

## FREQUENCY OF REMISSION AFTER TREATMENT WITH HYPER CVAD PROTOCOL IN NEWLY DIAGNOSED PATIENTS OF ACUTE LYMPHOBLASTIC LEUKEMIA PRESENTING TO JINNAH HOSPITAL LAHORE

### ABSTRACT:

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**OBJECTIVE:** The objective of this study was to determine the frequency of complete and partial remission after 2 courses of hyper CVAD regimen in newly diagnosed patients of acute lymphoblastic leukemia (ALL).

**MATERIAL AND METHODS:** This study was conducted on 100 patients of ALL presenting to the oncology department of Jinnah Hospital, Lahore and fulfilling the inclusion criteria from 01-01-2016 to 30-12-2016. Patients were undergone treatment with hyper CVAD regimen according to the standard protocol. Complete or partial remission rate was checked after 2 session of hyper CVAD regimen. CT scan (chest and abdomen) was performed for confirmation of extramedullary disease.

**RESULTS:** The mean age of study population was  $35.68 \pm 8.69$  years. There were 48% male patients while female patients were 52%. Complete remission was present in 72% patients. Partial remission was present in 24% patients. There was no significant association between complete remission and age ( $p$ -value=0.497). No significant association was found between partial remission and age ( $p$ -value=0.103). Significant association was found between partial remission and complete remission with gender having  $p$ -value=0.001 and 0.01 respectively.

**CONCLUSION:** The frequency of complete and partial remission after 2 courses of hyper CVAD regimen in newly diagnosed patients of ALL was 72% and 24% respectively. Effect modifiers have no significant influence except gender.

**KEYWORDS:** Acute Lymphoblastic Leukemia, Complete and Partial Remission, Hyper CVAD.

### INTRODUCTION:

Acute lymphoblastic leukemia (ALL) alludes to a gathering of hematopoietic neoplasms including cells focused on the lymphoid heredity. Philadelphia chromosome positive ALL ( Ph+ALL) is a naturally and clinically unmistakable variation of ALL delegated with t(9;22) (q34;q11.2); BCR-ABL1 in the WHO arrangement system<sup>[1]</sup>. Ph+ALL represents around 20 to 30 percent of ALL in adults and 2 to 3 percent of ALL in youngsters<sup>[2,3]</sup>. At the point when treated with chemotherapy alone, patients with Ph+ALL have a consistently poor anticipation with couple of survivors at five

years after treatment. Allogeneic hematopoietic cell transplantation (allo-HCT) gives better outcomes, relieving around 30 to 60 percent of patients with Ph+ALL. The fuse of BCR-ABL1 tyrosine kinase inhibitor (eg, imatinib, dasatinib) into the treatment regimen has brought about unrivaled remission rates, thereby enabling more patients to continue to

(allo-HCT) It is not yet known whether treatment with chemotherapy in addition to a tyrosine kinase inhibitor will give durable long haul abatements and preferable survival over allo-HCT. The treatment of Ph+ALL is particular from that of different sorts of ALL and involves a few phases that, altogether, may traverse three years of treatment.

More than 80 percent of adult patients with Ph+ALL will accomplish a total abatement (CR) with acceptance chemotherapy that joins a tyrosine kinase inhibitor. Not with standing, without extra cytotoxic treatment, for all intents and purposes these patients will backslide inside half a month or months in spite of proceeding with tyrosine kinase inhibitor. Conversely, patients who get post-induction treatment may expect five-year survival rates of 40 to 60 percent. Post-induction treatment incorporates an about allo-HCT or the continuation of chemotherapy in addition to tyrosine kinase inhibitor.

More than 90 percent of adult patients with Ph+ALL will achieve a hematologic finish remission (CR) with acceptance chemotherapy that joins a tyrosine kinase inhibitor (TKI). In any case, without extra cytotoxic treatment, for all intents and purposes these patients will backslide inside fourteen days or months. In contrast, patients who get post-induction therapy may expect five-year survival rates of 40 to 60 percent<sup>[4]</sup>.

Autologous HCT permits the utilization of myeloablative chemotherapy and isn't related with GVHD, yet does not furnish the GVL impact seen with allogeneic HCT. Treatment related dismalness and mortality are generally low ( $\leq 6\%$ ). Auto-HCT following imatinib-or dasatinib containing acceptance treatment yields a promising sub-atomic reduction, and individual long haul survivors have been depicted<sup>[5,6]</sup>.

Non-myeloablative chemotherapy has a low treatment related death rate ( $< 5\%$ ). Significant adverse reactions are commonly present and incorporate pancytopenia, hepatic debilitation, and neuropathy. Before the availability of TKIs, patients with Ph+ALL had a consistently poor anticipation with couple of survivors at five years after treatment with chemotherapy alone

[7-14]

## **METHODOLOGY:**

This cross sectional study was conducted on 100 patients of ALL, presenting to the oncology department of Jinnah Hospital, Lahore and fulfilling the inclusion criteria from 01-01-2016 to 30-12-2016. Information regarding their demographic data was noted in the proforma. Patients underwent treatment with hyper CVAD regimen according to the standard protocol. Complete or partial remission rate was checked after 2 session of hyper CVAD regimen. All patients undergone complete blood count after taking 3ml of blood sample under aseptic technique along with CT scan (chest and abdomen) for confirmation of extramedullary disease. They were also undergone bone marrow biopsy and examination by consultant histopathologist and results were noted in the proforma as well. Confidentiality of the data was ensured.

## **RESULTS:**

From 100 patients, it was observed that the minimum age was 20 years and maximum age was 50 years with mean and standard deviation of the age was  $35.68 \pm 8.69$  years. There were 48% male patients while female patients were 52%. Complete remission was present in 72% patients while complete remission was not present in 28% patients ( $p=0.001$ ) in table-I. Partial remission was present in 24% patients while partial remission was not present in 76% patients ( $p=0.01$ ) in table-II. By applying chi-square test, there is no significant association between complete remission and age having  $p$ -value=0.497 It observed that significant association is not found between partial remission and age having  $p$ -value=0.103. There is significant association between complete remission and gender having  $p$ -value=0.001 in table-I, also with partial remission with gender having  $p$ -value=0.01 in table-II.

**Table-I: Distribution of patients by complete remission (n=100)**

Gender	Complete remission		Total
	Yes	No	
Male	31	17	48
Female	41	11	52
<b>Total</b>	72	28	100

$\chi^2=16.3$  P-value=0.001

**Table-II: Distribution of patients by partial remission (n=100)**

Gender	Partial remission		Total
	Yes	No	
Male	14	34	48
Female	10	42	52
<b>Total</b>	24	76	100

$\chi^2=12.1$  P-value=0.01

## DISCUSSION:

In our investigation the mean age was  $35.7 \pm 8.7$  years. There were 48% male and 52% female patients. Finish reduction (CR) was available in 72% patients. Halfway abatement was available in 24% patients. As indicated by the investigation of Terwilliger et al<sup>[15]</sup> Acute lymphoblastic leukemia (ALL) is the second most acute leukemia in grown-ups, with an occurrence of more than 6500 cases for every year in the United States alone. In grown-ups, 75% of cases create from antecedents of the B-cell genealogy, with the rest of cases comprising of dangerous T-cell forerunners. Generally, chance stratification has been founded on clinical factors such as age, white platelet check and reaction to chemotherapy; in any case, the recognizable proof of intermittent hereditary changes has refined individual guess and guide the executives<sup>[15]</sup>.

In an investigation led in Iran, three hundred and one patients experienced changed hyper-CVAD chemotherapy regimen. Finish reduction and in general survival (OS) rates were estimated as essential endpoints. About 81.7% achieved finish abatement amid the initial a half year of treatment<sup>[16]</sup>.

Past examination demonstrated that 34% patients were determined to have ALL, and included 53% males and 47% females with a mean age of 34 years. Acceptance

chemotherapy with healing expectation was managed to 94% patients. Twenty-seven patients got intrathecal chemotherapy as prophylaxis (n=24) or as treatment for CNS involvement (n=3). Twenty-eight patients (82%) accomplished finish abatement (CR) after enlistment chemotherapy. The median survival (OS) time was 22 months and the five-year OS for ALL patients was 38%. The median disease free survival (DFS) time was a year, while the five-year DFS was 38%. Multivariate investigation demonstrated that age <40 years, WBC <30×10<sup>9</sup>/L, accomplishment of CR after first acceptance, and CNS prophylaxis were prescient components for OS and DFS<sup>[17]</sup>.

In another examination, 185 patients (91%) accomplished finish reduction (CR) and 12 (6%) kicked the bucket amid enlistment treatment. Evaluated 5-year survival and 5-year CR rates were 39% and 38%, individually. The frequency of CNS backslide was low (4%). Contrasted and 222 patients treated with vincristine, doxorubicin, and dexamethasone (VAD) regimens, our patients had a superior CR rate (91% v 75%, P <0.01) and CR rate after one course (74% v 55%, P <0.01) and better survival (P<0.01), and a littler rate had over 5% day 14 impacts (34% V 2.48%, P=0.01). Hyper-CVAD treatment is better than our past regimens and ought to be contrasted and set up regimens in grown-up ALL<sup>[18]</sup>.

## CONCLUSION:

The achievement of finish (CR) and incomplete reduction (PR) after 2 courses of hyper CVAD regimen in recently analyzed patients of Acute lymphoblastic leukemia was 72% and 24% separately. Impact modifiers have no noteworthy impact with the exception of gender.

## CONFLICT OF INTEREST:

There is no declared conflict of interest.

## ETHICAL REVIEW COMMITTEE:

Ethical review committee of the said institute has reviewed and approved this article.

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