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The Study of Management of Acute Lymphoblastic Leukemia

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Abstract

This study was conducted to analyze the management of Acute Lymphoblastic leukemia, which is a chronic disease. Total 15 cases were collected from Oncology Ward in North West General Hospital Peshawar. Maximum cases were reported from developed cities, such as Peshawar and Kabul. Complete blood count, bone marrow aspiration, triphene biopsy, cytogenetics and flowcytometry are used for the detection of Acute Lymphoblastic leukemia. Cases were collected randomly from patient medication file of each ward of Oncology North West General Hospital Peshawar during one month. The result of this study revealed the intensity of Acute Lymphoblastic leukemia in Peshawar (46.6%), (26.6%)cases from Kabul, and (26.8%)cases were reported

from other areas. The research show the prevalence of Acute Lymphoblastic leukemia which was 3:2 in male and female. This indicates that the level of Acute Lymphoblastic leukemia was high in the district Peshawar than maximum permissible level due to Ethnicity, race, genetics and environmental conditions. The cause and ideal treatment for Acute Lymphoblastic leukemia are still under research.

INTRODUCTION

Acute lymphoblastic leukemia and lymphoblastic lymphoma constitute a family of genetically heterogeneous lymphoid neoplasms derived from B- and T-lymphoid progenitors. ALL (Acute lymphoblastic leukemia) starts in the bone marrow (these of tinner part of certain bones, where new blood cells are made). Most often, the leukemia cells invade the blood quickly. They can also sometimes spread to other parts of the body, including the lymph nodes, liver, spleen, central nervous system (brain and spinal cord), and testicles (inmales). Some cancers can also start in the organs and then spread to the bone marrow, but these cancers are not leukemia (Zanette, Rivadavia et al. 2007).

Most ALL (Acute lymphoblastic leukemia) cases occur in children, with an incidence of 3 to 4/100,000 in patients 0to14 years of age and1/100,000 in patients older than15 years. In children, ALLs represent 75% of all acute leukemia's (which in turn represent 34% of all cancers in this age group),with a peak incidence at 2 to 5years of age. This percentage is much lower in adults, in whom acute myeloid leukemia's (AMLs) and chronic lymphocytic leukemia common (Hoffman, Benz Jr et al. 2013)

The clinical onset of ALL (Acute lymphoblastic leukemia) is most often acute, although a small percentage of cases may evolve insidiously over several months. The presenting symptoms and signs correlate with the leukemic cell burden and the degree of marrow replacement, leading to cytopenias (Uckun, Sather et al. 1997, Onciu 2009)

There are several types of leukemia, which are divided based mainly on whether the leukemia is acute (fast growing) or chronic (slower growing), and whether it starts in myeloid cells or lymphoid cells. Knowing thes pecific type of leukemia helps doctors better predict each person' sprognosis (outlook) and select the best treatment. (Rehman, Abbaset al. 2018)

Acute lymphocytic leukemia (ALL) can cause many different signs and symptoms. Most of these occur in all kinds of ALL, but some are more common with certain subtypes of ALL (Uckun, Sather et al. 1997.Hoffman, Benz Jr et al. 2013).

Leukemia cells may build up in the liver and spleen, making them larger. This might be notice dasafullness or swelling of the belly, or feelingfull after eating only a small amount. The lower ribs usually cover these organs, but when the organs are enlarged the doctor can feel them (Uckun, Sather et al. 1997.Hoffman, Benz Jr et al. 2013)

ALL that has spread to lymph nodes close to the surface of the body(such as on the sides of the neck, in the groin, or in underarm areas), might be noticed as lumps under the skin. Lymph nodes inside the chest or abdomen may also swell, but these can be detected only by imaging tests such as CT or MRI scans (Benz Jret al. 2013).

Sometimes leukemia cells build up near the surface of the bone or inside the joint, which can lead to bone or joint pain (Hoffman, Benz Jr et al. 2013). A morphological bone marrow assessment represents the first step in the diagnostic pathway, for the primary diagnosis of ALL and for the differentiation from acute myeloid leukemia (AML) To confirm a diagnosis of acute lymphoblastic leukaemia, the haematologist will take a small sample of your bone marrow to examine under a microscope (Kawasaki,Clarketal. 1988).

METHODOLOGY

The histories of medical record were collected during clinical pharmacy clerkship at Northwest general hospital, Peshawar. The data are collect from different patient, which admitted in oncology ward at Northwest general hospital, Peshawar. The current research of acute lymphoblastic/lymphocytic leukemia on hospitalized patients was conducted in the oncology Ward at Northwest general hospital, Peshawar. The data were collected on the prescribed Performa designed By the Department of Pharmacy, Sarhad University Peshawar Pakistan. It comprises of patient demographic data, laboratory data, chief complaints, diagnosis, prescribed medication, non-prescribed medication, patient complaints and patient counseling, adverse effects and medication toxicity from the present therapy in leukemic patients. After the collection of data/case histories according to the prescribed Performa designed for the acute lymphoblastic leukemia patients, it was screened properly in order to find out the irrational use of

medications/therapy, drug interactions and with special emphasis on Adverse drug reactions. The data were properly tabulated according to different parameter, which includes male to female ratio,risk factors concurrent ailments, main adverse effects, their percentage and others as the case maybe. Then it was analyzed by applying possible statistical approaches such as descriptive analysis, tabulated tools. Before joining the hospital for the clerkship, we were trained by our supervisor that how to collect the patient medical history. All the information and questions to be asked are summarized in a Performa. I collected the data according to the instructions.

Duration and Date of Collection

The duration of histories collection was 45 days. The data collected during clinical pharmacy clerkship started from July 2022 to August 2022.

Excluding Criteria for Data Collection

Pregnant women, all patient with final stages of cancer disease. Patient with diabetic ketoacidosis, patient having age of less than 2 years and patient having complication like Down Syndrome

Including Criteria

All patient recently suffer from acute lymphocytic /lymphoblastic leukemia, precursor B or T lymphocytic/lymphoblastic leukemia, patient which are admitted in hospital for the management of ALL, patient age of above 2 years and below 100 year are included.

Data Collection

Total 20 cases of ALL has been collected in order to accomplish the objectives of this report. Following data were collected:

a) Patient's identification and demographics information
b) Chief Complaints (CC)
c) History of present illness(HOPI)
d) Past medical history
e) Personal history
f) Medication history
g) Other relevant histories
h) Findings on physical examination
i) Laboratory test results

j) Diagnosis

k) Treatment provided at hospital

Data Analysis

a) Medication histories were analyzed for drug allergies, response to previous medications, adverse effects, compliance and any other relevant point.

b) Hospital based treatment was analyzed for indications and outcomes.

c) Drug Therapy was reviewed for dosage appropriateness.

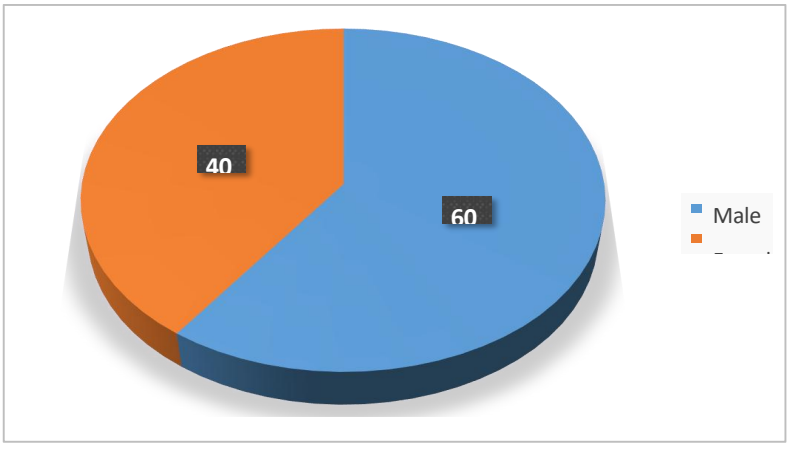
d) Drugs prescribing patterns, patients' signs/symptoms and laboratory profiles; and activities related to patient education and counseling was reported

RESULTS

Gender Wise Distribution Of Patient

Study was conducted on total 15 patients of Acute Lymphoblastic Leukemia attended in Oncology ward of North West general hospital Peshawar in the month of august and September. Management of ALL in different sex, as shown in fig.1, the management of ALL is more in male as compared to female. In 15 patients, a sum of 9 were male and the rest of 6 were female patients. In terms of percentage, ALL is found in 60% male and 40% female.

Figure1: Gender wise distribution of patient



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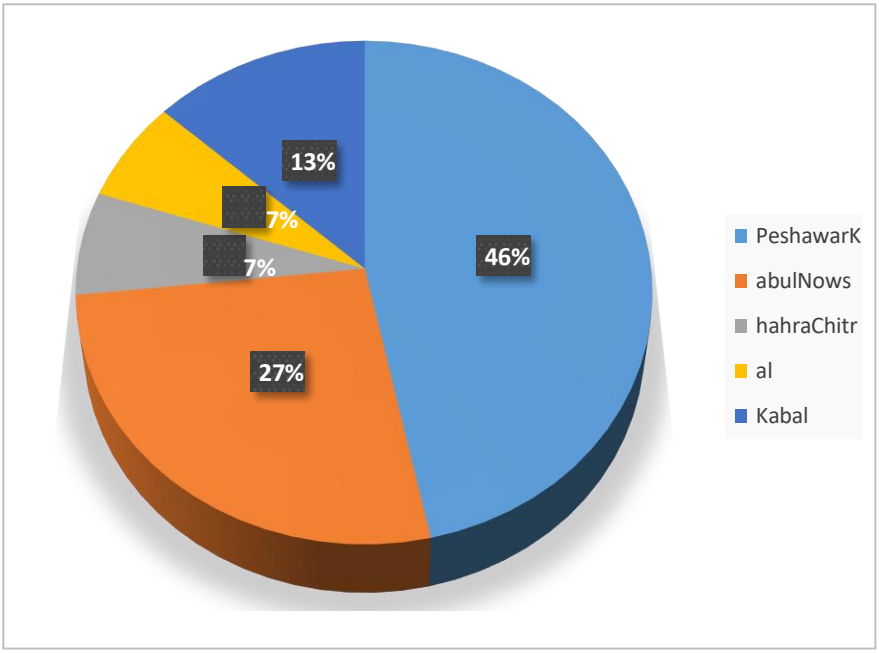

Figure 2: Area wise distribution

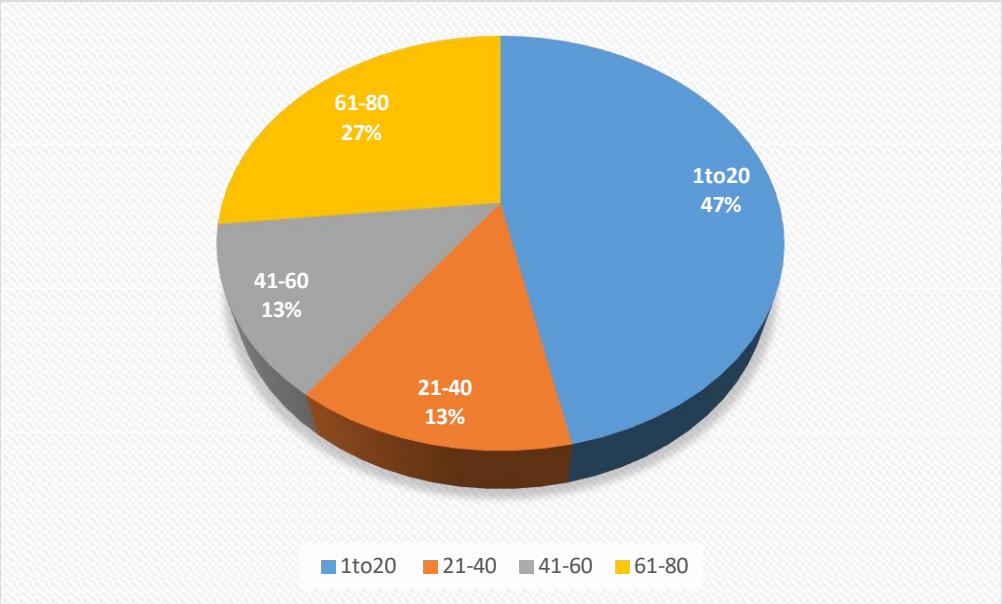

Figure 3: Age wise distribution

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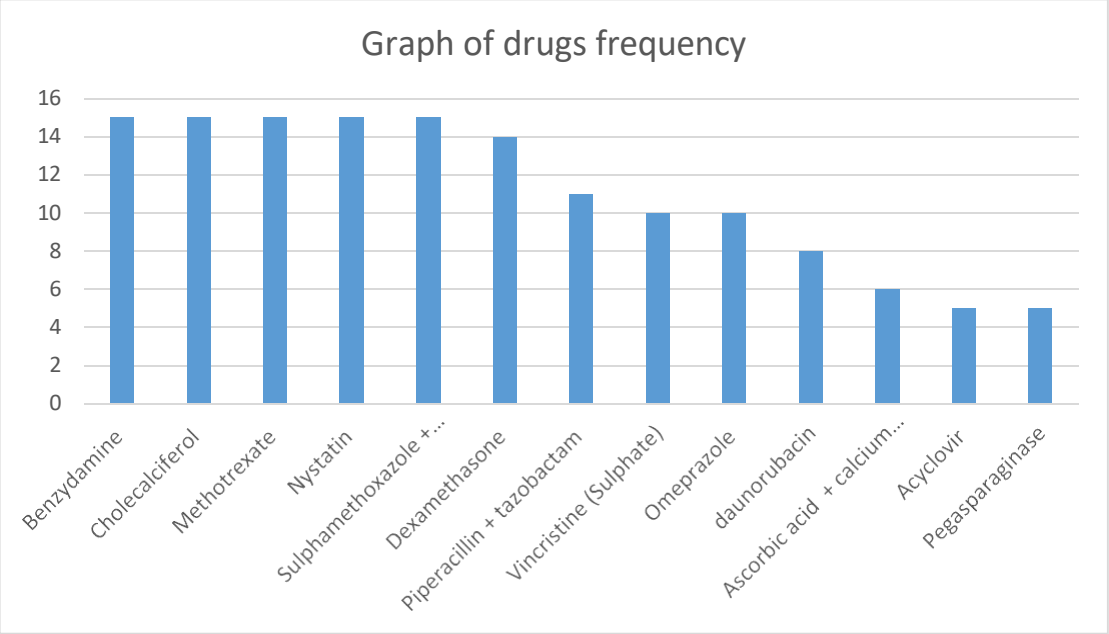

Figure 4 : Graph Of Drugs Frequency

S.No	Drug interaction	Interaction type	Effectsand management
1	Piperacillin/Tazobactam, Methotrexate	Major	Concomitant use of large doses ofpenicillinsmayelevateserum methotrexate concentrations.
2	Methotrexate,Amoxicillin / Clavulanate	Major	Concomitant use of large doses ofpenicillinsmayelevateserum methotrexate concentrations.
3	Methotrexate, Omeprazole	Major	Coadministration with proton pump inhibitors (PPIs) may increase the serum concentrations of methotrexate (MTX)anditspotentiallyactive 7-hydroxy metabolite

4	Methotrexate, Sulfamethoxazole	Moderate	Sulfonamide antibiotics may potentiate the toxicities of methotrexate, possibly by interfering with the plasma protein binding and/or renal clearanceofmethotrexateandits toxic metabolite
5	Methotrexate, Daunorubicin	Moderate	The concomitant or sequential administration of multiple antineoplastic agents may result in additive toxicities, particularlyinthebonemarrow andgastrointestinaltract
6	sulfamethoxazole-trimethoprim	Minor	Limited data suggest that sulfamethoxazole-trimethoprim (SMX-TMP)mayrarelyprolong the Q interval of the electrocardiogram. Theoretically, coadministration with other agents that can prolongtheQTintervalmay result in additive effects and increased risk of ventricular arrhythmiasincludingtorsadede pointes and sudden death
7	Methotrexate, Omeprazole	Major	Coadministration with proton pump inhibitors (PPIs) may increase the serum concentrations of methotrexate (MTX)anditspotentiallyactive 7-hydroxy metabolite.

8	Ondansetron,Tramadol	Major	Concomitant use of 5-HT3 receptor antagonists with tramadol may potentiate the risk of serotonin syndrome and/or reduce the analgesic efficacy of tramadol. Serotonin syndrome has been reported with both 5- HT3 receptor antagonists and tramadol, and combined use of thesedrugsmayincreasetherisk of this rare but serious and potentially fatal condition.
9	Paracetamol (Acetaminophen), Methotrexate	Moderate	Coadministration of methotrexate with other agents known to induce hepatotoxicity may potentiate the risk of liver injury
10	lidocaine, midazolam	Moderate	Using midazolam together with lidocaine can increase nervous system side effects such as dizziness, drowsiness, and confusion.
11	Methotrexate, Dexamethasone	Moderate	Although they are often used together in clinical practice, limited data suggest that corticosteroidsmayincreasethe riskofmethotrexate toxicity
12	Methotrexate, Vincristine	Moderate	Coadministration of methotrexate with other agents known to induce hepatotoxicity aypotentiatetheriskofliver injury.

13	Lidocaine,Trimethoprim	Major	Local anesthetics such as lidocaine may cause methemoglobinemia, a rare conditionthatcanleadtooxygen deprivation in tissues and vital organs due to reduced oxygen- carrying capacity of the blood. The risk is increased when combined with other medicationsthatcanalsoinduce methemoglobinemiasuchas trimethoprim
14	Dexamethasone,Vincristine	Moderate	Combining thesemedications May reduce the blood levels and effects of vincristine.
15	Methotrexate, Cytarabine	Moderate	Coadministration of Methotrexatewitho ther agents knowntoinducehepatotoxicity, such as cytarabine, may potentiatethe risk of liver injury
16	Methotrexate,(Pegaspargase)	Moderate	Pegaspargase may reduce the effects of methotrexate in the treatment of some conditions.
17	Dexamethasone, Levofloxacin	Major	Concomitant administration of corticosteroids may potentiate the risk of tendinitis and tendon rupture associated with fluoroquinolone treatment.The mechanism is unknown.

Table 1: Drug-drug interactions and its types

S.No	Conditions	NO OFCASES	TOTAL CASES	%AGE
1	elevatedUricacid	1	15	6.7%

2	Throathyperemicand mildlycongested	1	15	6.7%
3	Bruisingon legs	1	15	6.7%
4	FebrileNeutropenia	1	15	6.7%
5	Diabetes mellitus	1	15	6.7%
6	Hypertension	1	15	6.7%
7	Dyslipidemia	1	15	6.7%
8	Albumin++	2	15	13.3%
9	Bilateral subconjunctival haemorrhages	1	15	6.7%
10	Non-neutropenicfever	1	15	6.7%

Table2 :percentage of Co morbidity found in patient along with current disease

DISCUSSION

ALL represents approximately less than 1% of adult cancers, and 25% of all childhood cancers. In the USA, among all ages, it represents less than 0.4% of all cancers, 13.6% of all leukemias, and 29.6% of all lymphocytic leukemias. Age-adjusted incidence rates for ALL vary several-fold, internationally, with the highest rates occurring in Spain, among Hispanicsin Los Angeles, and in Caucasians in Quebec and Ontario,Canada, and in New Zealand. The lowest rates are found in developing countries, among US blacks, Israeli Jews, Chinese and Asian Indians, whose rates may be many times lower than those in more developed countries (Wartenberg et al., 2008)

Incidence rates for total leukemia, and to a lesser extent for ALL, are higher among males than among females, and this gender difference is considerably more pronounced among whites (70% more leukemia in males and 60% more ALL in males) than among blacks (30% and 15%, respectively) (Wartenberg et al.,2008). However, this study showed the prevalence of ALL is more in male as compared to female. In 15 patients, asum of 9 were male and the rest of 6 were female patients. In terms of percentage, ALL is found in 60% male and 40% female. In the USA, for leukemia, for males, females, and all

combined, whites have higher incidence rates than blacks (30–40% excess), and this same pattern is seen even more strongly forALL(85–215%excess). A similar pattern is seen form or tality in that context as well (Wartenberg et al., 2008). Here in Northwest General hospital the ratio of patient from Peshawar was greater as compared to other developing areas including Afghanistan (Kabul) from Peshawar 7 or 46.6%,from Kabul 4 or 26.6%, fromNowshera1or6.6%,

From chitral1 or6.6%, and from Kabal 2 or13.3%respectively.

In the United States (USA) Leukemia incidence increases from birth through age 3, then decreases until about age 50, when rates begin to increase slowly. ALL incidence rates increase more dramatically from birth to age 3 (up to more than 9 cases per 100000 per year), drop off to lower level suntila boutage 50 (less than1 per 100000 per year), and then Increases lightly, but never approach the rates observed between ages 1 and 14 Similar rise has been detected during the study of cases in Northwest General hospital in which distribution by age wise,7 patient cases were having age of 1-20 years which make 46.6%. 2 patients were having age of 21-40 years making 13.3%.2 patients were having age of 41-60 years making13.3%.4 patients were having Age of 61-80 years making 26.6%

CONCLUSION

According to the data collected during the clinical clerk ship in Northwest General hospital Peshawar, the management of Acute Lymphoblastic/Lymphocytic Leukemia was performed in better way in which the medication were based on rational therapy and patients were hemodynamically stabilized during the course of chemotherapy .During data collection, it was concluded that the male are slightly more prominent in developing ALL as compared to female; however, the effect of the chemotherapy and management ratio were same between both genders. During the course of this study, it was concluded that the age of the patient had greater influence on the therapy and children of age 1-14 showed more effective management through chemotherapy compared to the patients above 20 years. It was concluded that the patients were treated according to UK ALL protocol 2011, in which the patients lower than age 10 having highest white cell count received Regimen A induction chemotherapy which consisted of a group of 3 drugs. The elder patients having low WCC were treated

according to Regimen Binduction chemotherapy, which consisted of a 4 drugs including Asparaginase. It was concluded that the overall procedure have least involvement of pharmacist for the dilution, dose calculation and drug-drug interaction of chemotherapeutic agents.

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