RACIAL DISPARITIES IN HEMATOLOGIC DISORDERS

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OBJECTIVES

• Review burden of selected hematologic diseases in U.S.

• Review definition of disparity

• Review epidemiology of disparities in leukemia, multiple myeloma, and lymphoma

• Review potential etiologies of disparities
CANCER BURDEN IN AMERICA

- According to the American Cancer Society, there will be an estimated \textbf{1,688,780 new cancer cases} diagnosed and \textbf{600,920 cancer deaths} in the United States in 2017.

- A significant proportion of these diagnoses (172,910) and cancer deaths (58,300) will be in patients with hematologic malignancies.

- Much of current data focuses on general cancer trends, incidences, and survival data on patients with solid tumors. There is not a significant amount of information on disparities amongst patients with hematologic diseases.
DEFINITION OF DISPARITY

- In 2000, *Minority Health and Health Disparities Research and Education Act* was passed which helped to legally define a health disparity population:

  “[a] population is a health disparity population if there is a significant disparity in the overall rate of disease incidence, prevalence, morbidity, mortality, or survival rates in the population as compared to the health status of the general population.”
LEUKEMIA

- In 2017, there will be more than 21,000 cases of newly diagnosed acute myeloid leukemia (AML) and over 5,000 new cases of acute lymphoblastic leukemia (ALL) in the US.
**LEUKEMIA EPIDEMIOLOGY**

<table>
<thead>
<tr>
<th></th>
<th>Acute leukemia n (%)</th>
<th>AML n (%)</th>
<th>ALL n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>26,480 (67.9)</td>
<td>20,264 (73.6)</td>
<td>6,216 (54.2)</td>
</tr>
<tr>
<td>Black</td>
<td>2,797 (7.2)</td>
<td>2,075 (7.6)</td>
<td>722 (6.3)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>6,599 (16.9)</td>
<td>3,030 (11.0)</td>
<td>3,569 (31.1)</td>
</tr>
<tr>
<td>API</td>
<td>3,126 (8.0)</td>
<td>2,156 (7.8)</td>
<td>970 (8.5)</td>
</tr>
</tbody>
</table>
Age-adjusted incidence rates of childhood acute lymphocytic leukemia (ALL) and acute myeloid leukemia (AML) by ethnicity and subtype, SEER 13, 1992-2011.

# DISTRIBUTION OF GENETIC FACTORS IN AML

<table>
<thead>
<tr>
<th>Race</th>
<th>AML n (%)</th>
<th>t(8;21) n (%)</th>
<th>t(11q23) n (%)</th>
<th>t(15;17) APL n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>20,264 (73.6)</td>
<td>269 (1.3)</td>
<td>125 (0.6)</td>
<td>1,276 (6.3)</td>
</tr>
<tr>
<td>Black</td>
<td>2,075 (7.6)</td>
<td>29 (1.4)</td>
<td>8 (0.4)</td>
<td>184 (8.9)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3,030 (11.0)</td>
<td>41 (1.4)</td>
<td>19 (0.6)</td>
<td>407 (13.4)</td>
</tr>
<tr>
<td>API</td>
<td>2,156 (7.8)</td>
<td>43 (2.0)</td>
<td>17 (0.8)</td>
<td>156 (7.2)</td>
</tr>
</tbody>
</table>

HAZARD OF MORTALITY, ALL LEUKEMIA AND STRATIFIED BY SUBTYPE (ACUTE LEUKEMIA, SEER 1999–2008)

<table>
<thead>
<tr>
<th>Race</th>
<th>All acute LEUKEMIA HR (95% CI)</th>
<th>p value</th>
<th>AML HR (95% CI)</th>
<th>p value</th>
<th>ALL HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>1.00 (Referent)</td>
<td></td>
<td>1.00 (Referent)</td>
<td></td>
<td>1.00 (Referent)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1.17 (1.12, 1.23)</td>
<td>&lt;0.0001</td>
<td>1.12 (1.06, 1.18)</td>
<td>&lt;0.0001</td>
<td>1.45 (1.28, 1.65)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.13 (1.08, 1.17)</td>
<td>&lt;0.0001</td>
<td>1.06 (1.01, 1.11)</td>
<td>0.01</td>
<td>1.46 (1.36, 1.57)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>API</td>
<td>0.97 (0.92, 1.02)</td>
<td>0.22</td>
<td>0.96 (0.91, 1.01)</td>
<td>0.1</td>
<td>1.06 (0.94, 1.20)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

LEUKEMIA

- Despite a higher percentage of favorable genetic mutations in AML for black and Hispanic patients, no protective effect was seen after statistical adjustment.

- For ALL, there is a nearly 50% higher probability of death for blacks and Hispanics compared to whites.
MULTIPLE MYELOMA

- In 2017, there will be more than 30,000 cases of newly diagnosed multiple myeloma in the US
MULTIPLE MYELOMA

• Multiple myeloma is the most common hematologic malignancy in US Blacks

• One study analyzed SEER database from 1973-2005
  > Blacks had a younger age of onset compared to whites (65.8 vs 69.8 – p<.001)
  > Age-adjusted incidence among Blacks about twice that among whites (11.0 vs 4.9 per 100,000 person-years – p <0.001)

> Limited data on other minority groups since SEER did not include information on regions with multiple ethnicities until ~1992

Disease-specific survival 1973-2005 (SEER-9), by race and age group.

A. All Ages

B. <50 Years

C. 50-69 Years

D. ≥70 Years

Advances in the diagnosis and treatment of MM.

1960s — Melphalan-Prednisone\textsuperscript{37}

1973 — Start of NCI SEER Registry\textsuperscript{33}

1978 — Recognition of MGUS\textsuperscript{35}

1980 — Smoldering Myeloma Described\textsuperscript{36}

1994 — High-Dose Melphalan with Autologous Stem Cell Transplantation\textsuperscript{24,25}

1999 — Thalidomide Salvage Therapy\textsuperscript{27}

2002 — Thalidomide Initial Therapy\textsuperscript{28}

2003 — Bortezomib Salvage Therapy\textsuperscript{31}

2006 — Tandem Autologous Transplantation\textsuperscript{26}

2008 — Lenalidomide Salvage Therapy\textsuperscript{29}

2010 — Bortezomib Initial Therapy\textsuperscript{32}

2010 — Lenalidomide/Dexamethasone (Low Dose) Initial Therapy\textsuperscript{30}


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Five-year RSRs by race and age group (SEER-9). *P < .05; **P < .01; ***P < .001; and –, P ≥ .05.
MULTIPLE MYELOMA

- Blacks have younger age of onset and better survival (from 1973-2005) compared to whites

- Whites had significant survival improvement over time after introduction of novel therapies. Blacks had non-significant changes in survival – possibly due to unequal access to and/or disparate responsiveness to new modalities of treatment

- Limited data on other racial groups, though some data suggest worse OS in Hispanic patients compared to whites. Asians are thought to have similar overall survival to whites.
LYMPHOMA

• In 2017, it is estimated there will be more than 80,000 new cases of Hodgkin and non-Hodgkin’s lymphoma
HODGKIN LYMPHOMA

- Bi-modal distribution?
  - True for white population. Not true for other groups
    - African American men have constant incidence rate after age 30
    - Hispanics only had small incidence peak in the 20s and then highest incidence rate >65
HODGKIN LYMPHOMA

- Inferior 5, 10, and 15 survival for African Americans and Hispanics compared to Caucasians

- Survival for patients diagnosed with Hodgkin lymphoma is worse for patients living in lower SES. After adjustments for SES are made, Blacks and Hispanics still had worse survival than Caucasians and Asian/Pacific Islanders.

NON-HODGKIN LYMPHOMA

- Three largest subtypes of NHL are diffuse large B-cell lymphoma, follicular lymphoma, and chronic lymphocytic leukemia

- Racial disparities in survival exist but without a consistent pattern
POTENTIAL CAUSES OF DISPARITIES
VARIABLE ACCESS/STRUCTURAL BARRIERS

• Much of the solid tumor literature has focused on improving access to screening (colorectal, cervical, lung, and breast cancer). This is something we cannot necessarily do for hematologic diseases

• Studies on variable access for hematologic diseases focus on access to treatment rather than screening
VARIABLE ACCESS/STRUCTURAL BARRIERS

• Access to treatment is different between groups
  
  -> Blacks 49% less likely to receive stem cell transplantation for myeloma compared to whites
  -> Black patients less likely to receive chemotherapy for DLBCL
  -> No data regarding language/English comprehension for patients with hematologic malignancies. Studies on this do exist in solid tumor literature.

• Socioeconomic status

COMPLIANCE

• Some studies have demonstrated poor adherence to medications (e.g. anti-hypertensive medications and oral chemotherapy for solid tumors) and follow-up care amongst Hispanics, African-Americans, and other minority groups.

• While limited data exist on patients with hematologic diseases, some studies refute the claim that there is differences in compliance.

Differential metabolism of chemotherapy drugs has been hypothesized as a possible reason for disparate outcomes.

Is race a poor proxy for genetic diversity?

Cardiology trials have demonstrated differential benefit of drugs for African Americans.


CLINICAL TRIAL PARTICIPATION

• Minority recruitment and enrollment in clinical trials is low compared to white patients

• Representative example: many of the trials leading to the approval of nivolumab for non-squamous lung cancer and advanced renal cell carcinoma had study populations involving nearly 90% white patients and less than 10% underrepresented minorities

• How do we generalize clinical trials to minority patients when they are not included?
SUMMARY

• The percentage of racial/ethnic minorities in this country is increasing

• Certain groups continue to have worse outcomes compared to whites for unclear reasons

• More epidemiologic and interventional studies should be done with minorities in mind in order to help improve care

• Increased minority recruitment and enrollment in clinical trials is necessary
REFERENCES

