality rate of 1.8 per 100,000 population followed by Georgia (2.8), Connecticut (2.9) and Alabama (3.0). Among high AAMR states, Rhode Island had the highest notable AAMR of 9.5 per 100,000 population. Other significantly higher AAMR states were Vermont (9.3), South Dakota (9.1) and Ohio (9). (Fig.5,6)

Fig 5: State Wise Distribution of Mortality: AAMR per 100,000 in the U.S. population from 1999 to 2020

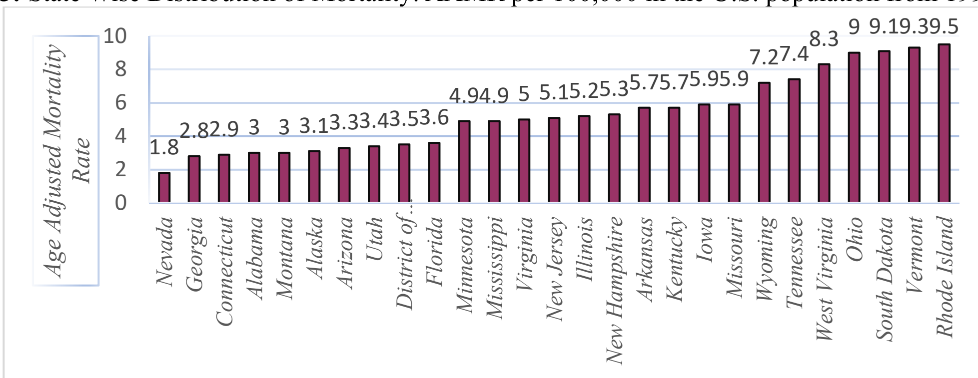
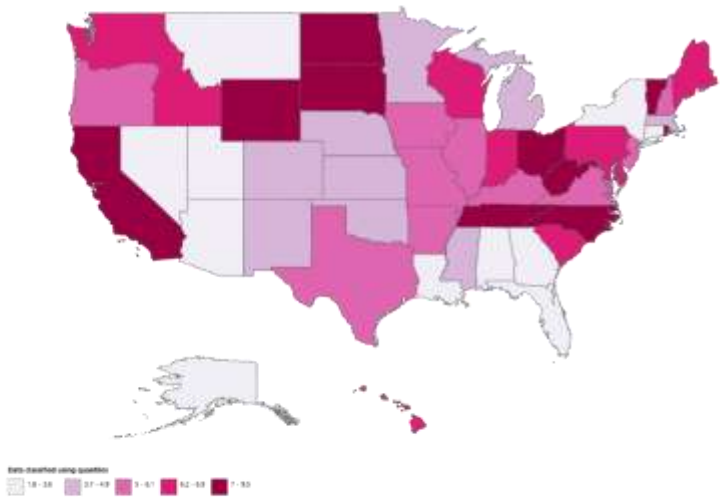


Fig 6: State Wise Heatmap of Mortality: AAMR per 100,000 in the U.S. population from 1999 to 2020



DISCUSSION

Our study evaluates the mortality data of Acute myocardial infarction (I21) with metabolic disorders (E70-E89) as a comorbid condition. Analysis of this data showed significant unusual trends of mortality rate with sharp significant inflection in mortality from 1999-2003; then non-significant upward rather steady slope from 2003-2018. The concerning period to demonstrate is 2018-2020 when fatalities due to Acute myocardial infarction (AMI) increased even after mind-blowing advancements in healthcare facilities during the last 20 years. As demonstrated by the American Heart Association (AHA), COVID-19 pandemic reversed a decade of progress in reducing the deaths due to cardiovascular diseases.[20] This sharp increase in 2020 stands out, likely tied to this pandemic, which disrupted healthcare access, delayed treatment for acute conditions, and potentially worsened cardiovascular risks. Similar trends were observed when mortality was stratified across gender and Hispanic origins. In this case, Males and non-Hispanics displayed a higher number of fatalities among others. In terms of racial division, mortality rates were observed to be significantly higher in African Americans followed by whites during the period of 2018-2020. States like Ohio, Rhode Island, and South Dakota stand out, with crude mortality rates of 9.1, 10.2, and 9.8 per 100,000, respectively, significantly higher than the national average (approximately 4.34 per 100,000). In contrast, Nevada and Alaska report much lower rates at 1.6 and 2.2, highlighting stark regional disparities.

In our findings, we assessed that male exhibited consistently higher AAMR than their counterpart females. This finding is supported by the fact that this variation could be due to numerous biological and sociocultural factors. However, Fabijanic et al. reported that higher in-hospital mortality rates due to AMI are associated with females.[20] Among females, approximately double in-hospital mortality rates are accompanied with younger females than the men in the same age group (less than 50 years of age), as demonstrated by Vaccarino et al.[21] This disparity of gender provides valuable insights of younger women being the high-risk population with poorer short-term outcomes. This finding is highly suggestive of the fact that targeted and age-specific interventions are necessary for better outcomes. Lanas et al. identified that history of Diabetes Mellitus and other metabolic disorders is strongly attributed to 2.59-fold increased risk of AMI in Hispanic population.[23] This finding further gives strength to our results that from 2018-

2020, Hispanics showed higher Annual percentage changes (APC) of mortality rates as compared to non-Hispanics. Meanwhile, Herrera et al. reported strong biological association of AMI with DM in the Hispanic population accounting for higher prevalence (43%) in participants.[24]

A study by Nancy Lapid in 2024 reported a 180% increase in obesity-related heart disease mortality in the U.S. from 1999 to 2020, with male and female accounting for 243% and 131% rise, respectively.[25] This finding exhibits a strong association of metabolic disorders such as obesity with risk of AMI and associated conditions. Furthermore, Lapid's findings during the same time period reinforce the fact that metabolic dysfunction is strongly correlated with AMI mortality. Additionally, Lapid's reported higher obesity increase in males coincides with higher AAMR in males.

Madssen et al. assessed that dyslipidemia, another metabolic factor, disproportionately impacts males, making them more vulnerable to AMI related outcomes.[26] Ramirez et al. identified low HDL level as an independent risk factor of AMI.[27] A study by Carroll et al. reported higher prevalence (24.7%) of low-HDL levels in Hispanic population as compared to non-Hispanics with prevalence of 17.6% and 12.2% in non-Hispanics whites and blacks, respectively.[28] These findings further bolster the results of our study in which the Hispanic population was strongly associated with raised mortality rates due to high prevalence of low HDL levels.

Our results showed a significant increase in mortality rates for African Americans and whites, followed by stabilization for whites. This suggests that African Americans with diabetes have a slightly lower mortality risk compared to whites, despite similar socioeconomic and healthcare access. Baqqiyah et al. supported this finding, suggesting that disparities in mortality trends may be influenced by comorbidities and healthcare utilization, such as cardiovascular disease (CVD) and hypertension. The stabilization of white mortality rates from 2005 to 2018 may indicate better healthcare interventions or management of metabolic diseases in this group. However, African Americans, despite having a lower baseline prevalence of CVD, experienced higher mortality risks when comorbidities were present. The sharp increase in mortality rates from 2018 to 2020 for both groups may be attributed to systemic stressors like the pandemic, which disproportionately affected individuals with pre-existing conditions, especially in underserved communities.[29]

Our study found significant increases in mortality rates in certain regions, with the Northeast consistently showing the highest rates. Fakhar et al. study emphasized the role of factors such as age, comorbidities like metabolic diseases, and disparities in healthcare access contribute to these trends. Older adults aged 75 and above have higher mortality rates from chronic heart disease. Disparities in healthcare access and socioeconomic factors between metropolitan and non-metropolitan areas explain regional variations in mortality. Regions with lower socioeconomic status, like the South and parts of the Midwest, may have higher mortality rates due to inadequate healthcare infrastructure and higher prevalence of risk factors. The sharp increases in mortality rates from 2018 to 2020 coincide with the COVID-19 pandemic.[30]

Bin yu et al study similarly supported our findings that regions with limited access to quality healthcare services may experience higher mortality rates due to delayed diagnosis and treatment of MI. Economic disparities can lead to differences in lifestyle, diet, and access to preventive care, contributing to regional variations in MI outcomes. Higher prevalence of diabetes and obesity in certain regions may exacerbate MI mortality rates.[31]

Zakariah et al. study found a link between urbanization and higher rates of Type 2 Diabetes, which aligns with our observation of increased mortality in urban areas. Urbanization can worsen health disparities, leading to higher mortality rates in Micropolitan and non-core areas due to limited healthcare access. Rural areas may face higher mortality rates due to delayed diagnosis and treatment of metabolic diseases like myocardial infarction. Rapid urbanization can create unhealthy environments with reduced physical activity and increased processed food consumption. Aging populations in certain regions may also contribute to higher mortality rates. Disparities in public health policies and resources across regions can impact health outcomes.[32]

Similarly; Bin Dong et al. found that higher urbanization levels (UI $\geq$ 40) are associated with a reduced risk of myocardial infarction (MI) measured through urbanization index. Our study also shows stable or declining mortality trends in more urbanized areas during certain periods. Less urbanized areas face higher MI risks due to limited healthcare access and higher prevalence of risk factors like hypertension and diabetes. Urbanized areas may have better health policies and access to resources. The COVID-19 pandemic likely contributed to recent spikes in mortality rates due to healthcare system strain and delayed care for chronic conditions.[33]

Limitations: Our CDC based analysis has many limitations, as the data were extracted from death certificates of patients, making it more prone to misclassification or underreporting of the data especially for broad underlying conditions like metabolic syndrome. As CDC lacks individual level patient details, there's no method to deal with confounders. It also doesn't provide insights about socioeconomic status, clinical severity or medication use. This data is solely based on the US population; hence it doesn't provide any information regarding geographical or temporal variations of these conditions around the globe.

CONCLUSION

Our nationwide analysis of mortality trends in Acute Myocardial Infarction as major cause and Metabolic syndromes as contributing factor provided valuable insights regarding disparities in mortality trends across various demographic and geographic groups from 1999-2020. Hispanics, Black or African Americans and whites displayed rising trends in mortality from 2018-2020, highlighting the high-risk population in recent years. All the census region as classified by the U.S. Census Bureau Classification showed increasing mortality rates from 2017 to 2020. Among states, Rhode Island and Vermont were states with most vulnerable population. These findings suggest the implementation of immediate measures and targeted interventions, especially for the population at risk, in order to provide better healthcare and to attain better prognosis of these particular conditions.

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