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Research Article

TO DETERMINE THE INDUCTION-REMISSION RATE IN ADULT PATIENTS OF ACUTE MYELOID LEUKEMIA

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A B S T R A C T

Objective: The purpose of this study was to determine the rate of induction-remission among the patients of Acute Myeloid Leukemia in medical oncology department of the Jinnah Postgraduate Medical Centre, Karachi, Pakistan.

Methodology: This was a cross sectional observational study conducted using convenient sampling technique for seven months, from September 2017 till March 2018 in Oncology ward of Jinnah Postgraduate Medical Centre, Karachi after taking ethical approval. A total of 100 patients, who were admitted in haematology oncology unit diagnosed with acute myeloid leukemia were included in the study. Informed consent was taken from the patients with complete concealment of the data. The demographic data including age, gender and ethnicity of the patients was documented. Complete blood picture and other laboratory investigations included LFT's (Total bilirubin, SGPT, ALT, ALK PO4), uric acid, LDH. The signs and symptoms recorded were fever, bleeding gums, weight loss, hepatomegaly, splenomegaly and lymphadenopathy. Bone marrow biopsy was taken. Remission acquired of AML was recorded. Descriptive analysis was done using SPSS version 20.0

Results: Among the total of 100 AML patients selected for this study, 60 (60%) were male and 40 (40%) were females. Mean age of patients was 31.89 ± 13.79 years. 29 (29%) of patients presented with complains of bleeding gums, 24 (24%) patients experienced weight loss, 12 (12%) patients had hepatomegaly, 7 (7%) patients had splenomegaly, 8(8%) patients had lymphadenopathy, and 53 (53%) of patients had acquired remission while 47 (47%) of patients did not acquire remission. Mean days of follow up were 26.47 ± 32.67 days. Mean level of haemoglobin was 9.94 ± 8.22 mg/dl. Mean level of total leukocyte count was 39.55 ± 57.78 mm3. Mean dose of Daunorubicin was 71.77 ± 8.84 mg and Cytarabine was 142.24 ± 21.71 mg.

Conclusion: The present study predicted that half of the patients acquired remission. A considerable number of patients with acute myelogenous leukemia, still fail toachieve complete remission (CR) with initial remission induction treatment

INTRODUCTION

Acute leukemia is a worldwide disease with an incidence of approximately 4/100000 per year; 70% of the cases are acute myeloid leukemia (AML) [1]. Although acute lymphoblastic leukemia (ALL) predominates in childhood, AML is by far the most common type among adults. The incidence rises steeply after 50 years of age with a median age of approximately 70 years[2]. The salient pathologic feature of AML is the accumulation of immature myeloid blast cells in the bone marrow (BM). This maturation arrest, a characteristic of acute leukemia, prevents normal hematopoiesis and leads directly or indirectly to a lack of differentiated granulocytes (neutrophils, eosinophils and basophils), monocytes, thrombocytes and erythrocytes[3]. AML is characterized by clonal expansion of undifferentiated myeloid precursors, resulting in impaired hematopoiesis and bone marrow failure. Although many

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patients with AML have a response to induction chemotherapy, refractory disease is common, and relapse represents the major cause of treatment failure[4].

AML is a form of cancer that causes infiltration of bone marrow, blood and other tissues by proliferative, clonal, abnormally differentiated, and occasionally poorly differentiated cells of the hematopoietic system[5]. Although the cytogenetic heterogenicity of AML has been recognized for more than 30 years, the enormous molecular heterogenicity of the disease has become increasingly apparent over the past 15 years. The prognostic importance of this biologic heterogenicity is well accepted, but translation of this new information into improved therapy is just beginning [6].

Approximately 20% of adult patients with acute myeloid leukemia (AML) fail to achieve remission with initial induction chemotherapy, and approximately 50% ultimately experience relapse after achieving complete remission[7,8]. Even though potentially curative therapy including allogeneic hematopoietic stem cell transplantation, is now available for many patients, this therapy is expensive and is associated with significant morbidity[9]. Thus, identifying patients at high risk for relapse would be clinically useful and is the basis of current risk stratification approaches, which include conventional karyotyping, clinical features, and the mutational status of a limited panel of genes[10,11].

Genomic approaches have identified somatic mutations in coding genes that are associated with outcomes, however, no study has yet addressed whether mutations in noncoding and regulatory regions may further improve outcome predictions for adults with de novo AML[12]. Furthermore, it is not yet clear whether genomic approaches can be used to assess the clearance of leukemia cells after chemotherapy, which has historically been done by morphologic examination and more recently, by multicolour flow cytometry[13]. The known prognostic value of persistent clonal cytogenetic abnormalities in remission samples which is relevant for the 50%-60% of AML cases with clonal cytogenetic abnormalities at presentation, suggests that higher-resolution genomic approaches that can be applied to all AML samples may provide useful prognostic information[14].The purpose of this study was to determine the rate of induction-remission among the patients on Acute Myeloid Leukemia.

METHODOLOGY

This was a cross sectional observational study through convenient sampling technique conducted for September 2017 till March 2018 in Oncology ward of Jinnah Postgraduate Medical Centre, Karachi. Approval was taken from the Institutional review board of JPMC, Karachi.

A total of 100 patients, who were admitted in haematology oncology unit was selected for the study. Patients diagnosed with acute myeloid leukemia were included in the study. Incomplete data and the patients who did not give informed consent were excluded from the study. Informed consent was taken from the patients with complete concealment of the data. The demographic data including age, gender and ethnicity of the patients was documented. Complete blood picture parameters included haemoglobin, total leucocyte count, blast cells, platelets and peripheral picture. Other laboratory investigations included liver function tests, total bilirubin, SGPT. ALT, ALK PO4), uric acid, LDH. Date and dose of chemotherapy induction was recorded. The signs and symptoms recorded were fever, bleeding gums, weight loss, hepatomegaly, splenomegaly and lymphadenopathy. Bone marrow biopsy was taken. Remission acquired of AML was recorded.

Data Analysis

The statistical software SPSS version 20.0 was used for data analysis. The quantitative data was expressed as mean and standard deviation. Qualitative data was presented as frequency and percentages

RESULTS

Among the total of 100 AML patients selected for this study, 60 (60%) were male and 40 (40%) were females Mean age of patients was 31.89 ± 13.79 years. Mean days of follow up were 26.47 ± 32.67 days. Mean level of haemoglobin was 9.94 ± 8.22 mg/dl. Mean level of total leukocyte count was 39.55 ± 57.78 mm^3. Mean level of platelets was 119.19 ± 130.12 mm^3. Mean % of blast cells was 45.74 ± 23.89 %. Mean level of total bilirubin was 1.11 ± 1.08 mg/dl. Mean SGPT was 37.44 ± 21.05 IU/L. Mean ALT was 90.51 ± 141.27 IU/L. Mean ALP was 147.20 ± 99.94 IU/L. Mean level of uric acid was 4.52 ± 4.29 mg/dl. Mean LDH level was 155.73 ± 65.21 U/L. Mean urea level was 28.98 ± 17.96 mg/dl. Mean level of creatinine was 1.06 ± 1.28. Mean dose of Injection Daunorubicin was 71.77 ± 8.84 mg. Mean dose of Injection Cytarabine was 142.24 ± 21.71 mg.(Table:1)

Table 1 Mean and standard deviation of age, follow up days and laboratory values

Variables		Frequency	Percent (%)
Gender	Male	60	60
	Female	40	40
	Total	100	100
Ethnicity	Sindhi	36	36
	Pushto	30	30
	Balochi	11	11
	Urdu	17	17
	Hazara	6	6
	Total	100	100

Among ethnicity, 36 (36%) of the patients were Sindhi, 30 (30%) were Pushto, 17 (17%) were Urdu speaking, 11(11%) were Baloch and 06 (6%) patients were from Hazara. (Table:2).

Table 2 Demographic representation of AML patients

Variables		Frequency	Percent (%)
Gender	Male	60	60
	Female	40	40
	Total	100	100
Ethnicity	Sindhi	36	36
	Pushto	30	30
	Balochi	11	11
	Urdu	17	17
	Hazara	6	6
	Total	100	100

29 (29%) of patients presented with complains of bleeding gums, 24 (24%) patients experienced weight loss, 12 (12%) patients had hepatomegaly, 7 (7%) patients had splenomegaly, 8 (8%) patients had lymphadenopathy.(Table:3). 53 (53%) of patients had acquired remission while 47 (47%) of patients did not acquire remission. (Figure: 1)

Table 3 Frequency of symptoms among AML patients

Variables	Yes	No
	n (%)	n(%)
Gum Bleed	29 (29%)	71 (71%)
Weight Loss	24 (24%)	76 (76%)
Hepatomegaly	12 (12%)	88 (88%)
Splenomegaly	07 (7%)	93 (93%)
Lymphadenopathy	08 (8%)	92 (92%)

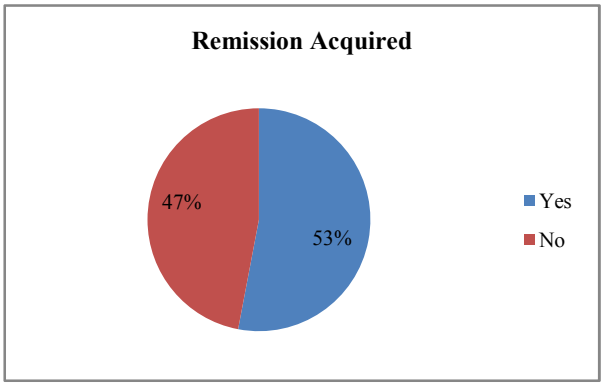

Table 1 Frequency of remission among AML patients

DISCUSSION

In our study of 100 AML patients among which 60 (60%) were males and 40 (40%) were females, the overall induction-remission acquiring rate was 53 (53%). The most common clinical feature experienced by the patients was bleeding gums, present in 29 (29%) of patients and 24 (24%) patients experienced weight loss. Similar acquisitions of induction-remission have been observed in other studies. In a study by Naseer *et al*., among their 42 patients with AML followed up for a period of 5 years, 56% of patients developed induction remission with 44% patients failing treatment. Among their 32 treated patients, 6 (18%) had post induction death due to sepsis and bleeding gums [15]. In another study by Brown *et al*., in which among their 55 adult patients of AML, after chemotherapy achieved a remission rate of 32 (58%) and 23 (42%) patients had failure of treatment [16].A study by Stringaris *et al*., showed that from the total of 32 patients in their study, 14 (44%) of patients had complete remission of AML wile 18 (56%) of patients had either induction failure/partial remission/supportive care only[17]. In contrast to our study, Serna *et al*., which included 792 patients of AML on chemotherapy were found to have a induction-remission failure in 66 (9%) of patients. As compared to this study our study had 53% induction-remission failure[18].Low socio-economic strata, poor supportive care and non-availability of bone marrow transplantation facility in countries like Pakistan causes increased rate of treatment failure among the patients. High risk patients have always had an increased tendency of having failure of treatments. Non-complaint patients also play a part in failing of treatment.In a study by Lee JH *et al* on 383 AML patients it was reported that 275 (72 %) of patients on Daunorubicin had induction-remission failure and 316 (82.5%) patients developed induction-remission failure who were on Cytarabine. In their study, 206 (54%) were males and 177 (46%) females. Majority of the patients were above 40 years old i.e. 223 (58%). Majority of patients, 223 (58%) had normal hemoglobin. The most common adverse event experienced by the patients were Infection, by 291 (76%) of patients followed by Metabolic derangements by 81 (21%) of patients[19]. In our study, mean age was 31.89 years of the patients with 53 % of patients having acquired induction-remission. Mean hemoglobin of our patients was 9.9 gm/dl. Most common adverse event experienced by our patients was bleeding gums, by 29 (29%) of patients followed by weight loss, by 24 (24%) of patients.Another study by Fernandez HF *et al* showed that in 657 AML patients on chemotherapy, 376 (57.3%) of patients developed induction-remission failure, that were on Daunorubicin and 463 (70.6%) of patients on Cytarabine developed induction-remission failure [20].

It has been widely recognized that most treatment failures are due to death during induction from infection and hemorrhage. With recent advances in chemotherapy and supportive care, it is again important to estimate how many initial induction failures result from inherent resistance to chemotherapy andhow many result from fatal infection and/or hemorrhage before chemotherapy can achieve CR. Determination if pretreatment characteristics can identify patients at increased risk of a given fatalcomplication on of having refractory disease would allow alternate chemotherapeutic regimens to be given to those likely to be resistant to standard treatment and different approaches to supportive care to be explored in those patients most likely to benefit from them. Furthermore, if specific periods of high risk could be identified, optimal supportive cane could be given atthe most appropriate time [21].

CONCLUSION

The present study predicted that half of the patients acquired remission. A considerable number of patients with acute myelogenous leukemia, still fail toachieve complete remission (CR) with initial remission induction treatment

References

1. Döhner H, Weisdorf DJ, Bloomfield CD. Acute myeloid leukemia. *New England Journal of Medicine*. 2015 Sep 17;373(12):1136-52.
2. Yang JJ, Park TS, Wan TS. Recurrent Cytogenetic Abnormalities in Acute Myeloid Leukemia. Methods in molecular biology (Clifton, NJ). 2017;1541:223-45.
3. Arber DA. Acute Myeloid Leukemia 11. Atlas of Bone Marrow Pathology. 2018 Jan 17:173-91
4. Papaemmanuil E, Gerstung M, Bullinger L, Gaidzik VI, Paschka P, Roberts ND, *et al*. Genomic classification and prognosis in acute myeloid leukemia. *New England Journal of Medicine*. 2016 Jun 9;374(23):2209-21.
5. Saultz JN, Garzon R. Acute myeloid leukemia: a concise review. *Journal of clinical medicine*. 2016 Mar 5; 5(3):1-17
6. Medinger M, Lengerke C, Passweg J. Novel prognostic and therapeutic mutations in acute myeloid leukemia. Cancer Genomics-Proteomics. 2016 Sep 1;13(5):317-29.
7. Döhner H, Estey E, Grimwade D, Amadori S, Appelbaum FR, Buechner T, *et al*. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. *Blood*. 2017;129(4):424-47.
8. Shihadeh F, Reed V, Faderl S, Medeiros LJ, Mazloom A, Hadziahmetovic M, *et al*. Cytogenetic profile of patients with acute myeloid leukemia and central

nervous system disease. *Cancer*. 2012 Jan 1;118(1):112-7.
9. Feldman EJ, Gergis U. Management of refractory acute myeloid leukemia: re-induction therapy or straight to transplantation?. *Current hematologic malignancy reports.* 2012 Mar 1;7(1):74-7.
10. Wouters BJ, Delwel R. Epigenetics and approaches to targeted epigenetic therapy in acute myeloid leukemia. *Blood*. 2016 Jan 7;127(1):42-52.
11. De Kouchkovsky I, Abdul-Hay M. Acute myeloid leukemia: a comprehensive review and 2016 update. *Blood cancer journal*. 2016 Jul;6(7):441:1-8
12. Chen X, Xie H, Wood BL, Walter RB, Pagel JM, Becker PS, Sandhu VK, *et al*. Relation of clinical response and minimal residual disease and their prognostic impact on outcome in acute myeloid leukemia. *Journal of Clinical Oncology*. 2015 Mar 2;33(11):1258-64.
13. Loken MR, Alonzo TA, Pardo L, Gerbing RB, Raimondi SC, Hirsch BA, Ho PA, *et al*. Residual disease detected by multidimensional flow cytometry signifies high relapse risk in patients with de novo acute myeloid leukemia: a report from Children's Oncology Group. *Blood*. 2012 Aug 23;120(8):1581-8.
14. Inaba H, Coustan-Smith E, Cao X, Pounds SB, Shurtleff SA, Wang KY, *et al*. Comparative Analysis of Different Approaches to Measure Treatment Response in Acute Myeloid Leukemia. *Journal of Clinical Oncology*. 2012 Sep 10;30(29):3625-32.
15. Naseer M, Kanvinde P, Bhutada S, Mudaliar S, Agrawal B. Acute myeloid leukemia: Correlation of cytogenetics and outcome in resource limited setting. *Pediatric Hematology Oncology Journal*. 2017 Dec 31;2(2):17-8.
16. Brown FC, Cifani P, Drill E, He J, Still E, Zhong S, *et al*. Genomics of primary chemoresistance and remission induction failure in paediatric and adult acute myeloid leukaemia. *British journal of haematology*. 2017 Jan;176(1):86-91.
17. Stringaris K, Sekine T, Khoder A, Alsuliman A, Razzaghi B, Sargeant R, *et al*. Leukemia-induced phenotypic and functional defects in natural killer cells predict failure to achieve remission in acute myeloid leukemia. *Haematologica*. 2014 May 1;99(5):836-47.
18. de la Serna J, Montesinos P, Vellenga E, Rayón C, Parody R, León A, *et al*. Causes and prognostic factors of remission induction failure in patients with acute promyelocyticleukemia treated with all-trans retinoic acid and idarubicin. *Blood*. 2008 Apr 1;111(7):3395-402.
19. Lee JH, Joo YD, Kim H, Bae SH, Kim MK, Zang DY, *et al*. A randomized trial comparing standard versus high-dose daunorubicin induction in patients with acute myeloid leukemia. *Blood*. 2011 Oct 6;118(14):3832-41.
20. Fernandez HF, Sun Z, Yao X, Litzow MR, Luger SM, Paietta EM, *et al*. Anthracycline dose intensification in acute myeloid leukemia. *New England Journal of Medicine*. 2009 Sep 24;361(13):1249-59.
21. Estey EH, Keating MJ, McCredie KB, Bodey GP, Freireich EJ. Causes of initial remission induction failure in acute myelogenousleukemia. *Blood*. 1982 Aug 1;60(2):309-15.

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