Real world data on unique challenges and outcomes of older patients with AML from resource limited settings: Hematology Cancer Consortium INwARD registry

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Despite significant advances in the treatment of acute myeloid leukemia (AML), outcomes in older patients continue to be suboptimal, due to adverse disease characteristics and increasing prevalence of co-morbidities. This challenge is further magnified in resource-limited settings where logistical and financial barriers often preclude effective therapy. In addition, a significant number of patients do not undergo any evaluation after diagnosis, resulting in very little real-world data on treatment outcomes in this cohort. We present data on epidemiology and treatment patterns in older patients with AML from the Indian Acute Leukemia Research Database [INwARD] established by Hematology Cancer Consortium (HCC).

Retrospective data from 17 centres was collected to include patients older than 55 years diagnosed between January 2018 and April 2021. . A lower age cut off of 55 years was used based on previous data indicating physiologic characteristics comparable to a 65 year old individual in the West. No exclusion criteria were specified. The primary objectives were to ascertain the proportion of patients receiving therapy and one-year overall survival among treated patients. Patient status was assessed as on March 31, 2022.

A total of 733 patients (M:F=1.48) were included in this study, of which only 339(46%) patients underwent further evaluation and treatment. The most common reasons for not initiating treatment were to begin evaluation at another centre(37%) and financial constraints(13%). Among treated patients, the median age at diagnosis was 63 years (IQR, 59-69), with 130(40.2%) having an ECOG performance score ≥ 2 and 203(60.4%) having at least one comorbidity. No differences in baseline attributes were noted among treated or untreated patients.(Table 1) Of the 339 patients who received treatment, initial therapy comprised hypomethylating agents (HMA) in 247 (72.8%) patients, standard or modified 7+3 regimen in 64 (18.8%) and other intensive regimens in 2 (0.59%) patients. Infections requiring treatment were diagnosed in 117 (40.3%) patients, with 36 (13.79%) requiring intensive care. A second induction was required in 26 patients, of which 5(19%) received intensive chemotherapy and 8 (30%) received HMA. Early mortality (within 60 days of diagnosis) was noted in 58(20.1%) out of 288 evaluable patients at this time point. Poor performance status at baseline was significantly associated with early mortality(p=0.015) with no effect of age or associated co-morbidities. Among patients who died within 60 days, a significantly higher white cell count was observed at baseline (median, 20310 vs 7200/mm^3,p=0.005). Complete remission (CR) was achieved in 24(36%) patients after intensive chemotherapy. Among 146(59%) evaluable patients receiving HMA, 62(42%) achieved CR at any time point after therapy. The probability of achieving CR significantly decreased with increasing age (p=0.037). Allogeneic stem cell transplant was utilized for only 11 (3.2%) patients in the treated cohort.

After a median follow up of 5 months (IQR 1.4 to 14.6 months), 102 (32.2%) patients were lost to follow up and only 72 (26%) had completed treatment. For survival analysis, patients lost to follow up were considered dead at the date of last follow up. At the end of one year, probability of survival was 32.9%, (Figure 1) with the median overall survival being 190 days (95% CI, 143 to 236) in the treated cohort. Among 145 patients with available data, the most common cause of death was progressive disease (52%), followed by infectious complications(29%).

Our data highlights dual challenges of low rates of treatment initiation and significant treatment discontinuation within one year in patients older than 55 years of age with AML in India. Poor disease biology is also highlighted by low rates of CR irrespective of initial therapy and low probability of survival at one year. Financial challenges emerge as major modifiable factors leading

to incomplete treatment. This large registry dataset indicates the need for more effective, affordable and safer treatment options for this group of patients.

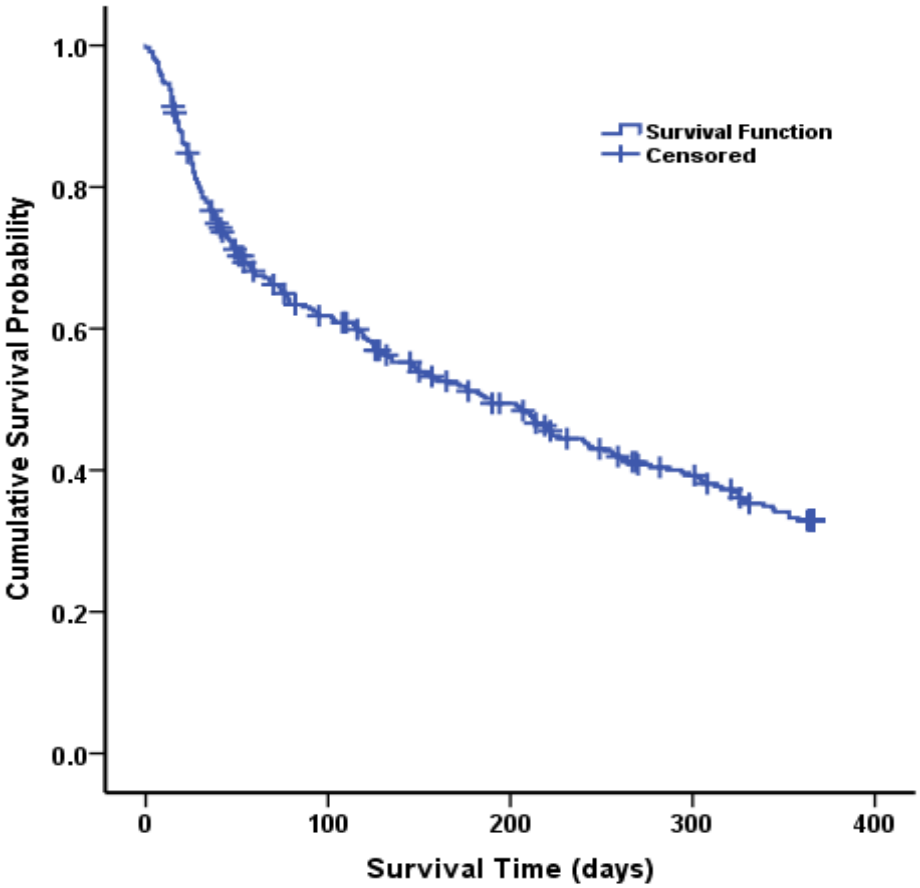

Figure 1: Kaplan Meier curve showing one year overall survival among patients who initiated treatment.

Variable	Group A	Group B
Age in Years (Median, IQR)	63 (59, 69)	63 (59, 69)
Hb, g/dl (Median, IQR)	7.80 (6.60, 9.10)	8 (6.70, 9.30)
TLC at diagnosis in/mm3 (WBC) (Median, IQR)	8430 (2910, 33700)	11700 (347, 49750)
Gender	**N(%)**	**N (%)**
Male	202 (59.59)	236 (59.90)
Female	137 (40.41)	158 (40.10)
ECOG Performance status		
Fully active	39 (12.07)	16 (4.78)
Restricted in physically strenuous activity	154 (47.68)	179 (53.43)
Ambulatory and capable of all self care	77 (23.84)	66 (19.70)
Capable of only limited self care	42 (13.0)	57 (17.01)
Completely disabled	11 (3.41)	17 (5.07)
ELN Risk Group		
Low	51 (16.50)	21 (7.72)
Intermediate	164 (53.07)	61 (22.43)
High	56 (18.12)	32 (11.76)
Unknown	38 (12.30)	158 (58.09)
Infection at Diagnosis (Fungal/Documented)		
No	64 (71.91)	5 (83.33)
Yes	25 (28.09)	1 (16.67)

Table 1: Baseline characteristics among patients who received treatment (Group A) and patients who did not (Group B)