Global Incidence and Survival of Acute Myeloid Leukemia with 20–29% Blasts: A Systematic Literature Review

Poster
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Background & Objectives

Acute myeloid leukemia (AML) is a form of bone marrow-related cancer accounting for approximately 1% of all cancers and is generally more commonly diagnosed among older people[1]. Per the 2002 WHO classification, the blast threshold for AML was reduced from 30%–20% blasts in the blood and bone marrow on the basis of prior studies indicating that patients with 20%–29% blasts had a similar response to therapy and survival as those with 30% or more blasts[2]. AML with 20-29% blasts is potentially less aggressive than AML with ≥30% blasts, with its clinical course similar to that of myelodysplastic syndromes (MDS) with 10–19% bone marrow blasts[3]. Current treatment options are limited and are not tailored towards AML with 20–29% blasts. The objective of this study was to describe the global incidence and prevalence of AML with ≥30% blasts and AML with 20–29% blasts and related secondary outcomes (such as treatment patterns, the prevalence of mutations, and mortality) in recent years (2008–2020).

Methods

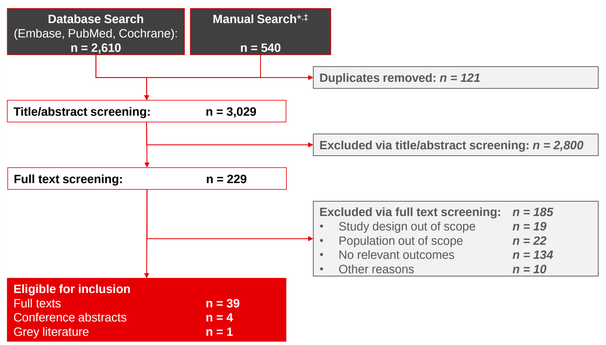
Database and manual search

Comprehensive searches were developed and conducted in MEDLINE, EMBASE and the Cochrane library, covering studies published between January 1st, 2008, and October 7th, 2020. The search string was designed to identify any studies reporting epidemiology, incidence, or prevalence outcomes of AML. Relevant conference proceedings (published between 2018–2020) and grey literature were searched. The reference lists of eligible systematic reviews were also searched to identify primary studies.

Screening and data extraction

Two independent reviewers screened all titles/abstracts and full-text articles. One reviewer extracted data from included studies, and a second reviewer verified all data. Observational studies reporting incidence/prevalence of AML and/or AML with 20–29% blasts in populations aged 18 years and older were eligible for inclusion. Data on secondary outcomes of interest (such as treatment patterns, prevalence of mutations and mortality) were extracted from studies that met the inclusion criteria.

Figure 1. PRISMA flow diagram



* The reference lists of five systematic reviews and one meta-analysis were manually searched for relevant studies
‡ Hand searching corresponds to the targeted Google searches and grey literature searches

Results

Study selection

A total of 44 studies were included (Figure 1), reporting estimates from 39 countries and covering data from 1961–2020. The majority of included studies reported data from large population-based cancer registries, while 13% of the studies were center-based. Most of the included studies were conducted in the USA.

Incidence of AML

Incidence was reported in 24 studies (Figure 2). Key insights are listed below:

- The most recent age-adjusted global incidence estimate of AML was 1.54 per 100,000 person-years, but regional estimates showed considerable variation.
- The most recent estimate from the USA was 4.3 per 100,000 persons in 2020 (modeled rate based on 2014–2018 SEER data), while the most recently reported incidence in Europe ranged from 2.62 cases per 100,000 person-years in Andorra to 4.05 in the UK in 2017 (all estimates were age-adjusted).
- Higher rates were generally reported in males in comparison to females. The most recent age-adjusted global estimate in males was 1.81 per 100,000 person-years, while the rate in females was 1.33 per 100,000 person-years.
- Studies assessing the incidence over time found an increasing trend in Asian countries (n = 2) as well as the USA (n = 2). Varying trends on incidence (increasing, decreasing, or stable) were seen in Europe (2 studies in 7 countries) and Oceania (2 studies in 3 countries). The global incidence between 2008 and 2017 was reported to have remained stable.
- Incidence rates in both males and females showed an increasing trend with age. A study from the USA reported an incidence of 27.6 per 100,000 persons in people aged 75–84 years and 30 per 100,000 persons in people aged 85 years and above. The national average during the same period was 4.2 per 100,000 persons.

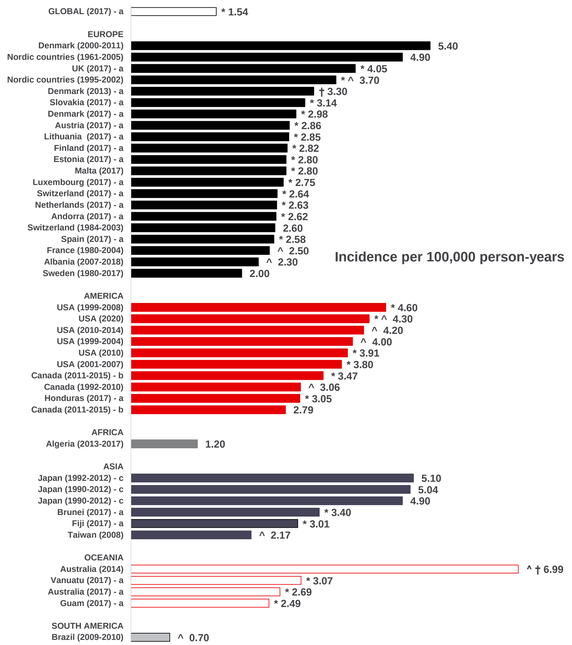
Prevalence of AML

Prevalence was reported in three studies, ranging from 1.5 per 100,000 persons in Brazil (2009–2010) to 13.7 per 100,000 persons in Sweden (1997–2013). One study spanning multiple European countries reported a prevalence of 11 per 100,000 persons over the years 1995–2002. Four studies reported the proportion of AML among a broader group of malignancies, estimates of AML prevalence ranging from 70.1% among patients with AML/MDS (USA), over 27.8% among patients with hematological malignancies (Ukraine) to 1.8% among all cancer patients (USA).

Key findings among patients with AML with 20–29% blasts

In total, four studies reported data on patients with AML with 20–29% blasts. One population-based study from Poland reported an overall incidence of 0.1 per 100,000 person-years in males and 0.2 per 100,000 person-years in females in 2012[4]. Three center-based studies[5-7] reported data on patients with AML with 20–29% blasts among a sample of patients with AML, whereby the overall percentage of AML with 20–29% blasts among incident cases with AML ranged from 17% to 34%. The proportion of AML with 20-29% blasts differed slightly between male (17% to 38%) and female patients (15% to 28%). The three center-based studies also reported on additional characteristics and outcomes of patients with AML with 20–29% blasts in comparison to patients with AML with ≥30% blasts (Table 1). FLT3(-ITD) and NPM1 mutations were more common among patients with AML with ≥30% blasts in all three studies. Two studies concluded that the mutational profile of AML with 20–29% blasts resembles MDS more than AML with ≥30% blasts. While intensive chemotherapy was most frequently received by patients with AML with ≥30% blasts, hypomethylating agents were more commonly given to patients with AML with 20–29% blasts. One study reported a similar proportion of patients receiving allogeneic stem-cell transplantation in both groups (29% in AML with 20–29% blasts/27% in AML with ≥30% blasts). Two studies reported lower overall survival (OS) in patients with AML with ≥30% blasts compared to AML with 20–29,% blasts while one study found the opposite.

Figure 2. Global Incidence of AML (n=24 studies)



* Indicates age-adjusted estimates; ^ Indicates an incidence per 100,000 persons; † Primary AML incidence estimate.; **a** All modeled estimates from a single study (Yi 2020); **b** Estimates from a single study (Shysh 2018); lower estimate corresponds to subnational data; **c** Data from a nationwide Japanese cohort with a large proportion of current or former smokers.

Table 1. Patient and treatment characteristics of patients with AML with 20–29% compared to AML with ≥30% (n of studies = 3)

Outcome	AML with 20-29% blasts	AML with ≥30% blasts
Mutations	FLT3-ITD: **4% to 6%** (n = 2) FLT3: **10%** (n = 1) NPM1: **2% to 10%** (n = 3) KRAS or NRAS: **10%** (n = 1) DNMT3A: **10%** (n = 1) KIT: **4%** (n = 1) CEBPA: **16%** (n = 1)	FLT3: **20% to 24%** (n = 2) FLT3: **20%** (n = 1) NPM1: **16% to 31%** (n = 3) KRAS or NRAS: **13%** (n = 1) DNMT3A: **2%** (n = 1) KIT: **6%** (n = 1) CEBPA: **11%** (n = 1)
Treatment Patterns	Induction chemotherapy: **44% to 58%** (n = 3) Hypomethylating agents: **23% to 35%** (n = 3) Supportive care: **8%** (n = 1)	Induction chemotherapy: **59% to 99%** (n = 3) Hypomethylating agents: **18%** (n = 2) Supportive care: **8%** (n = 1)
Stem-cell Transplantation (STC)	Allogeneic SCT at any time: **29%** (n = 1)	Allogeneic SCT at any time: **27%** (n = 1)
Mortality	OS: **16 months to 20.5 months** (n = 3)	OS: **12 months to 25 months** (n = 3)

Limitations

- Due to the lack of validated tools to assess the quality of epidemiological studies, no adequate quality appraisal of included studies could be conducted. Nonetheless, many population-based studies were identified.
- Exclusion of non-English studies led to scarce representation of certain geographies.
- The direct comparability of reported incidence rates and prevalence estimates is limited as some studies focused on patient subgroups with primary AML only.
- Summarized data on patient and treatment characteristics and mortality outcomes were heterogeneous as these data were not systematically searched for.

Conclusions

- AML remains relatively rare in comparison to other leukemias (incidence across Europe/North America: 2.0–5.4/100,000 person-years) and is therefore classified as a rare disease according to the Rare Diseases Act of 2002[8]. Among older patients, however, AML incidence and prevalence are markedly higher compared to younger generations.
- Most published data on AML epidemiology are from European and North American countries with established cancer registries. Estimates from countries in Asia, Africa, and South America were infrequently reported.
- Epidemiological data on AML with 20–29% blasts were scarce, which might be due to poor reporting of blast count percentages. However, the available data suggest differences in patient characteristics, treatment choice, and survival outcomes between this disease subtype and AML with ≥30% blasts. Accordingly, additional research is warranted for disease characterization of AML with 20-29% blasts.

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Abbreviations

AML, Acute Myeloid Leukemia; MDS, Myelodysplastic Syndromes; OS, Overall Survival; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SCT, Stem Cell Transplant

Disclosures

FK and MD are employees of Millennium Pharmaceuticals, Inc., Cambridge, MA, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited. EM and AR are employees of Cytel. CJ is a former employee of Millennium Pharmaceuticals, Inc.

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