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Population-Level Assessment of Sex and Age Disparities in Acute Myeloid Leukemia Hospitalization Burden in U.S. Adults Using a Retrospective Healthcare Utilization Framework (2009–2018)

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ABSTRACT

Acute myeloid leukemia (AML) represents a clinically aggressive hematological malignancy with substantial hospitalization burden, particularly among older adults. Despite advances in molecular diagnostics and risk stratification, population-level evidence describing sex- and age-specific disparities in AML-related hospitalizations remains limited. This study presents a retrospective, population-based technical assessment of AML hospitalization patterns in U.S. adults from 2009 to 2018 using a healthcare utilization framework derived from national inpatient surveillance data structures. The objective is to evaluate differential hospitalization burden across sex and age strata and to interpret observed disparities within an epidemiological and molecular context.

Findings from prior population-level studies indicate persistent sex-based survival and incidence differences in AML, with males exhibiting consistently higher disease burden compared to females across multiple age groups (Hossain & Xie, 2015; Utuama et al., 2019). Age remains a dominant determinant of AML hospitalization intensity, with a marked concentration among older adults (Shallis et al., 2019). Molecular heterogeneity further complicates disease trajectory, as leukemogenic pathways and biomarker variability influence both progression and treatment response (rada-Arismendy et al., 2017). This technical synthesis integrates epidemiological patterns with healthcare utilization structures to conceptualize AML hospitalization disparities in a population-level framework.

The study emphasizes the need for stratified healthcare planning, improved risk prediction models, and integration of molecular epidemiology into population surveillance systems. Limitations include reliance on secondary data constructs and absence of individual-level clinical variables.

KEYWORDS

Acute Myeloid Leukemia, Hospitalization Burden, Sex Disparities, Age Stratification, Epidemiological Analysis, Healthcare Utilization, NIS Database, Population Health, Hematological Malignancy, Retrospective Study.

INTRODUCTION

1.1 Background and Problem Statement

Acute myeloid leukemia (AML) is a biologically heterogeneous malignancy characterized by clonal proliferation of myeloid precursors with impaired differentiation. It remains one of the most lethal hematological cancers in adults, with survival strongly influenced by age, sex, genetic mutations, and comorbid conditions. Epidemiological evidence indicates that AML incidence and outcomes are not uniformly distributed across populations, with significant disparities observed in both hospitalization rates and survival outcomes (Shallis et al., 2019).

Population-level analyses have consistently demonstrated that males exhibit higher AML incidence and poorer survival outcomes compared to females, suggesting the presence of sex-linked biological and behavioral determinants (Hossain & Xie, 2015). Similarly, older adults experience disproportionately higher hospitalization rates due to age-associated hematopoietic decline, comorbid disease burden, and reduced treatment tolerance (Utuama et al., 2019).

From a molecular perspective, AML pathogenesis is driven by heterogeneous genetic and epigenetic alterations. Biomarker-based classification systems have significantly improved disease stratification and prognostication (rada-Arismendy et al., 2017). However, integration of molecular insights into population-level hospitalization frameworks remains limited, creating a gap between clinical genomics and health services research.

Healthcare utilization studies using national datasets such as the Nationwide Inpatient Sample (NIS) provide a critical platform for evaluating disease burden at scale (HCUP, 2012). These datasets allow for assessment of hospitalization trends, resource utilization, and demographic disparities across large populations.

1.2 Research Objectives

This study aims to:

1. Evaluate sex-based differences in AML hospitalization burden among U.S. adults.

2. Assess age-stratified hospitalization patterns over a 10-year period (2009–2018).

3. Conceptualize hospitalization disparities within a healthcare utilization framework.

4. Integrate epidemiological findings with molecular insights from AML literature.

5. Identify structural gaps in population-level AML surveillance.

1.3 Scope and Significance

The significance of this technical analysis lies in its integration of epidemiological, demographic, and molecular perspectives to interpret AML hospitalization disparities. Understanding these patterns is essential for optimizing healthcare resource allocation, improving early risk identification, and developing precision health strategies for vulnerable populations.

2. Literature Review

2.1 Epidemiology of AML and Hospitalization Burden

AML epidemiology is characterized by increasing incidence with age and marked heterogeneity in clinical outcomes. Shallis et al. (2019) emphasize that AML remains a major public health challenge due to its rising incidence in aging populations and persistent survival disparities. Hospitalization burden is particularly high due to intensive induction chemotherapy, complications such as infections, and treatment-related toxicities.

2.2 Sex-Based Disparities in AML

Sex differences in AML outcomes have been consistently documented. Hossain and Xie (2015) report significant survival disparities between males and females in younger populations, suggesting underlying biological and possibly hormonal influences. Utuama et al. (2019) further extend these findings, demonstrating persistent sex-based differences in leukemia survival across adult populations in the United States.

These disparities may arise from differential gene expression, immune response variation, and exposure risk profiles. However, healthcare utilization patterns may also contribute, including differences in healthcare-seeking behavior and access to specialized care.

2.3 Age-Related Variability in AML Outcomes

Age is one of the most significant determinants of AML prognosis. Older adults exhibit higher hospitalization rates and poorer outcomes due to increased comorbidity burden and reduced tolerance to intensive chemotherapy (Shallis et al., 2019). Age-related hematopoietic stem cell mutations also contribute to increased susceptibility.

2.4 Molecular Biomarkers and Pathophysiological Insights

Molecular characterization of AML has transformed understanding of disease heterogeneity. rada-Arismendy et al. (2017) highlight the importance of molecular biomarkers in AML classification, prognosis, and therapeutic targeting. These biomarkers include genetic mutations, cytogenetic abnormalities, and epigenetic modifications that influence disease progression.

Importantly, biomarker variability may also contribute to observed population-level disparities, as molecular subtypes differ in prevalence across demographic groups. This introduces a biological dimension to hospitalization patterns that is often absent in administrative datasets.

2.5 Healthcare Utilization Frameworks

The Nationwide Inpatient Sample (HCUP, 2012) provides a foundational dataset for evaluating hospitalization trends in the United States. Such datasets enable researchers to quantify disease burden, identify disparities, and assess healthcare resource utilization at a national level.

Castellanos et al. (2022) demonstrate the utility of population-based hospitalization data in identifying disparities in leukemia outcomes, reinforcing the importance of large-scale administrative datasets in epidemiological research.

2.6 Research Gap Identification

Despite extensive literature on AML epidemiology, several gaps remain:

- Limited integration of molecular biomarkers into population-level hospitalization studies.
- Insufficient sex- and age-stratified analyses of hospitalization burden over extended time periods.
- Lack of unified frameworks combining clinical, demographic, and healthcare utilization perspectives.

This study addresses these gaps by synthesizing epidemiological and healthcare utilization evidence within a structured analytical framework.

3. Methodology

3.1 Study Design

This study adopts a retrospective population-based technical analysis framework. It synthesizes findings from existing epidemiological literature and healthcare utilization structures to model AML hospitalization disparities in U.S. adults between 2009 and 2018.

3.2 Conceptual Framework

The analytical framework integrates three core dimensions:

1. Demographic dimension – sex and age stratification of hospitalization burden.
2. Clinical dimension – disease severity and molecular heterogeneity.
3. System-level dimension – healthcare utilization patterns derived from national inpatient data systems.

This triadic framework enables interpretation of AML hospitalization trends as an interaction between biological determinants and healthcare system structures.

3.3 Data Source Architecture

The Nationwide Inpatient Sample (NIS) serves as the foundational reference structure for understanding hospitalization trends (HCUP, 2012). Although primary data extraction is not performed in this technical note, the dataset framework informs the analytical model used to interpret population-level trends.

3.4 Analytical Strategy

The methodological approach includes:

- Stratified analysis logic based on sex (male/female) and age groups.
- Temporal trend conceptualization across a 10-year period.
- Integration of epidemiological and molecular literature to interpret observed disparities.
- Comparative synthesis of prior findings to validate hospitalization burden patterns.

3.5 Role of Molecular Biomarkers in Analytical Interpretation

Molecular biomarkers play a critical interpretative role in this framework. rada-Arismendy et al. (2017) emphasize that AML progression is driven by genetically distinct subtypes, which may influence hospitalization intensity through differential disease aggressiveness and treatment response variability. These molecular characteristics are indirectly incorporated into the analytical interpretation of population-level disparities.

4. Results / Findings

4.1 Overall Hospitalization Burden Patterns

The synthesized epidemiological evidence indicates that acute myeloid leukemia (AML) hospitalizations in U.S. adults demonstrate a consistently high burden among older age groups, with a pronounced concentration in individuals aged ≥60 years. Across population-based surveillance systems, AML-related admissions are strongly age-dependent, reflecting cumulative genomic instability, age-associated clonal hematopoiesis, and reduced physiological resilience to intensive therapy (Shallis et al., 2019).

Sex-stratified observations reveal a persistent male predominance in hospitalization burden. Males consistently exhibit higher AML-related hospitalization rates compared to females across nearly all adult age categories. This pattern aligns with prior population-level findings indicating sex-based survival and incidence disparities in leukemia outcomes (Hossain & Xie, 2015; Utuama et al., 2019).

4.2 Age-Specific Disparities in Hospitalization

Age emerges as the most significant determinant of hospitalization intensity. The highest burden is observed in older adults, particularly those aged 60–79 years, followed by those ≥80 years. This pattern is consistent with the established epidemiological profile of AML as a disease of aging hematopoiesis (Shallis et al., 2019).

Younger adults (18–39 years) demonstrate comparatively lower hospitalization rates; however, relative sex disparities are more pronounced in this subgroup. The differential gap suggests that biological sex effects may be more visible when baseline age-related risk is lower, allowing underlying biological and behavioral

differences to become more apparent.

4.3 Sex-Based Disparities Across Age Strata

Across all age categories, males exhibit higher hospitalization burden than females. The disparity is especially notable in younger adult cohorts, where relative differences are more pronounced despite lower absolute hospitalization rates.

This sex-based divergence may reflect multiple interacting mechanisms:

- Hormonal modulation of immune and hematopoietic function
- Differential exposure to environmental or occupational risk factors
- Genetic susceptibility linked to sex chromosomes
- Healthcare utilization and diagnostic timing differences

These observations are consistent with prior evidence demonstrating sex-related survival differences in AML populations (Hossain & Xie, 2015; Utuama et al., 2019).

4.4 Integration of Molecular Heterogeneity

Molecular heterogeneity plays a critical interpretive role in explaining variability in hospitalization burden. AML is not a single disease entity but a spectrum of genetically distinct subtypes characterized by driver mutations, cytogenetic abnormalities, and epigenetic alterations.

rada-Arismendy et al. (2017) emphasize that molecular biomarkers significantly influence disease aggressiveness, treatment response, and relapse risk. These molecular differences likely contribute indirectly to hospitalization burden by determining:

- Disease progression speed
- Intensity of induction chemotherapy required
- Frequency of complications such as infections or relapse

Therefore, observed population-level disparities may partially reflect underlying molecular subtype distributions across demographic groups.

4.5 Healthcare System-Level Observations

Hospitalization trends derived from national inpatient surveillance frameworks (HCUP, 2012) indicate that AML remains a high-resource utilization condition. Admissions are frequently associated with:

- Intensive chemotherapy cycles
- Supportive transfusion therapy
- Infection management and critical care utilization

Castellanos et al. (2022) highlight that hematologic malignancies demonstrate significant disparities in inpatient outcomes, reinforcing the importance of system-level evaluation in understanding AML burden.

4.6 Summary of Key Findings

Overall, three dominant patterns emerge:

1. Age dependency – hospitalization burden increases sharply with age.
2. Sex disparity – males consistently exhibit higher hospitalization rates.
3. Biological heterogeneity – molecular diversity likely modulates observed epidemiological patterns.

5. Discussion

5.1 Interpretation of Age-Driven Hospitalization Patterns

The strong age gradient observed in AML hospitalizations reflects fundamental biological processes of hematopoietic aging. Age-related accumulation of somatic mutations and decline in DNA repair mechanisms increase susceptibility to malignant transformation. Additionally, older adults are less tolerant of intensive chemotherapy, leading to prolonged hospital stays and increased complication rates.

Shallis et al. (2019) emphasize that AML in older populations is associated with both higher incidence and poorer outcomes, reinforcing the interpretation that hospitalization burden is not merely a function of disease occurrence but also treatment complexity and systemic fragility.

5.2 Mechanistic Basis of Sex Disparities

Sex-based differences in AML hospitalization burden are multifactorial. Biological explanations include hormonal regulation of immune responses and sex-linked genetic expression patterns influencing hematopoietic regulation. Behavioral factors, such as differences in healthcare-seeking behavior and occupational exposures, may also contribute.

Importantly, Utuama et al. (2019) demonstrate that sex disparities persist across multiple age groups and racial/ethnic strata, suggesting that these differences are structurally embedded rather than context-specific.

Hossain and Xie (2015) further reinforce that sex differences are evident even in younger populations, where confounding age-related comorbidities are minimal.

5.3 Role of Molecular Biomarkers in Explaining Heterogeneity

Molecular classification provides a critical explanatory layer for understanding hospitalization variability. rada-Arismendy et al. (2017) highlight that AML is driven by diverse genetic lesions, including mutations affecting signaling pathways, transcription factors, and epigenetic regulators.

These molecular differences influence:

- Disease aggressiveness (rapid vs. indolent progression)
- Treatment response variability
- Likelihood of relapse requiring rehospitalization

Thus, hospitalization burden is not solely a demographic phenomenon but also a reflection of underlying biological diversity.

5.4 Healthcare System and Utilization Implications

From a systems perspective, AML represents a high-intensity resource utilization condition. The reliance on inpatient care for chemotherapy administration, infection management, and transfusion support contributes to sustained hospitalization burden.

The HCUP framework (2012) provides essential infrastructure for quantifying these trends, enabling national-level surveillance of disease burden. However, administrative datasets often lack molecular and clinical granularity, limiting their ability to fully explain observed disparities.

5.5 Contradictions and Limitations in Existing Evidence

Although epidemiological studies consistently report sex and age disparities, inconsistencies remain in the magnitude of these differences across datasets. Variability may arise from:

- Differences in coding practices in administrative datasets
- Heterogeneity in treatment protocols across institutions
- Lack of integration between molecular and demographic data

Additionally, Castellanos et al. (2022) highlight that hospitalization outcomes in hematologic malignancies may also be influenced by racial and socioeconomic variables, which are not fully captured in this analysis framework.

5.6 Theoretical Implications

This study supports a multi-layered theoretical model of AML hospitalization burden in which:

- Biological layer (molecular mutations) drives disease aggressiveness
- Demographic layer (age, sex) modulates susceptibility and outcomes
- System layer (healthcare utilization) determines hospitalization intensity

The integration of these layers provides a more comprehensive understanding of AML epidemiology.

6. Conclusion

This technical synthesis demonstrates that AML hospitalization burden in U.S. adults is strongly shaped by age and sex disparities, with older adults and males disproportionately affected. The findings reinforce that AML is not only a biologically heterogeneous malignancy but also a condition deeply influenced by demographic and healthcare system structures.

Molecular insights from rada-Arismendy et al. (2017) further clarify that genetic heterogeneity likely contributes to variability in disease progression and hospitalization intensity, bridging the gap between clinical biology and population-level outcomes.

The study contributes to epidemiological understanding by integrating healthcare utilization frameworks with demographic and molecular perspectives. Future research should focus on integrating genomic datasets with administrative hospitalization records to develop predictive models capable of identifying high-risk populations earlier in the disease course.

Limitations include reliance on secondary literature synthesis and absence of patient-level clinical data. Nevertheless, the framework provides a scalable model for analyzing hematologic malignancy burden at the population level.

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