

Acute Respiratory Failure-Related Mortality Among US Infants, 1999–2023

Yang Meng

my7496@126.com

Yancheng First People's Hospital

XinYu Wang

Yangzhou First People's Hospital

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Additional Declarations: No competing interests reported.

Abstract

Objective Acute respiratory failure (ARF) is a major mortality driver in pediatric critical care, and infants under 1 year account for more than half of pediatric ARF cases. National long-term epidemiologic data focusing specifically on ARF-related mortality among US infants remain scarce. This study aimed to characterize temporal trends and sociodemographic disparities in ARF-associated deaths among US infants from 1999 to 2023.

Methods Mortality data were retrieved from multiple cause-of-death dataset. Infants aged < 1 year were enrolled, and ARF deaths were defined by ICD-10 codes J96.0, J96.9 and P28.5. Mortality rates per 100,000 live births were calculated with 95% CIs; race and ethnicity-stratified rates were calculated per 100,000 population estimates and limited to 1999–2020 due to post-2020 revisions in federal racial classification standards. Temporal trends were analyzed using Joinpoint regression to estimate the average annual percent change (AAPC) and annual percent change (APC).

Results A total of 67,051 ARF-related infant deaths were identified over 25 years, with an overall mortality rate of 67.6 per 100,000 live births. The overall AAPC was 0.76% (95% CI: 0.44–1.08; $p < 0.001$), with a notable upward trend from 2011 to 2023 (APC = 1.99%; 95% CI: 1.50–2.49; $p < 0.001$). Significant disparities existed: male infants, neonates, Black infants and infants in the Southern US had higher mortality (all $P < 0.001$). Black infants presented a bimodal mortality trend with a sharp decline during 2006–2012 followed by a rapid increase from 2012 to 2018.

Conclusions ARF mortality among US infants increased continuously after 2011, accompanied by prominent sociodemographic inequities. Targeted perinatal and neonatal critical care interventions for high-risk infant subgroups are needed to reduce ARF-related mortality disparities.

Introduction

Acute respiratory failure (ARF) is a leading cause of mortality in pediatric critical care (1). The pediatric population bears a disproportionate ARF burden, with over half of cases occurring in infants under 1 year (2–4). While prior studies have explored national trends and geographic disparities in ARF-related mortality, data specific to US infants remain limited (5). This study analyzed 25 years of national mortality data to characterize trends and sociodemographic disparities in ARF-related infant deaths, informing targeted interventions to address persistent inequities.

Methods

Data source

Data were extracted from the multiple cause-of-death dataset of the US Centers for Disease Control and Prevention (CDC) Wide-ranging Online Data for Epidemiologic Research (WONDER) database, which aggregates national mortality records from death certificates (2). The study included infants aged < 1

year from 1999 to 2023, adhering to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Outcome definition

ARF-related deaths were identified using International Classification of Diseases, 10th Revision (ICD-10) codes J96.0 (Acute respiratory failure), J96.9 (Respiratory failure, unspecified), and P28.5 (Respiratory failure of newborn). This coding strategy aligns with prior population-based studies of respiratory failure mortality in the US (5). Cases were included regardless of whether ARF was coded as the immediate, underlying, or contributing cause of death; this study therefore describes ARF-associated mortality, not mortality directly caused by ARF.

Mortality rates and denominators

Crude mortality rates per 100,000 live births, with 95% confidence intervals (CIs), were calculated for the overall cohort and for subgroups stratified by sex, age group, and census region. Race and ethnicity-stratified rates were calculated per 100,000 population estimates due to data availability and privacy constraints. These two rate metrics use different denominator structures and are not directly comparable.

Race and ethnicity-stratified analyses were limited to the period 1999–2020 due to revisions to the federal standard for racial and ethnic classification implemented after 2020, which introduced inconsistencies in category definitions across the study period.

Statistical analysis

Differences in mortality rates across subgroups were assessed using two-tailed two-sample z-tests. Reference groups were predefined as follows: female for sex comparisons, post-neonates (28–364 days) for age comparisons, White infants for race and ethnicity comparisons, and the Northeast region for census region comparisons. No formal adjustment for multiple comparisons was applied; all p-values should be interpreted as exploratory. Temporal trends were analyzed using Joinpoint regression software (version 5.3.0) to calculate the average annual percent change (AAPC) and segment-specific annual percent change (APC), with corresponding 95% CIs. A permutation test method was used for model selection, with a maximum of three joinpoints (inflection points) permitted per model based on statistical significance and interpretability. Statistical significance was set at two-tailed $p < 0.05$. Additional methodological details are provided in the eMethods in the Supplement.

Results

Between 1999 and 2023, 67,051 ARF-related infant deaths occurred among 99,053,300 live births, yielding an overall mortality rate of 67.6 per 100,000 live births. Significant sociodemographic disparities

were observed. In 2023, male infants had higher mortality than females (84.9 vs 74.3 per 100,000), and neonates (< 28 days) had 3-fold higher mortality than post-neonates (28–364 days) (60.5 vs 19.2 per 100,000).

In 2020, Black or African American infants had the highest mortality rate (117.7 per 100,000 population), exceeding rates among American Indian or Alaska Native (63.7 per 100,000), White (63.4 per 100,000), Hispanic or Latino (62.8 per 100,000), and Asian or Pacific Islander (43.0 per 100,000) infants (all $p < 0.001$ vs White infants).

Geographically, Southern states had the highest 2023 mortality burden (86.6 per 100,000 live births), followed by the Midwest (79.6 per 100,000), West (74.1 per 100,000), and Northeast (70.1 per 100,000) (all $p < 0.001$ vs Northeast) (Fig. 1).

The overall AAPC was 0.76% (95% CI: 0.44–1.08; $p < 0.001$), with a significant upward trend from 2011 to 2023 (APC = 1.99%; 95% CI: 1.50–2.49; $p < 0.001$). Stratified trends were generally consistent across sex, age, and regional subgroups. Notably, Black infants had a non-significant overall AAPC of –0.49% (95% CI: –2.12 to 1.17; $p = 0.55$), with a sharp decline segment (2006–2012: APC = –4.25%; 95% CI: –6.38 to –2.06; $p < 0.01$) followed by a significant increase segment (2012–2018: APC = 5.35%; 95% CI: 3.02–7.72; $p < 0.001$) (Fig. 2).

Discussion

This study identified a concerning increase in ARF-related infant mortality in the US from 2011 to 2023, which differs from previously reported declines in all-cause infant mortality and several pediatric respiratory disease mortality rates in earlier decades (5). Several potential explanations for this upward trend have been proposed in prior literature, including contractions in rural obstetric care capacity, shifts in perinatal risk profiles, changes in death certification practices, and disruptions to healthcare access during the COVID-19 pandemic (6). However, the present descriptive study cannot directly test or confirm these causal hypotheses.

Significant sociodemographic disparities persisted across the study period: male infants, neonates, Black infants, and infants residing in the Southern US consistently carried the highest ARF-related mortality burden. These patterns align with well-documented racial and geographic inequities in perinatal and pediatric critical care access reported in previous studies, but the underlying mechanisms cannot be determined from this ecological analysis.

This study has several important limitations. First, ARF-related deaths were identified using multiple-cause death certificate codes, which may be subject to variation in coding practices across regions and over time; misclassification of the cause of death could affect observed rates and trends. Future sensitivity analyses restricting to underlying-cause only or expanding to include primary neonatal respiratory conditions (e.g., respiratory distress syndrome, meconium aspiration) will help clarify the robustness of these findings. Second, the study cannot distinguish ARF as an underlying cause of death

from ARF as a terminal event or contributing condition, and the selected ICD-10 codes do not capture all primary conditions that may lead to fatal acute respiratory failure in infants (such as respiratory distress syndrome, meconium aspiration, or congenital pneumonia). Third, different denominators were used for live birth-based rates and population-based race and ethnicity rates, which limits direct comparison across these subgroups. Fourth, the study is ecological in design and lacks individual-level clinical data, including prematurity, birth weight, congenital anomalies, and details of healthcare utilization; therefore, causal inferences are not appropriate. Finally, race and ethnicity analyses were limited to 2020 due to changes in federal classification standards, which restricts assessment of more recent trends in these subgroups.

Overall, these findings provide national, long-term descriptive data on ARF-related infant mortality disparities and trends. Further individual-level and health services research is needed to identify the underlying drivers of the observed upward trend and inequities, and to inform targeted public health and clinical strategies to reduce preventable infant respiratory mortality.

Declarations

Funding Declaration

No funding was received for the conduct of this study or preparation of the manuscript.

Ethics, Consent to Participate, and Consent to Publish

Ethics, Consent to Participate, and Consent to Publish declarations: not applicable. This study used only publicly available de-identified population-level mortality data without access to individual identifiable clinical information, therefore formal ethical approval and written informed consent were not required.

Availability of data and materials

The dataset(s) supporting the conclusions of this article are available in the Centers for Disease Control and Prevention (CDC) WONDER repository, <https://wonder.cdc.gov/>. All de-identified aggregated mortality data are open-access and free to access for research purposes without academic restrictions.

Author Contributions

M.Y. conceived and designed the study, extracted and analyzed CDC WONDER data, performed statistical analysis, drafted the full manuscript, and revised the manuscript. W.X.Y. collected literature references, organized supplementary materials, drew all figures, and participated in manuscript revision. All authors read and approved the final submitted version of the manuscript.

Competing Interests

The authors declare that there are no competing interests associated with this work.

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Figures

Figure 1

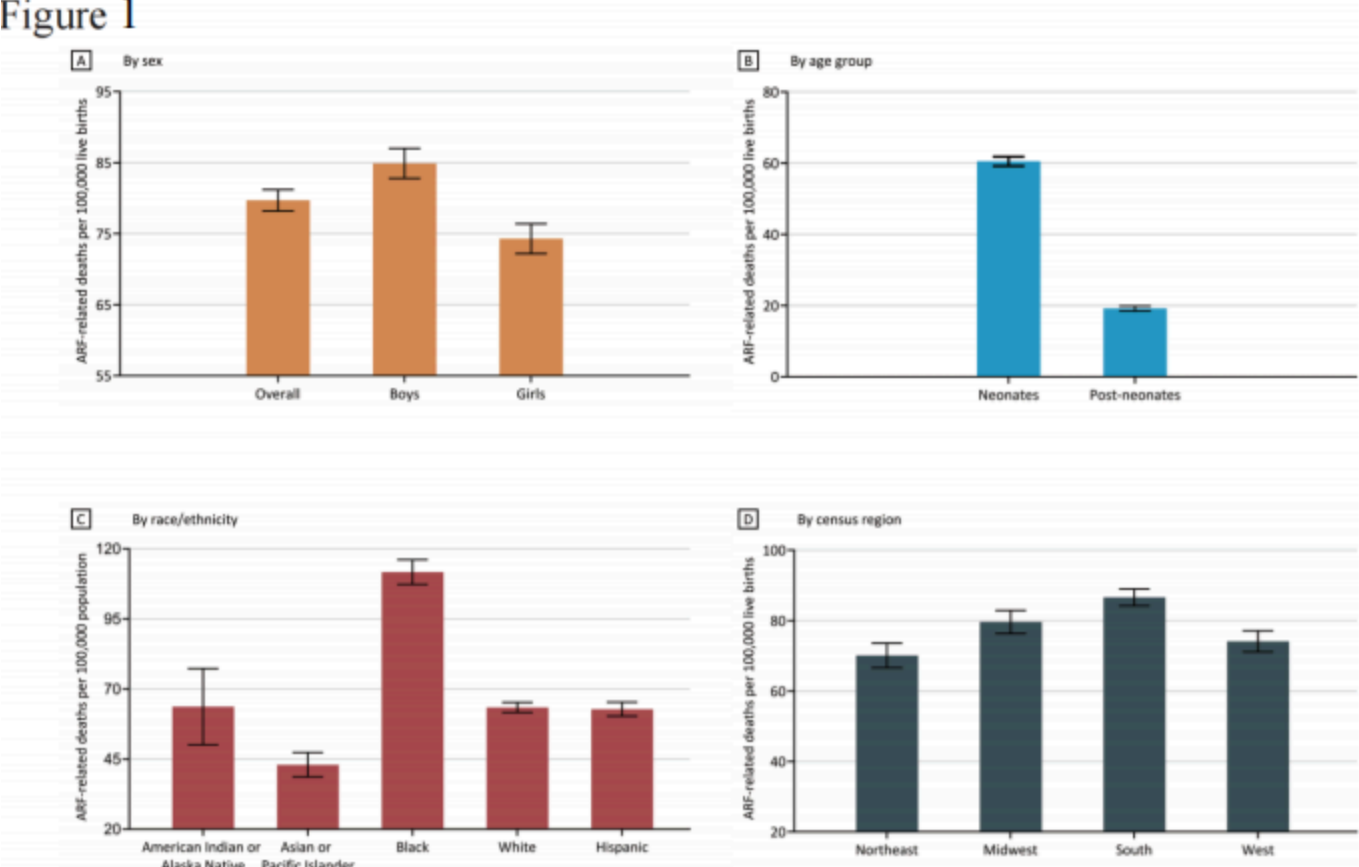


Figure 1

Comparison of ARF-Related Mortality Among US Infants, Stratified by Sex, Age Group, Census Region (2023), and Race and Ethnicity (2020)

Comparisons of ARF-related mortality rates among infants, stratified by sex (A), age(B), race and ethnicity (C), and census region (D). Data were obtained from the US Centers for Disease Control and Prevention (CDC) Wide-Ranging Online Data for Epidemiologic Research (WONDER). We limited our results stratified by race and ethnicity to 2020 due to changes in the classification of races after 2020. All mortality rates were presented per 100,000 live births, except for rates stratified by race and ethnicity, which were presented per 100,000 population estimates due to privacy constraints. Error bars represent the 95% confidence intervals (CIs).

Figure 2

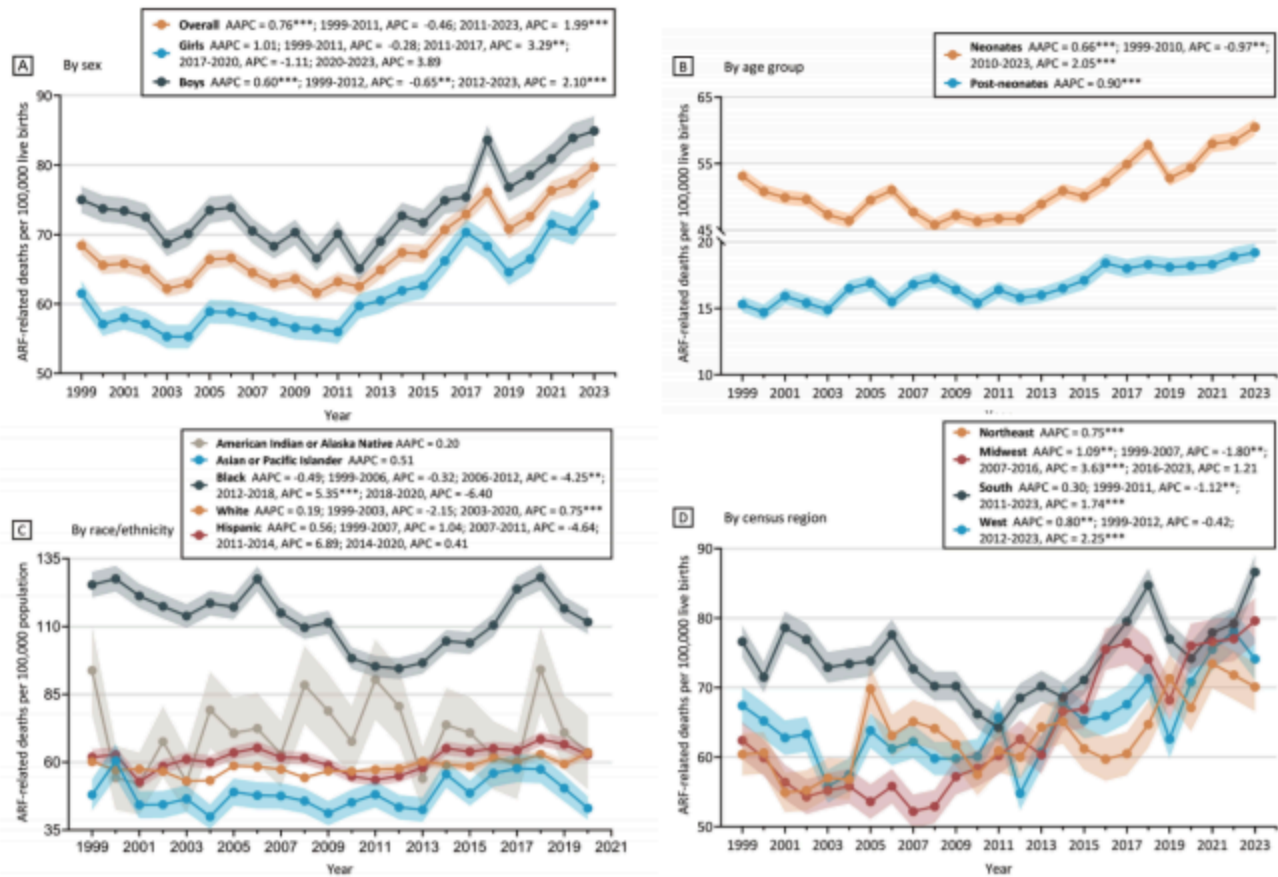


Figure 2

Trends in ARF-Related Mortality Among US Infants, Stratified by Sex, Age Group, Census Region (1999-2023), and Race and Ethnicity (1999-2020)

Trends in ARF-related mortality rates among infants, stratified by sex (A), age (B), race and ethnicity (C), and census region (D). Data were obtained from the US Centers for Disease Control and Prevention (CDC) Wide-Ranging Online Data for Epidemiologic Research (WONDER). We limited our results stratified

by race and ethnicity to 2020 due to changes in the classification of races after 2020. All mortality rates were presented per 100,000 live births, except for rates stratified by race and ethnicity, which were presented per 100,000 population estimates due to privacy constraints.

Abbreviations: AAPC, average annual percent change; APC, annual percent change.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [ARFeMethods.07.06docx.docx](#)