ORIGINAL ARTICLE

PATTERN OF LEUKAEMIA PATIENTS ADMITTED IN AYUB TEACHING HOSPITAL ABBOTTABAD

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Background: Any tissue of the body can give rise to cancer. However, those tissues which multiply rapidly are at high risk of developing cancer and haematopoietic system is one of them. Neoplasms of this system are known as leukaemia and lymphoma, according to the types of white cells involved. Study of cancer patterns in different societies, however can contribute a substantial knowledge about the aetiology of cancer. The present Study was designed and aimed to estimate the frequency of different types of leukaemia in patients admitted in Ayub Teaching hospital Abbottabad. **Methods**: Data from the patients admitted at oncology Department of Ayub Teaching Hospital Abbottabad from 2010 to 2015 was collected and analysed to calculate cumulative and year-wise frequency of leukaemia and its major types. Frequency distribution with reference to gender and age was also calculated. **Results**: In our analysis about 16% patients had acute myelocytic leukaemia and 32% patients had acute lymphocytic leukaemia; while chronic myeloid leukaemia outnumbered chronic lymphocytic leukaemia (11% and 3%); Hodgkin lymphoma was seen in 18% cases while Non Hodgkin lymphoma (NHL) was present in 20% cases. Out of the total, 150 cases (75%) belonged to mountainous areas of Hazara, i.e., 40 cases belonged to Kohistan, another 40 cases were residents of Battagram, 45 cases belonged to hilly areas of Mansehra and 25 cases to Kaghan valley, while only 50 (25%) cases were from the plain areas of Abbottabad and Haripur districts, i.e., 20 and 30 cases respectively. **Conclusion**: Leukaemia is more common in hilly areas of Hazara, since majority of the cases belonged to well-known mountainous regions of Kohistan, Battagram, Kaghan or Mansehra and only few cases belonged to the plain areas of Abbottabad and Haripur districts.

Keywords: leukaemia, lymphoma, myeloid leukaemia, lymphoid leukaemia
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INTRODUCTION

In the United States of America, cancer is the second leading cause of death; however, physical and emotional sufferings inflicted by these malignancies are even more agonizing. In 2008, there were about 1,450,000 new cases diagnosed and about 565,000 deaths from cancer, showing 23% of the total mortality rate in the residents of United States.[1] Leukaemia, clinically the most important disorder of white cells, arise from uncontrolled, clonal proliferation and production of abnormal cells of haematopoietic system recognized by Virchow.[2] It is caused by cancerous mutation of myelogenous or Lymphogenous type of white cells, known as Myelocytic or Lymphocytic leukaemia (Lymphoma) according to its origin, either in bone-marrow or lymphoid tissue.

In children, Acute Lymphocytic Leukaemia (ALL) is the most common subtype, representing more than 80% of acute leukaemias.[3] Genetic abnormalities that lead to genomic defects such as; Bloom syndrome, Fanconi's anaemia, & Ataxia telangiectasia are at more risk of acute leukaemia; e.g., Down syndrome and Neurofibromatosis are associated with childhood leukaemia.[4] The most commonly occurring leukaemia in the United States are Hodgkin and Non-Hodgkin lymphoma, about 100,000 new cases being diagnosed yearly.[5] Non-Hodgkin lymphoma is the second fastest growing cancer in terms of the mortality, now representing about 4–5% of all the new cases of leukaemia.[6] Lymphoma is the third most frequent malignancy among children,, representing 15% of the all paediatric malignancies with 1700 new cases diagnosed each year.[7] Leukaemia is not a very uncommon malignancy in Pakistan. A study carried out in Northern Areas of Pakistan revealed that leukaemia is the second most common malignancy in males and third one in the females.[8] Idris *et al* reported that myeloid leukaemia is the commonest type of haematological Malignancy in Hazara division.[9] A similar study conducted in Northern Pakistan also revealed that leukaemia is the second most common cancer in males and third one in the females.[10]

Hazara Region is located in the Khyber Pakhtunkhwa (KPK) province of Pakistan. However, due to insufficient medical facilities and lack of

health awareness in Hazara, treatment is either very difficult or impossible when it is diagnosed at a very advanced stage. The present Study was aimed and designed to estimate the frequency of different types of leukaemia in patients admitted in Ayub Teaching Hospital, KPK and also to observe any association with predisposing epidemiological factors, specifically in mountainous areas.

MATERIAL AND METHODS

It was a hospital based descriptive case series, carried out at the Oncology Department of Ayub Teaching Hospital Abbottabad (ATH), which is almost the sole recipient of patients from all over the region. The study was conducted from 2010 to 2015. Data on study variables was collected from the patients admitted in Oncology Department of ATH during the study period. During this research hundreds of patients were seen but only those who fulfilled the criteria set for the study were included for further procedure.

Two hundred leukemic cases of all ages, ethnic groups and both genders were admitted during the study period. The cases of any age, both genders and permanently resident by birth of Hazara Division were included. Patients belonging to Hazara division but lived out of the area for many years were excluded from the study. All patients having non–neoplastic Haematopoietic diseases, specifically Leucocytosis, Leucopoenia, thrombocytopenia, drug and infection- induced Neutropenia were excluded.

The required haematological investigations were carried out at the laboratory of Ayub Medical Institution Abbottabad. Cumulative and year wise frequency of different types were calculated for both males and females. A detail history was taken from every patient, including history of the present and past illness, particularly any drug intake prescribed by quacks and any blood transfusion. Socioeconomic history was taken in detail to know whether the patient would be able to afford the treatment. Every patient was interviewed in detail regarding common signs and symptoms observed by him or her, mode of onset and duration of the disease. Each patient was also examined, including general physical/systemic examination and signs especially anaemia, fever and bleeding tendency etc. were observed. The diagnosis was based on the clinical history and laboratory investigations with particular emphasis on haematological and histological findings.

All patients underwent investigations including CBC, TLC, DLC, Hb estimation, platelet and reticulocyte count, blood film examination, bone marrow aspiration and cytochemistery. While peripheral smear, blood urea, glucose, electrolytes, liver function tests, x-ray chest, HbsAg, HCV anti DNA antibodies were also determined in specific cancers, wherever required. Hb estimation was done by Sahli's method, while TLC, DLC and platelet count by visual method. Weight was measured in kg, blood pressure as mm of mercury, temperature in centigrade. Geiasma stain was used to prepare blood film for examination of cell morphology. Posterior iliac spine in adults and tibia in the children was aspirated for routine bone marrow examination, iron stain and cytochemistery. Wherever the bone marrow aspirate was inadequate trephine biopsy was performed. Each subject was briefed and assured about the safety and confidentiality of the personal data and test procedure.

Data was analysed using SPSS version 20. Quantitative variables were explained as Mean and standard deviation, whereas categorical variables were described as frequencies and percentages. To know significant differences between groups with regard to quantitative variables, t-test was used and for the same differences between categorical variables chi-square test was performed. A $p \leq 0.05$ was considered as statistically significant.

RESULTS

A total of two (200) hundred cases of leukaemia were admitted in the Oncology ward from 2010 to 2015. Out of these 120 cases fulfilled the inclusion criteria and were included in the study.

Distribution of 120 cases with respect to hilly and plain areas of Hazara is shown in table-1. Among 120 cases, males were 78 (67%) and females were 42(33%). With regard to age groups, 40 (33.4%) were children less than 16 years with an average age of 8.5 years, 49 (40.8%) were adults (16–50 years) with a mean age of 36 years and 31 (25.8%) were old age patients with a mean age of 61 years.

Table-2 describes the cumulative and year-wise frequency of major types of leukaemia. In the analysis about 16% patients had acute myelocytic leukaemia, while 32% patients had acute lymphocytic leukaemia; chronic myeloid leukaemia outnumbered chronic lymphocytic leukaemia (11% and 3%); Hodgkin lymphoma was seen in 18% cases while Non Hodgkin Lymphoma was present in 20% cases. Mortality rate found was about 30% in Acute (ALL) and Chronic Lymphocytic Leukaemia (CLL), almost 20% in Acute (AML) and Chronic Myelocytic Leukaemia (CML), approximately 10% in Hodgkin and Non-Hodgkin lymphoma. Table-3 describes age wise distribution of various types of leukaemia.

Table-1: Area-wise distribution of leukaemia

Area	No of cases	Percentage
Kohistan	22	18
Battagram	18	16
Mansehra	29	25
Torghar	10	08
Kaghan	11	09
Abbottabad	17	14
Haripur	13	10
Total	120	100

Table-2: Frequency distribution of various types of leukaemia.

Type of leukaemia	No of patients	%age
AML	19	16
ALL	39	32
CML	14	11
CLL	04	03
HL	20	18
NHL	24	20
Total	120	100

Table-3: Age wise distribution of various types of leukaemia.

Age group in years	No of Cases						Total
	AML	ALL	CML	CLL	HL	NHL	
Children <15 years	04	22	02	00	09	04	40
Adults (16–50 years)	12	11	04	01	08	13	49
Old age (>50 years)	03	06	08	03	04	07	31
Total cases	19	39	14	04	20	24	120

DISCUSSION

According to the results observed, majority of the cases belonged to mountainous areas of four districts of Hazara, i.e., Mansehra, Kohistan, Battagram and Torghar. After categorizing and analyzing data, it became evident that among leukaemia ALL occurred commonly[9] as expected (50 cases) and among lymphoma, NHL was more common (25 cases)[10] with slight male predominance. While, AML (45 cases) is most commonly occurring neoplasm among children and CML (30 cases) in adults, again males being effected more than females, with similar observations made by earlier studies.[11] AML is more prevalent among younger age groups as seems in West, incidence of AML is more than our setups, regarding earlier domestic and foreign 6studies. In the present study, AML was the commonest malignant leukaemia, closely followed by ALL. HL was found in only 2% of cases, frequency being much less compared to those reported in literature. our study show 12% of NHLs tumours were seen in young adults.[19] ALL was second most common group of indolent leukaemia, consistent with our findings.[20] CLL are rare that occurs predominantly in young women. Metastases to other parts of body are relatively frequent with the most common to breast, colon, stomach and liver. However, in present study there was only one case of NKL cell tumour. Immuno-histo-chemistry is an important diagnostic tool in evaluation of leukaemia, especially useful in diagnosing tumours with early metastasis. A similar study conducted by Adel *et al*, also showed male predominance like our study, may be due to the fact that males consult doctors earlier as compared to females, latter being the neglected sex in our society. In USA male to female ratio is 2:1, the exceptionally high ratio in Hazara may be due to social considerations.

In contrast to European and USA studies, where CML is more common in females, it is almost opposite in Hazara, having low malignant potential, favourable prognosis and relatively early age at onset. In the case of CLL male to female ratio is 1:2, sex males are predominant.[12] ALL is found rare in children but its frequency increases with age and peaks at the age of 60 and 70 years. No case of ALL was found in 1st decade and only two in 2nd decade. The results of ALL were almost similar to that in Europe and USA but in AML the pattern of rest of the Pakistan is in consonance with ours, as reflected in a study by Mohammed Idris *et al*. [13] Our figures are comparable to international figures regarding ALL and comparable to local figures when AML is considered. In general, 85% of ALL's occur in children while 90% of CLL's occur in adults and old age with peak incidence at 56 years.[14] As for as age of high occurrence of HL is concerned it is most common in adolescent men and NHL equal in all age groups. Overall age distribution of the patients in our study ranged between 2 to 70 years. Out of 200 patients 45 were between 12–20 years, 25 were 21–40 years and 10 were above 60 years. This shows that leukaemia is more prevalent among young people earlier studies also showed similar results, where 70% of the cases were below the age of 40 years. Our findings are almost similar to the earlier studies.[15] Median age of presentation of the three commonest types of these leukaemias, i.e., AML, ALL and NHLs was 25 years, 6 years and 23 years ranging between 5–65 years, 3–12 and 5–65 years respectively. For Non-Hodgkin's Lymphoma our results are different from previous study performed exclusively on NHLs with an average age 46 years.[16] Reasons are not exactly known, small sample size in our study could be the major factor. For AML and ALL our results were not much different from those of previous researches**.** Median age of representation for CLL and multiple myeloma was about 54 years each (ranging 46–75 and 45–66 years respectively), this is remarkably different from the results of earlier studies.[17] The median age for CML is 24 years (ranging between 15–70 years) as compared to 34 years in an past studies.[18] The median age for HL was 23 years (ranging 6–34 years) than coincides with all

may be attributed to the type of investigations performed. However we diagnosed a single case of HL in a 42 year old lady, this relatively low incidence in our community may not be true reflection of the reality as our population is not disease conscious. Results strongly recommended that leukaemia has high incidence in mountainous areas of Hazara and also reflected that environmental agents are the major predisposing factors and have valuable significance in clinical practice.

CONCLUSION

In developed and developing world, despite educational programs designed to prevent leukaemia, incidence and mortality rate for the disease has soared steadily. A gradual rise was observed in total haematological cancers in this area during past 5 year's period. Mortality rate found was about 30% in Acute (ALL) and Chronic Lymphocytic Leukaemia (CLL), almost 20% in Acute (AML) and Chronic Myelocytic Leukaemia (CML), approximately 10% in Hodgkin and Non-Hodgkin lymphoma. Further studies are required on larger scale and sample size, with the help of more modern diagnostic techniques to have a better knowledge about the break-up of leukaemia in this area. Government and private sector organizations need to pay attention towards this dreadful health problem. Private sector organizations (NGOs) should come ahead to assist the government sector in its battel against Leukaemia. Maintenance of disease registers is very important in this regard which will help future researches in the field. Health education of our community is need of the day to prevent complications and to get real figures of the disease.

REFERENCES

1. Pui CH, Relling MV, Downing JR. Acute lymphoblastic leukaemia. N Engl J Med 2004;350(15):1535–48.
2. Handin RI, Lux SE, Stossel TP. Blood: principles and practice of hematology. Vol. 1. Lippincott Williams & Wilkins; 2003.
3. Wang W. Emergence of a DNA-damage response network consisting of Fanconi anaemia and BRCA proteins. Nat Rev Genet 2007;8(10):735–48.
4. Baris D, Zahm SH. Epidmiology of lympomas. Curr Opin Oncol 2000;12(5):383–94.
5. Greiner TC, Mederiros LJ, Jaffe ES. Non-Hodgkin's lymphoma. Cancer 1995;75(1 suppl):370–80.
6. Parkin D, Stiller C, Draper G, Bieber C, Terracini B, Young J. International incidence of childhood cancer. Lyon: International Agency for Research on Cancer. IARC Sci Publ (87):1998.
7. Imperial Gazetteer of India in 26 assorted volumes (London: Oxford 1931), v.13, p.76.
8. Zahid M. Khalid A, Ahmed ZD, Aziz Z. Acute leukaemias of childhood: A retrospective analysis of 62 cases. J Pak Med Assoc 1996;46(7):147–9.
9. Ahmed M, Khan AH, Mansoor A, Khan MA, Saud S. Non-Hodgkin's lymphoma-clinicopathological pattern. J Pak Med Assoc 1992;42(9):205–8.
10. Sevage DG, Szydlo RM, Goldman JM. Clinical features at diagnosis in 430 patients with chronic myeloid leukaemia seen at a referral centre over a 16 year period. Br J Haematol 1997;96(1):111–6.
11. Hassan K, Qureshi M, Shafi S, Ikram N, Akhtar MJ. Acute myeloid leukaemia-FB classification and its correlations with clinico-haematological features. J Pak Med Assoc 1993;43(10):200–10.
12. Idris M, Shah SH, Farid J, Gul N. An experience with sixty cases of haematological malignancies; a clinico haematological correlation. J Ayub Med Coll Abbottabad 2004;16(4):51–4.
13. Vallespi T, Montserrat E, Sanz MA. Chronic lymphocytic leukaemia: Prognostic value of lymphocyte morphological subtypes. A multivariate survival analysis in 146 patients. Br J Haematol 1991;77(4):478–85.
14. Hassan K, Bukhari KP, Zafar A, Malik MZK, Akhtar MJ. Acute leukaemia in children-French-American-British (FAB) classification and its relation to clinical features. J Pak Med Assoc 1992;42(2):29–33.
15. Pasqualetti P, Festuccia V, Acitelli P, Collacciani A, Gluski A, Casale P. Tobacco smoking and risk of haematological malignancies in adult: A case-control study. Br J Haematol 1997;97(3):659–62.
16. Dunn GP, Bruce AT, Ikeda H, Old LJ, Schreiber RD. Cancer immunoediting: from immunosurveillance to tumor escape. Nat Immunol 2002;3(11):991–8.
17. Knudson AG. Cancer genetics. Am J Med Genet 2002;111(1):96–102.
18. Hoeijmakers JH. Genome maintenance mechanism for preventing cancer. Nature 2001;411:336–74.
19. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin 2005;55(2):74–108.
20. Hussain Sp, Schwank J, Staib F, Wang XW, Harris CC. TP53 mutations and hepatocellular carcinoma: insights into the etiology and pathogenesis of liver cancer. Oncogene 2007;26(15):2166–76.

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