Original Article

Survival of Patients with Acute Myeloid Leukemia after Allogeneic Stem Cell Transplantation: An Experience in Developing Country

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ABSTRACT
Background: Allogeneic stem cell transplantation (allo-SCT) is the highest potential treatment for long-term survival as post-remission therapy for acute myeloid leukemia (AML). The aim of this study was to estimate the overall survival (OS) of patients with AML after allo-SCT and to identify the factors affecting them as a prognostic factor for the survival of patients.
Material and Methods: In this retrospective cohort study, data of patients with AML who underwent allo-SCT at Taleghani bone marrow transplantation and cell therapy center in Tehran, Iran, from May 2009 to September 2016 were used. A total of 101 patients were enrolled and death time was considered as a failure event for them. Kaplan-Meier method, log-Rank tests, and Cox proportional hazard model were used to evaluate OS and to identify the risk factors of patient's survival. The SPSS software version 21 was used for the analysis of data and $P<0.05$ was considered as a significant level.
Results: Of 101 patients with AML, 49 (48.5%) were males. The median age at allo-SCT was 32.76 years and 42 patients (41.6%) died. The 5-year OS and disease-free survival (DFS) was 56% (95%CI: 51-61%) and 52% (95%CI: 57-47%), respectively. Multivariate analysis by Cox regression indicated that OS has a significant relationship with WBC count and relapse ($P=0.001$).
Conclusion: Our results showed that allo–SCT has nearly the same outcome in developing countries and the WBC count and relapse are effective factors on the chance of survival in AML patients after allo-SCT.

Keywords: Acute myeloid leukemia; Allogeneic stem cell transplantation; Survival analysis; Prognostic factors

INTRODUCTION

Acute myeloid leukemia (AML) a cancer of myeloid cells in the bone marrow is the most common acute leukemia in the adult population[1,2]. Without treatment, AML is typically fatal within weeks to months[3]. The burden of AML became heavier during

the past 28 years, which might need more health resource especially in developing countries who had the most AML incidences and deaths[4]. The goal of AML therapy is to achieve and sustain remission, and treatment conventionally consists of two phases. In the first phase of treatment, the goal is to induce remission with conventional-dose of chemotherapy[5]. After achieving a first complete remission (CR1), second phase of therapy is mandatory to prevent relapse[6,7]. Post-remission therapy in patients with AML may consist of continuing chemotherapy or transplantation using either autologous or allogeneic stem cells[8]. Data on cytogenetic abnormalities and somatic mutations has provided important information that is essential for therapeutic decision making [9]. Patients with AML can be classified into three prognostic groups based on cytogenetic; good, intermediate, and high-risk [10, 11]. Therefore, the intensity and type of post-remission therapy is usually determined by cytogenetic and molecular factors[6,12]. Chemotherapeutic consolidation is usually recommended for good-risk genetic subtypes of AML and allogeneic hematopoietic stem cell transplantation (allo-SCT) for intermediate and high-risk genetic subtypes of AML[13].

Allo-SCT is the highest potential treatment for long-term survival as post-remission therapy in those with an intermediate or high-risk subtype and as salvage therapy in those with relapsed or resistant disease[14,15]. The Center of International Blood and Marrow Transplant Research (CIBMTR) and the National Marrow Donor Program (NMPD) have been reported 65% survival rates in AML patients after stem cell transplantation, while the 5-year survival rate of adult subjects with AML without allo-SCT is approximately 24%[16-18]. However, the benefit of allo-SCT in overall survival may be compromised by relapse and treatment-related mortality (TRM) [19-21]. Relapse is the major cause of treatment failure and up 50% of AML patients finally relapse after allo-SCT depending on disease status and characteristics [22]. According to the CIBMTR, relapse rates following HLA-matched transplantation range was reported from approximately 25% and 60% for AML patients in CR1 and high-risk subtype patients, respectively[23]. A graft-versus-leukemia effect gives allo-SCT

superior anti-leukemic activity, with a greater chance of maintaining remission than is achieved with consolidation chemotherapy[24,25]. However, its benefit is limited by greater TRM, which can be as high as 20%–30%, and the morbidity and mortality associated with graft-versus-host disease (GVHD)[26,27].

Estimate the survival rate is very useful in monitoring and improving the quality of life of patients with AML, which can lead to conducting better screening programs and discovering new treatments. We conducted this study to evaluate the 5-year overall survival (OS) and disease-free survival (DFS) rates of patients with AML after allo-SCT and to identify the factors affecting them as a prognostic factor for the survival of AML patients, who referred to bone marrow transplantation and cell therapy center at Taleghani Hospital, Tehran, Iran.

MATERIALS AND METHODS
Study design and participants
All patients with AML who underwent a first allo-SCT from May 2009 to September 2016 at bone marrow transplantation and cell therapy center at Taleghani Hospital, Tehran, Iran were enrolled in the retrospective cohort study. AML patients who underwent autologous bone marrow transplantation were excluded from this study. All demographic characteristics and clinical data of patients and donor of stem cells were obtained. Age at transplantation, sex, date of initial AML diagnosis, AML subtype ,disease status at transplantation time(CR1or CR2), date of allo-SCT, sibling or alternative related donor, age of donor, blood type of patient and white blood cell (WBC) counts of patients at diagnosis were obtained. Furthermore, the post-transplant variables and outcomes such as; relapse status, date of last follow-up or death, and the cause of death were recorded. Approval for this study was conducted by the Ethical Committee of Taleghani bone marrow transplantation and cell therapy center of Shahid Beheshti University of Medical Science. Written informed consent was obtained from all patients.

Preparative regimen

All patients receive a Bu/Cy regimen (Busulfan 4 mg/kg/day orally or 3.2 mg/kg/day on days -6 to -3 and Cyclophosphamide 60 mg/kg/day by intravenous infusion on days -2 to -1) for conditioning therapy with subsequent infusion of donor marrow cells on day 0.

Definition

Remission status post-chemotherapy was documented on the basis of criteria laid down by Cheson et al. [28] and European Leukemia Net.[29] Primary induction failure was defined as patients who experienced a failure to achieve remission after two induction chemotherapies. CR1 was defined as remission achieved within one or two consecutive induction chemotherapy regimens. CR2 was defined as remission after receiving salvage chemotherapy for first relapse.

Relapse: Relapse was defined as a recurrence of leukemia confirmed by cytology. Overall Survival (OS) was defined as the time interval between allo-SCT and death of any cause or censoring. DFS was defined as the time from allo-SCT to death without any relapse. Censoring was defined as being alive at the last follow-up.

Statistical analysis

Frequency tables including number and percent were prepared for qualitative variables also mean and standard deviation (Mean ± SD) were presented for continuous variables. OS and DFS of patients were the end points of study. OS was defined as the time interval between allo-SCT and death from any cause related to AML. DFS was defined as the time from allo-SCT to death without any relapse. Censoring was defined as being alive at the last follow-up. Survival after allo-SCT was calculated using the Kaplan–Meier (KM) curve, and the log-rank test was used to compare survival probability between groups. Univariate and multivariate Cox proportional hazard regression was used to determine the prognostic factors of OS and DFS. The Cox proportional assumptions for hazard were not met in defining the relationship between different types of AML based on FAB categories and survival, we only compare three types of AML with high frequency in this study M4, M5 and M2. Hazard ratio (HR) and 95% confidence interval (CI) were reported to compare hazards between patients groups. For all tests, P≤0.05 was considered significant. Statistical analysis was performed using SPSS for windows version 21 (SPSS, Chicago, IL).

RESULTS

Patients characteristic

Between May 2009 to September 2016, 101 consecutive patients with AML in first or second complete remission (CR1/CR2) received allo-SCT from human leukocyte antigen (HLA)-identical matched sibling or non-sibling. The mean age of patients at transplant time was 32.76 ± 9.23 years (range: 3–53 years), and 49 of them (48.5%) were men. Among of our cases with AML, the subgroups frequency of M0, M1, M2, M3,M4, M5 and M6 were 1%, 7.9%, 18.8%, 4%, 36.6%, 29.7%, and 2%, respectively. Most of the patients (97%) underwent transplanted in CR1 and only (3%) of them were transplanted in CR2. Cause of death (n=42) included infection (n=20, 47.6%), GVHD (n=12, 28.6%) and leukemia relapse (n=10. 23.8%). Patients and transplant characteristics are presented in Table 1.

Donors characteristic

The mean age of donors at transplant time was 33.39 ± 10.71 years (range: 5–56 years) and 54 of them (53.5%) were male. In 92 patients (91.1%), the allo-SCT donation came from a sibling and in 9 patients (8.9%) it came from a related alternative donor (a double cousin). For 66 of the recipient–donor pairs (65.3%), an ABO blood group match was attained, 21 pairs (20.8%) had a minor ABO mismatch, and 14 pairs (13.9%) had a major ABO mismatch. In 50 patients (49.5%), the recipient–donor pairs were sexually matched while in others 51 (50.5%) was not. Of the 59 male recipients, 28 (47.4%) had a female donor, and of the 52 female recipients, 23 (44.2%) had a male donor. The main characteristics of donors are presented in Table 2.

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Survival analysis
The median follow up time was 13.16 months (mean: 24.09±2.41 months). Up to the end of the study, 42 (41.6%) patients died and 59 patients (58.4%) were censored. The mean survival time in patients was 53.70 months (95% CI: 44.89-62.51) and for DFS was 50.80 (95% CI: 41.87-59.73). The 1, 3 and 5-year OS was 60% (95% CI: 51-69%), 58% (95% CI: 51-64%) and 56% (95% CI: 51-61%), respectively. The 1, 3 and 5-year DFS was 58% (95% CI: 53-63%), 54% (95% CI: 49-60%) and 52% (95% CI: 47-57%), respectively. The KM curves of OS for comparing sex, age, relapse, WBC counts and different types of AML (M2, M4 and M5) are shown in Figures 1 to 3. The survival time was compared among groups according to the Log-Rank test. There is a statistical difference between categories of WBC counts (P=0.001) and relapse of leukemia (P=0.006) and the different types of AML (M4, M5 and M2) (P=0.03) in OS. The number of patients with post-transplant relapse of leukemia was 13 (12.9%) and the mean time from allo-SCT to relapse for them was 4.87±3.9 months (range: 0.9-14.73). Complete remission after allo-SCT was achieved in 56 (55.4%) patients.

Univariate Analysis for prognostic Factors
Univariate analysis showed a significant association between OS with WBC counts (P=0.001), relapse (P=0.008) and AML-M2 (P=0.004). There was no any significant association between other variables with OS. The hazard ratio (HR) and corresponding CIs for OS are presented in Table 3. The estimated hazard of death was 4.06 (95% CI, 1.88-8.80) for WBC more than (10×10^8/ml) and 2.97 (95% CI, 1.23-7.19) for WBC (5-10$\times10^8$/ml), indicating the adverse effect of this variable on survival time. Hazard of death for relapse was estimated to be 2.61 (95% CI, 1.28-5.34). This rate indicates the power of relapse in decreasing the survival time. Hazard of death for AML-M2 was estimated to be 10.3 (95% CI, 0.13-0.68). This rate indicates that the patients with AML-M2 had a shorter overall survival time. In addition, univariate analysis showed a significant association between DFS with WBC counts (P=0.001) and AML-M2 (P=0.004). The estimated hazard of death was 3.57 (95% CI, 1.69-7.56) for WBC more than (10×10^8/ml) and 2.9 (95% CI, 1.26-6.67) for WBC (5-10$\times10^8$/ml),

indicating the adverse effect of this variable on disease-free survival time. Hazard of death for AML-M2 was estimated to be 0.30 (95% CI, 0.13-0.68). This rate indicates the power of the AML-M2 variable in decreasing disease-free survival time. The HR and corresponding CIs for DFS are presented in Table 4.

Multivariate Analysis for prognostic Factors
In a multivariate model, OS had a strong association with WBS counts (P=0.001) and relapse (P=0.001) (table 3). The estimated hazard of death was 3.98 (95% CI, 1.84-8.68) for WBC more than (10×10^8/ml) and 2.76 (95% CI, 1.13-6.72) for WBC (5-10$\times10^8$/ml), indicating the adverse effect of this variable on survival time. Hazard of death for relapse was estimated to be 5.66 (95% CI, 2.6-12.34). This rate indicates the power of relapse in decreasing the survival time. Moreover, multivariate cox model only revealed a significant association for WBC counts (P=0.001) with DFS (table 4). The estimated hazard of death was 3.80 (95% CI, 1.78-8.10) for WBC more than (10×10^8/ml) and 2.58 (95% CI, 1.11-5.97) for WBC (5-10$\times10^8$/ml), indicating the adverse effect of this variable on disease-free survival time.

Table 1: Patients and transplant characteristics

Characteristics		Frequency (%)
Sex	Male	49 (48.5)
	Female	52 (51.5)
Age at transplant	(Mean ± SD)	32.76 ± 9.23
	(Range)	5-53
Age group	≤ 30	44 (43.6)
	>30	57 (56.4)
Diseases status at transplant	CR1∞	98(97.0)
	CR2	3(3)
Blood group	A^+	29(28.7)
	B^+	15(14.9)
	O^+	37(36.6)
	O^-	7(6.9)
	AB^+	13(12.9)
WBC ($\times 10^8$ /ml)	<5	17(16.8)
	5-10	15(14.9)
	>10	52(51.5)
	unknown	17(16.8)
M3 AML	M3	4(4.0)
	Non-M3	97(96.0)
All types of ALM	M0	1(1.0)
	M1	8(7.9)
	M2	19(18.8)
	M3	4(4.0)
	M4	37(36.6)
	M5	30(29.7)
	M6	2(2.0)
Relapse	Yes	13(12.9)
	No	88(87.1)
Cause of death	Infection	20 (47.6)
	GVHD	12 (28.6)
	Relapse	10 (23.8)

Table 2: Characteristics of donors

Characteristics		Frequency (%)
Sex	Male	54(53.5)
	Female	47(46.5)
Age	Mean ± SD	33.39 ±10.71
	Range	5-56
Age group	≤ 30	40 (39.6)
	> 30	61 (60.4)
sex of donor / recipient	Male/Female	28(27.7)
	Male/Male	26(25.7)
	Female/Female	24(23.8)
	Female/Male	23(22.8)
Blood group	A^+	25(24.8)
	A^-	1(1.0)
	B^+	27(26.7)
	O^+	36(35.6)
	O^-	4(4.0)
	AB^+	8(7.9)
Donor relatives	Sibling	92(91.1)
	Related alternative	9(8.9)

Table 3: Prognostic Factors of overall survival (OS) in patients with AML after

Variable		Survival time	Univariate		Multivariate	
		Mean ± SD (Months)	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Sex	Male	58.06 ± 6.38	0.76 (0.41-1.40)	0.38		
	Female	42.97 ± 4.91	1			
Age group of patients	≤ 30	52.69 ± 6.76	1.11 (0.61-2.04)	0.73		
	> 30	53.98 ± 5.94	1			
Diseases status at transplant	CR1	54.34 ± 4.56	0.69 (0.17-2.87)	0.61		
	CR2	20.52 ± 8.71	1			
WBC (×10^8/ml)	<5	68.94 ± 5.82	1		1	
	5-10	26.00 ± 6.8	2.97 (1.23-7.19)	0.02*	2.76 (1.13-6.72)	0.03*
	>10	22.09 ± 6.77	4.06 (1.88-8.80)	<0.001*	3.98 (1.84-8.63)	<0.001*
Donor relative	Sibling	55.91 ± 4.67	0.48(0.20-1.14)	0.09		
	Related alternative	14.63 ± 4.61	1			
Relapse	Yes	25.11 ± 9.45	2.61 (1.28-5.34)	0.008*	5.66 (2.6-12.34)	<0.001*
	No	57.94 ± 4.79	1		1	
Age group of donors	≤ 30	58.13 ± 6.86	0.82 (0.43-1.54)	0.53		
	> 30	48.15 ± 5.51	1			
Sex of donor - recipient	F-F	47.70 ± 7.11	1.35 (0.58-3.14)	0.48		
	F-M	59.45 ± 9.21	0.91 (0.36-2.32)	0.85		
	M-F	42.27 ± 6.37	1.18 (0.51-2.73)	0.70		
	M-M	57.3 ± 8.28	1			
AML	M3	20.55 ± 7.49	1.15(0.28-4.76)	0.84		
	Non-M3	54.00 ± 4.58	1			
Different types of ALM	M2	34.62 ± 9.11	10.3 (0.13-0.68)	0.04*	0.56 (0.21-1.49)	0.25
	M4	61.24 ± 6.43	1		1	
	M5	56.66 ± 7.89	0.51 (0.23-1.10)	0.09	0.72 (0.32-1.61)	0.42

Acute graft-versus-host diseases (aGVHD), chronic graft-versus-host diseases (cGVHD), first and second complete remission (CR1, CR2)

Table 4: Prognostic Factors of disease-free survival (DFS) in patients with AML after allo-SCT

Variable		Survival time	Univariate		Multivariate	
		Mean ± SD (Months)	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Sex	Male	51.95 ± 6.62	0.91 (0.51-1.64)	0.76		
	Female	42.87 ± 4.94	1			
Age group of patients	≤ 30	50.60 ± 6.79	1.06 (0.59-1.91)	0.84		
	> 30	50.13 ± 6.11	1			
Diseases status at transplant	CR1	51.33 ± 4.63	0.64 (0.15-2.65)	0.54		
	CR2	18.36 ± 9.64	1			
WBC (×10^8/ml)	<5	65.15 ± 5.82	1		1	
	5-10	23.21 ± 6.80	2.9 (1.26-6.67)	0.02*	0.39(0.15-1.00)	0.07
	>10	21.50 ± 6.77	3.57 (1.69-7.56)	0.001*	0.86 (0.28-2.62)	0.05
Donor relative	Sibling	52.73 ± 4.75	0.56 (0.23-1.32)	0.18		
	Non- sibling	14.63 ±4.61	1			
Age group of donors	≤ 30	55.82 ± 6.97	0.82 (0.45-1.52)	0.53		
	> 30	43.88 ± 5.43	1			
Sex of donor - recipient	F-F	41.56 ± 7.17	1.35 (0.58-3.13)	0.48		
	F-M	46.82 ± 9.59	1.28 (0.54-3.0)	0.58		
	M-F	42.36 ± 6.37	1.14 (0.49-2.64)	0.76		
	M-M	57.35 ± 8.39	1			
AML	M3	20.55 ± 7.49	1.15 (0.28-4.76)	0.84		
	Non-M3	50.99 ± 4.46	1			
Different types of ALM	M2	22.03 ± 5.89	0.30 (0.13-0.68)	0.04*	0.43 (0.17-1.11)	0.08
	M4	61.54 ± 6.37	1		1	
	M5	52.84 ± 8.14	0.51 (0.23-1.10)	0.08	0.57 (0.26-1.27)	0.17

Acute graft-versus-host diseases (aGVHD), chronic graft-versus-host diseases (cGVHD), first and second complete remission (CR1, CR2)
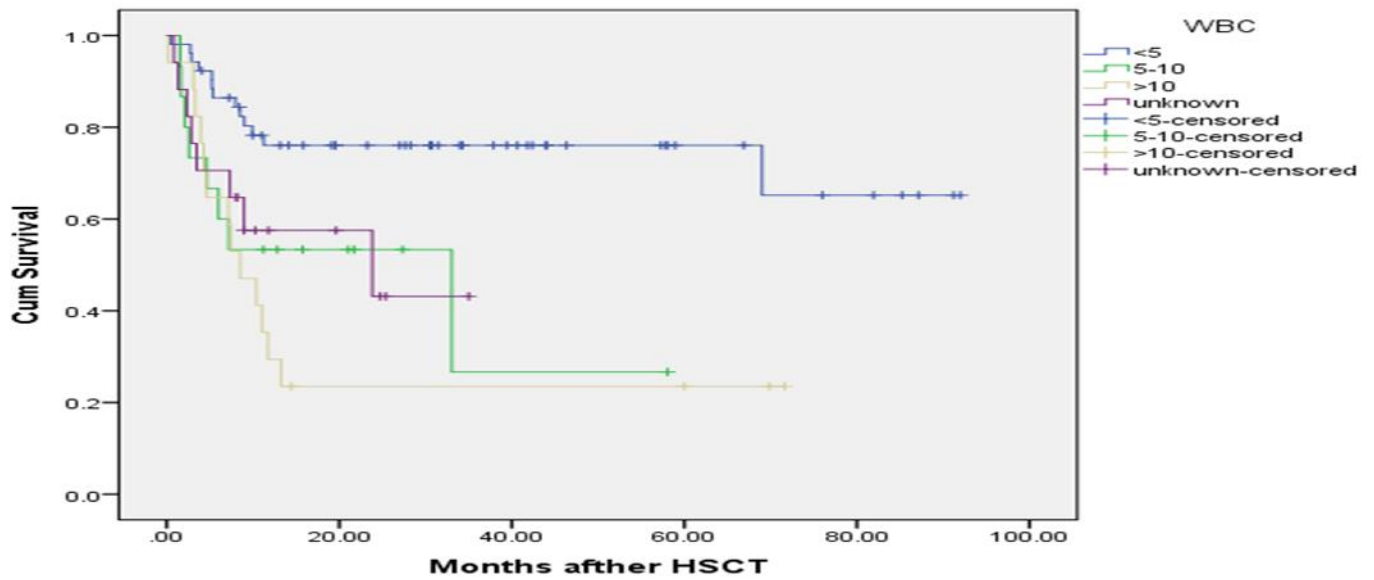
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Figure 1: Kaplan-Meier estimated overall survival of AML patients after allo-SCT according to WBC counts, there was a strong correlation between OS and WBC counts of patients after transplantation (P=0.001), those patients with WBC more than ($10×10^8$/ml), their OS was about 4.06 times shorter than the others.
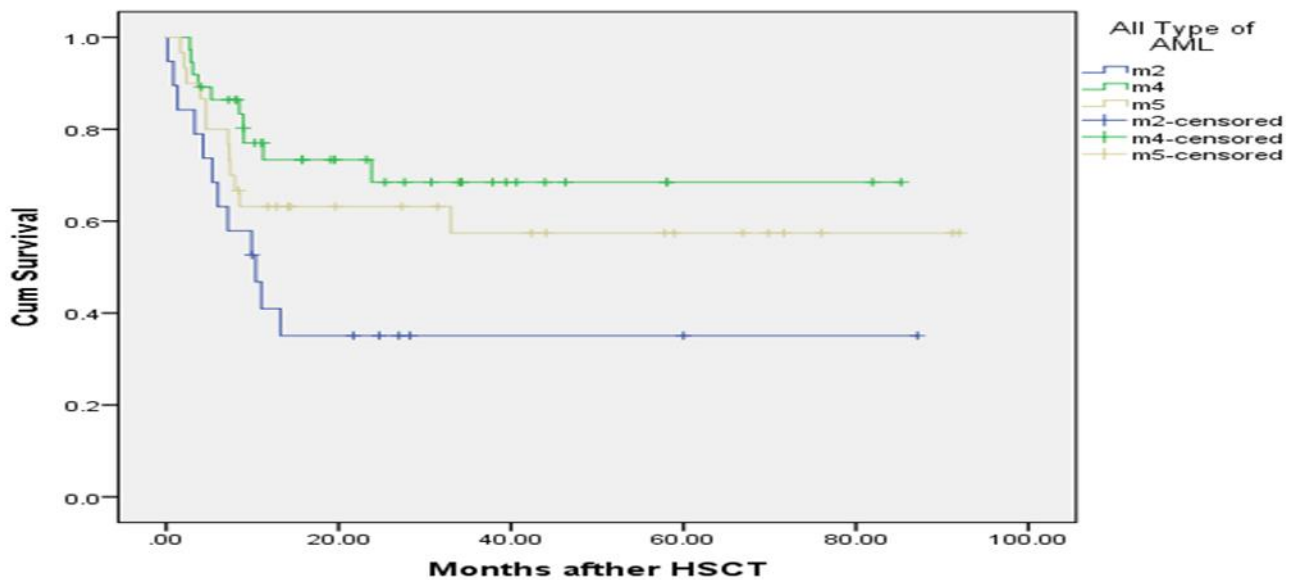

Figure 2 Kaplan-Meier estimated overall survival of AML patients after allo-SCT according to different types of AML (M2, M4 and M5), there was a correlation between OS and the type of AML of patients after transplantation (P=0.02), those patients with AML-M2, their OS was about 10.3 times shorter than the others (AML-M4 and AML-M5).

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DISCUSSION

In the present retrospective cohort study, we studied outcomes of 101 AML patients, who underwent allo-SCT (2009–2016) in CR1 or CR2 to determine the 5-year post-transplant OS, DFS and identify pre and post-transplant factors associated with survival rate. Our results indicated the 5-year post-transplant OS and DFS 56% (95% CI: 51-61%) and 52% (95% CI: 47-57%), respectively. The 5-year survival rate reported in our study is similar to previously reported by Mitus et al.[30] that reported the 5-year OS 55% and 3-year survival calculated by Baron et al. [31] was 54±1%. The results showed that OS and DFS of patients after allo-SCT were reduced with time and the results of the other studies confirm our findings. In a retrospective cohort study by Frazer et al. on 55 AML patients showed 60%, 45.5%, and 37.5% OS at 1, 3, and 5 years post-transplant, respectively [32].

In previous studies, the mean survival time in AML patients who did not have a history of transplantation were reported between 14 and 17 months [33,34.]. While in our study, the mean survival time in AML patients was 53.70 months (95% CI: 44.89-62.51) and for DFS was 50.80 (95% CI: 41.87-59.73). According to the CIBMTR and the NMPD have been reported 65% survival rates in AML patients after stem cell transplantation[16]. Thus, improvement in the survival of AML patients with allo-SCT seems to be similar in our center.

Various studies, including meta-analysis, suggest that allo-SCT in CR1 is the best option for consolidation in high and intermediate-risk patients with AML [21, 35, 36]. In addition, many studies have shown improved OS (in the range of 10% –15% at 5 years) in patients, who underwent allo-SCT in CR1[37,38]. In a retrospective descriptive study by Ganapule et al. on 254 patients with AML who underwent allo-SCT, the 5-year OS for the CR1 and CR2 was 53.1 ± 5.2% and 48.2 ± 8.3%, respectively[36]. The study of Sayehmiri et al. have shown the statistically significant of 5-year survival rates in AML patients at CR1 than CR2 (53% vs. 48.2%, *P*=0.001) [39]. In the present study, majority of patients (97%) received allo-SCT at CR1 and the mean survival time in these patients was (54.34 ± 4.56) months and it is

comparable to rates published in other studies [32, 40]. On the other hand, the mean survival time in patients who received allo-SCT at CR2 in our center was (20.52 ± 8.71) months. However, we observed no statistical significant differences between them (*P*=0.61). It could be due to very low percentage of patients who received the transplant in CR2 (3%).

In the present study multivariate analysis by Cox regression indicated that, OS has significant relationship with WBC count and relapse (*P*=0.001). Multiple studies have shown that the high WBC count at presentation is an unfavorable prognostic factor for treatment outcome in AML patients [41-44]. According to previous studies, our analysis revealed that WBC count had a significant impact on OS and DFS (*P*<0.001) in AML patients. So, our results demonstrate that high WBC count is prognostic factor in patients with AML. AML patients with a WBC count less than $5×10^8$/ml or between $5–10×10^8$/ml had a relatively favorable prognosis with a mean OS of (68.94 ± 5.8) and (26.00 ± 6.8) months, respectively. In contrast, patients with a WBC greater than $10×10^8$/ml evidently had a poor prognosis with a mean OS of (22.09 ± 6.77) months and hazard of death was 3.98 times higher in these patients.

Age of patients at transplant time is another prognostic factor associated with survival[45,46]. Altered disease biology and adverse prognostic cytogenetic are more frequently associated with increased age, and older adults are often unable to tolerate further intensive therapy, and are more likely to be managed supportively [47, 48]. The mean age at transplant time in our population was 32.76 ± 9.23 years (range: 3–53 years). In the current study, 97% of patients were age <40 years at the time of allo-SCT. No significant relationship between age at transplant time and survival was detected (P=0.73) in the study, It might be due to overall young age of study group which is consistent with the similar study by Shokouhi et al. on 587 AML patients with a mean age of 27.27 ± 12.45 years at transplant time[49]. Most studies have shown that people over the age of 60 years are less likely to survive than younger people [50, 51].

AML relapse after allo-SCT predicted poor survival. It remains as a major therapeutic challenge in AML patients. Bejanyan et al. studied outcomes of 1788

AML patients relapsing after allo-SCT (1990–2010) during CR1 or CR2 to identify factors associated with longer post-relapse survival and median time of post-transplant relapse was 7 months (range: 1–177)[40]. A study by the European Blood and Marrow Transplantation (EBMT) group showed cumulative incidence of relapse after allo-SCT 32% ± 1% among AML patients and the longer intervals from transplant to relapse, low bone marrow tumor burden at relapse, and the absence of aGVHD were identified as prognostic factors associated with survival improvement in these patients [52]. Similar to prior reports we observed poor survival following AML relapse after allo-SCT[49,53]. OS had a strong relationship with leukemia recurrence (P<0.001).

CONCLUSION

The results indicate that a hazard of death score in patients who had relapsed was 5.66 times worse than patients who had not relapsed. In conclusion, we conducted this retrospective cohort study to determine the 5-year post-transplant OS, DFS and identify pre and post-transplant factors associated with survival rate. Our results indicated the 5-year post-transplant OS and DFS 56% and 52%, respectively. Multivariate analysis by Cox regression indicated that the WBC count and relapse are effective factors on the chance of survival in AML patients after allo-SCT. Therefore, considering these factors can increase the chance of survival in AML patients. The limitation of this study is that cytogenetic and molecular studies which are the most important prognostic factors in AML patients were not available for most of the patients who referred to us . Patients referred to our center from different part of the countries and cytogenetic study was not available.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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