Original article

Prevalence of Acute and Chronic Forms of Leukemia in Various Regions of Khyber Pakhtunkhwa, Pakistan: Needs Much More to be done!

Shujaat Ahmad1, Kifayatullah2, Kiramat Ali Shah3, Haya Hussain4, Anwar Ul Haq5, Abid Ullah6, Asaf Khan7, Najm Ur Rahman8

Abstract:

Background and objective: Leukemia is one of the fatal diseases and their morbidity and mortality rates increases day by day all over the world. This piece of research study was designed in order to find out the prevalence of different types of leukemia in Khyber Pakhtunkhwa, Pakistan during January 2015 to December 2016. Material and Method: The retrospective research study was carried out at Institute of Radiotherapy and Nuclear Medicine (IRNUM) Peshawar. A data of 400 admitted patients of leukemia were evaluated. Result: It was observed that acute leukemia (80%) was more prevalent than chronic leukemia (20%). Amongst types of leukemia, Acute Lymphocytic Leukemia (ALL) 49.5% (n=198) was more prevalent than Acute Myelogenous Leukemia (AML) 31.25% (n=125), Chronic Myelogenous Leukemia (CML) 10% (n=40) and Chronic Lymphocytic Leukemia (CLL) 9.25% (n=37) was less prevalent in this study. It was also found that leukemia was more prevalent in male patients 64.5% (n=258) as compared to females 35.5% (n=142) and male to female ratio was 1.8:1. Most of the patients were under the age of 20 years. Conclusion: Acute leukemia was more prevalent than chronic leukemia during this study in this part of the country and needs to be address. Keywords: Leukemia; ALL; AML; CML; CLL; Khyber Pakhtunkhwa

Introduction:
The word leukemia literally means malignancies of white blood cells; a case rarely developing from red blood cells precursors, erythroleukemia, also called Di-Guglielmo’s disease1. ALL is the most common malignancy diagnosed in children. It is clinically and morphologically heterogeneous2. Morphologically, it is classified according to FAB (French, American and British) criteria into L-1, L-2 and L-3 sub-types, which are clinically reproducible3. Bone marrow aspiration with trephine biopsy is used as a standard for diagnosis of leukemia4. Currently, there is limited data regarding the prevalence of different types of acute leukemia in northern part of Pakistan5. At present, there are no cancer registry programs in Pakistan which can keep a track and notify regarding the prevalence and incidence of leukemia, because Pakistan is an Asian country and cancer is becoming a serious health issue, being the leading cause of death in Asia Pacific countries4. The incidence of leukemia across the world is 1 per 100,000 per year and contributes to 25% of childhood cancers5. Most common types of leukemia are; ALL, AML, CML and CLL. ALL and AML are further characterized

1. Shujaat Ahmad, Email: razmianbutterfly@gmail.com
2. Kifayatullah, Email: ullahkifayat0@gmail.com
3. Kiramat Ali Shah, Email: qazikiramat3366@gmail.com
4. Haya Hussain,
5. Anwar Ul Haq, Email: anwar@sbbu.edu.pk
6. Abid Ullah, Email: abid@sbbu.edu.pk
7. Asaf Khan, Email: hafizsbbu@gmail.com
8. Najm Ur Rahman, Email: najm@sbbu.edu.pk

Department of Pharmacy, Shaheed Benazir Bhutto University, Sheringal Dir (Upper), Pakistan

Correspondence to: Haya Hussain Email: haya@sbbu.edu.pk
into subtypes based on French American British (FAB) classification. Acute myeloid leukemia is primarily a cancer of adults and acute lymphoblastic leukemia is more prevalent in children under 15 years of age. The chronic leukemias distinguished from acute leukemia by their slower progression. Acute and chronic adult leukemia are a heterogeneous group of disorders. They are also an uncommon form of malignancy affecting approximately 5 persons per 100,000 in the United States annually. Hematological malignancies, especially leukemia and non-Hodgkin’s lymphoma are common in South-East Asia than in the U.S.A. and Europe. Leukemia is one of the most frequently occurring cancers in all races or ethnicities with relative proportion vary between 25-40%. In 2013, males have been accounted for more than 57% of the new cases of leukemia. High incidence of subtypes of leukemia in males was due to more exposed to occupational and environmental carcinogens. It further states that every 4 minutes, one person in the United States is diagnosed with a blood cancer. The second largest contributor to mortality from childhood cancer in Britain is leukemia, whereas in India, leukemia continues to be the largest contributor to cancer related mortality in children. ALL, the most common cancer diagnosed in childhood, with higher incidence for white than for black. Bone marrow aspiration of leukemia patients shows >20% blast cells. The mean age for CLL is greater than 50 years and the male to female ratio is 2:1. The illness seems to occur in 0.8 new cases per 100,000 persons per year in Brazil. Twice as many men as women are affected by CLL. Due to lack of information and sufficient work in this field and its significances to the development of health of the community and importance to the socioeconomic aspect for the development of the nation, this piece of research project was therefore designed to investigate the prevalence of different types of leukemia in various residential areas of Khyber Pakhtunkhwa, Pakistan. This data was collected at Institute of Radiotherapy and Nuclear Medicine (IRNUM) Peshawar which is the only recognized cancer hospital in this province and people frequently visits here for treatment.

**Patients and methods:**
A retrospective study was carried out in IRNUM Hospital Peshawar and 400 leukemic patients were treated during 2015-16. In 2015, 175 patients were treated and 225 patients were treated in 2016. The medical records were taken from the record room and patients were classified as suffering from acute or chronic form of leukemia on the basis of examining peripheral blood and bone marrow aspiration records as well as according to percentage of blast cells and premature cells.

**Study design:**
Retrospective research study was conducted with in-patients.

**Study population:**
The record charts of hospitalized patients diagnosed with leukemia as the source of research data.

**Inclusion criteria:**
The data collected from those hospitalized patients who were treated from January 2015 to December 2016.

**Exclusion criteria:**
Patients diagnosed with leukemia who stay less than 3 days in the hospital were excluded from this study.

**Data collection:**
The data was collected on a special proforma designed by the Department of Pharmacy Shaheed Benazir Bhutto University Sheringal Dir (Upper), Pakistan, consists of parameters regarding patients’ age, gender, date of admission, bed number, ward number, address, hospitalization time, chief complaints, medication history, biochemical tests, type of leukemia and address of the patients. FAB classification of acute leukemia was applied for subtyping.
Data analysis

The collected data was analyzed using Microsoft XL and Prisms Graph pad.

Ethical Issues:

Ethical clearance was obtained from UITH Ethical Research Committee. Written permission was also obtained from Department of Pharmacy, Shaheed Benazir Bhutto University, Sheringal Dir (Upper), Pakistan. A signed informed consent was obtained from every participant before being recruited.

Results:

In this piece of research study 400 leukemia patient’s data was evaluated containing 64.5% (n=258) and 35.5% (n=142). The data has been divided according to age group and sex (Table 1), most of the patients were children of age ≤ 10 years 38% (n=152) and 15.5% (n=70) of age group 11-20 years. 15% (n=60) patients lye in the age group 21-30 years while the others were mostly adults ones as shown in the (Table 1). The male to female ratio is 1.8:1. It is evident from the data that leukemia is more prevalent in younger patients.

Table 1: Distribution of patients according to Age and Sex

| Age group in years | Male | Female | Total n (%) |
|--------------------|------|--------|-------------|
| 0-10               | 108  | 44     | 152 (38)    |
| 11-20              | 45   | 25     | 70 (17.5)   |
| 21-30              | 40   | 20     | 60 (15)     |
| 31-40              | 20   | 16     | 36 (09)     |
| 41-50              | 19   | 15     | 34 (8.5)    |
| 51-60              | 14   | 03     | 17 (4.25)   |
| 61-70              | 08   | 07     | 15 (3.75)   |
| 71-80              | 03   | 08     | 11 (2.75)   |
| 81-90              | 01   | 04     | 05 (1.25)   |
| Total              | 258 (64.5 %) | 142 (35.5 %) | 400 (100)    |

The current research study has showed that acute leukemia is more prevalent than chronic leukemia and more common in male as compared to female patients. AML is prevalent 31.25% (n=125) and their male to female contribution is 18.7% (n=75) and 12.5% (n=50) respectively. CML has 10% (n=40) prevalent and common in male 6.25% (n=25) and 3.75% (n=15) in female individuals. ALL has 49.5% (n=198) prevalent which is more common amongst all types of leukemia and 32.5% (n=130) in male and 17% (n=68) in females patients. CLL contributed 37% (n=9.25) in which male patients suffered 7% (n=28) and female 2.25% (n=9) as given in the Table 2 and Figure 2.

Table 2: Distribution of patients according to Types of Leukemia

| Type of Leukemia | Male n (%) | Female n (%) | Total n (%) |
|------------------|------------|--------------|-------------|
| AML              | 75 (18.7)  | 50 (12.5)    | 125 (31.25) |
| CML              | 25 (6.25)  | 15 (3.75)    | 40 (10)     |
| ALL              | 130 (32.5) | 68 (17)      | 198 (49.5)  |
| CLL              | 28 (7.0)   | 09 (2.25)    | 37 (9.25)   |
| Total            | 258 (64.5 %) | 142 (35.5 %) | 400 (100)   |

According to the relation of leukemia with respect to age groups, it is evident that 38% (n=152) leukemia is prevalent in age group ≤ 10 years comprising AML 6.75% (n=27), ALL 31.25% (n=125). 17.5% (n=70) leukemia lye in the age group 11-20 years in which AML 6.50% (n=26), CML 1% (n=4) and ALL 10% (n=40) contributed. It is 15% (n=60) in the age group of 21-30 years having AML 6.25% (n=25), CML 2.5% (n=10) and ALL 6.25% (n=25). In the age group 31-40 years AML 4.25% (n=17), ALL 2% (n=8) are prevalent. In this piece of research study AML and ALL are mostly prevalent in young age group populations while CML and CLL are prevalent in adult age group populations as shown in the Table 3.
Table 3: Distribution of patients of different types of leukemia in relation to age groups

| Age group in years | AML n (%) | CML n (%) | ALL n (%) | CLL n (%) | Total n (%) |
|--------------------|-----------|-----------|-----------|-----------|-------------|
| 0-10               | 27 (6.75) | 00 (0.00) | 125 (31.25)| 00 (0.00) | 152 (38)    |
| 11-20              | 26 (6.50) | 04 (1.00) | 40 (10.00)| 00 (0.00) | 70 (17.5)   |
| 21-30              | 25 (6.25) | 10 (2.50) | 25 (6.25)| 00 (0.00) | 60 (15)     |
| 31-40              | 17 (4.25) | 05 (1.25) | 08 (2.00)| 06 (1.50) | 36 (9.0)    |
| 41-50              | 20 (5.00) | 03 (0.75) | 00 (0.00)| 11 (2.75) | 34 (8.5)    |
| 51-60              | 05 (1.25) | 04 (1.00) | 00 (0.00)| 08 (2.00) | 17 (4.25)   |
| 61-70              | 04 (1.00) | 00 (0.00) | 00 (0.00)| 11 (2.75) | 15 (3.75)   |
| 71-80              | 01 (0.25) | 05 (1.25) | 05 (1.25)| 05 (1.25) | 11 (2.75)   |
| 81-90              | 00 (0.00) | 00 (0.00) | 05 (1.25)| 00 (0.00) | 05 (1.25)   |
| Total              | 125 (31.25)| 40 (10)   | 198 (49.5)| 37 (9.25) | 400 (100)   |

Due to the near territories across the border most of the peoples from Afghanistan visit this hospital for cancer treatment and during this study 11.25% (n=45) Afghan peoples have one or more types of leukemia followed by leukemic patients from Bajaur Agency 8.75% (n=35), then Mardan and Peshawar 7.50% (n=30), Karak 6.75% (n=27), Kohat 6.25% (n=25) and 5.75% (n=23) patients from Mohmand Agency have been diagnosed with leukemia. Other regions includes Kurram Agency 2.25% (n=9), Charsada 5% (n=20), Orakzai Agency 1.25% (n=5), Dir Upper 3.75% (n=15), Dir Lower 3% (n=12), Swat 4.5% (n=18), Shangla 2% (n=8), Malak and 2.5% (n=10), Nowshehra 5% (n=20), North Waziristan 5.25% (n=21), Swabi 6.5% (n=26), Khyber Agency 3% (n=12) and 2.25% (n=9) leukemia patients were from Chitral district (Table 4).

Table 4: Area wise prevalence of leukemia patients treated at IRNUM Hospital

| Area                  | N | %  |
|-----------------------|---|----|
| Afghanistan           | 45| 11.25|
| Bajaur agency         | 35| 8.75 |
| Mardan                | 30| 7.50 |
| Peshawar              | 30| 7.50 |
| Karak                 | 27| 6.75 |
| Swabi                 | 26| 6.50 |
| Kohat                 | 25| 6.25 |
| Mohmand Agency        | 23| 5.75 |
| North Waziristan      | 21| 5.25 |
| Nowshehra             | 20| 5.00 |
| Charsada              | 20| 5.00 |
| Swat                  | 18| 4.50 |
| Dir Upper             | 15| 3.75 |
| Khyber Agency         | 12| 3.00 |
| Dir Lower             | 12| 3.00 |
| Malakand              | 10| 2.50 |
| Kurram Agency         | 09| 2.25 |
| Chitral               | 09| 2.25 |
| Shangla               | 08| 2.00 |
| Orakzai Agency        | 05| 1.25 |

Figure 3: Percentage prevalence of Leukemia in various regions of Khyber Pakhtunkhwa

Discussion:
Leukemia represents 31% of all cancer cases occurring among children younger than 15 years of age21. Acute leukemia is one of the most common cancers with about 20,000 cancer diagnoses and over 10,000 annual deaths in the United States22. The current study showed that acute leukemia is more prevalent than chronic leukemia in Khyber Pakhtunkhwa province including both sides of tribal areas across Pak Afghan border from January 2015 to December 2016. This piece of research study revealed that ALL (49.5%, n=198) is more common in children as earlier research studies reported that ALL suffered children more than adults in the past23. This study also revealed that ALL is more common and more prevalent under the age of 10 years than AML (31.25%, n=125). ALL is the most common pediatric malignancy. It represents 25% of all childhood cancers and approximately 75% of all cases of childhood leukemia19. There has been a gradual increase in the incidence of ALL in the past 25 years20. In the current study CLL is more common in adult patients and contributed 9.25% (n=37) of the total (n=400) leukemia patients as CLL is consider leukemia of old age population and more prevalent above 60 years and uncommon below 40 years of age24. This piece of research study indicated that CML
has suffered only 10% (n=40) patients and common above 20 years of age and found more frequently in adult patients as median age limit for CML has been suggested to be 40-50 years. The incidence of leukemia varies with age and gender. In our present study, the prevalence of leukemia is more common in males than females as similar to the findings of Shabbir, 2011. The reason may be linked to the life style, habits like smoking, occupation, contact with different chemicals and radiations other than genetic factors. Present study showed male to female ratio 1.8:1, which is similar as reported by Khalil et al. This piece of research study demonstrated the prevalence of leukemia in various regions of Khyber Pakhtunkhwa province including in some percentage of peoples from Afghan territories across the Pak Afghan border (Table 4 and Figure 3). It is essential weather the prevalence of leukemia in this study is representative of the whole country, if not, then similar study should be conducted to find out the overall prevalence of leukemia in Pakistan.

**Conclusion:**
The outcome of this research project shows that acute leukemia was more prevalent than chronic leukemia in the Khyber Pakhtunkhwa province of Pakistan. ALL was more common and more prevalent in young age male population of this part of the country followed by AML, CML and CLL. It is suggested that a proper policy regarding awareness and treatment of leukemia may be constituted to decrease the incidence as well as decrease the cost of cancer therapy throughout the country.

**Conflict of interest:** The authors declare no conflict of interest.

**Authors’ Contribution:**
Data gathering and idea owner of this study: Haya Hussain, Shujaat Ahmad, Kifayatullah
Study design: Kiramat Ali Shah, Haya Hussain, Anwar Ul Haq, Abid Ullah
Data gathering: Haya Hussain, Asaf Khan, Najm Ur Rahman
Writing and submitting manuscript: Shujaat Ahmad, Haya Hussain
Editing and approval of final draft: Haya Hussain, Anwar Ul Haq
References:
1. Rudden RW. Cancer biology: Oxford University Press, 2nd ed., 1987.
2. Jemal A, Siegel R, Xu J, Ward EJ. Cancer statistics 2010. CA Cancer J Clin 2010; 60: 277-300. https://doi.org/10.3322/caac.20073
3. Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DA, Gralnick HR. Proposals for the classification of the acute leukemias. French-American-British (FAB) co-operative group. Br J Haematol. 1976; 33: 451-58. https://doi.org/10.1111/j.1365-2141.1976.tb03563.x
4. Weinkauff R, Estey EH, Starostik P, Hayes K, Huh YO, Hirsch-Ginsberg C. Use of peripheral blood blasts vs bone marrow blasts for diagnosis of acute leukemia. Amer J Clin Pathol. 1999; 111: 733-740. https://doi.org/10.1093/ajcp/111.6.733
5. Hamayun M, Khan SA, Muhammad W. Investigation on the prevalence of leukemia in North West Frontier Province of Pakistan. Turk J Cancer. 2005; 35: 119-122.
6. Park S, Bae J, Nam HB, Yoo KY. Aetiology of cancer in Asia. Asian Pac J Cancer Prev. 2008; 9: 371-380.
7. Cartwright RA. Epidemiology: In: Leukaemia (ed. J.A. Whittaker), p3-33, Blackwell Scientific Publications, Oxford, 1992.
8. Johnson LE. Chronic lymphocytic leukemia. Practical Therapeutics. 1988; 38: 167-176.
9. Cranfield T, Bunh C. Acute leukemias. Med Int. 1995; 9: 503-508.
10. Pakistan Medical Research Council. Report of multicentre study on malignant rumors. Islamabad, PMRC, 1982; 5-7.
11. Mc Phedran P, HealthCW, Garcia JS. Racial variations in leukemia incidence among the elderly. J Natl Cancer Inst. 1970; 45: 25-29.
12. Sandler DP. Epidemiology of acute leukemias. Seminars in Oncology. 1987; 14: 359-368.
13. Arora RS, Eden TOB, Kapoor G. Epidemiology of childhood cancer in India. Indian J of Cancer. 2009; 46: 264-273. https://doi.org/10.4103/0019-509X.55546
14. Cancer Facts & Figures. Atlanta GA. Amer Cancer Soc. 2013.
15. Kumar A, Rathee R, Vashist M, Kamal N., Singh S, Gupta S. Acute Lymphocytic Leukemia: An epidemiological and hematological study from Haryana. Biosci Biotech Res Asia. 2012; 9: 813-817. https://doi.org/10.13005/bbra/1069
16. Leukemia and Lymphoma Society. USA (2010). Facts 2010-2011, p1-25.
17. Ross JA, Davies SM, Potter JD, Robison LL. Epidemiology of childhood leukemia, with a focus on infants. Epidemiol Rev. 1994; 16: 243-272. https://doi.org/10.1093/oxfordjournals.epirev.a036153
18. Hoelzer D, Gale RP. Acute lymphoblastic leukemia in adults: recent progress, future directions. Semin Hematol. 1987; 24: 27-39.
19. Greenlee RT, Murray T, Bolden S, Wingo PA. Cancer Statistics. CA Cancer J Clin. 2000; 50: 7-33. https://doi.org/10.3322/canjclin.50.1.7
20. Shah A, Coleman MP. Increasing Incidence of Childhood Leukemia: a controversy Re-examined. Br J Cancer. 2007; 97: 1009-1012. https://doi.org/10.1038/sj.bjc.6603946
21. U.S. Cancer Statistics Working Group. United States Cancer Statistics: 2000 Incidence; Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute: Atlanta GA, 2003.
22. Cutler SJ, Young JL, Connelly RR. Third national cancer survey: incidence data, US Dept. of Health, Education, and Welfare, Public Health Service, National Institutes of Health, National Cancer Institute, 1975.
23. Reaman G, Zeltzer P, Bleyer WA. Acute lymphoblastic leukemia in infants less than one year of age. J Clin Oncol. 1985; 3: 1513-1521. https://doi.org/10.1200/JCO.1985.3.11.1513
24. Pakkala S, Koeffler HP. Cancer treatment. 11th ed. 1993; 1082-1088.
25. Richman CM, Rowley JD, Golomb HM. Chronic granulocytic leukemia epidemiology and etiology, pathogenesis, cytogenetics, in vitro studies & clinical features. In: Hematology-leukemia London: Butterworths International Medical Reviews. 1984; 208-224.
26. Moss P. Chronic Leukemia. Med Int. 1995; 9: 509-513.
27. Shabbir A. Childhood cancers. J Rawalpindi Med Coll. 2011; 15: 38-39.
28. Khalil Ullah, Ahmed P, Raza S, Satti TM. Management of acute myeloid leukemia—5 years’ experience at Armed Forces Bone Marrow Transplant Centre, J Pak Med Assoc. 2007; 57: 434-439.