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Original Article

Association of Major Leuk emias with Different Age Groups

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ABSTRACT

Objective: To determine the association between major leukemias and age and assess differences with respect to gender, cytogenetics and hematological parameters among patients presenting at a tertiary care hospital.

Study Design: Cross sectional study.

Place and Duration of Study: Medical Oncology Department, Jinnah Postgraduate Medical Center, Karachi, Pakistan from Oct 2019 to Mar 2020.

Methodology: Two hundred and three patients of either gender >14 years presenting with confirmed diagnosis of acute or chronic leukemia based on bone marrow biopsy and immunophenotyping were enrolled in the study. Data regarding socio-demographics, duration of disease, family history, co-morbids and hematological parameters were collected.

Results: The mean age of the study sample was estimated as 35.46±15.14 years ranging from 14-85 years. Out of 203 patients, 69(34%) of the patients had Acute Myeloid Leukemia, 55(27.1%) had Acute Lymphoblastic Leukemia, 61(30%) had Chronic Myeloid Leukemia and 18(8.9%) had Chronic Lymphocytic Leukemia. AML and ALL are the most frequent leukemias in the age group 19-50 years while CML and CLL more frequently presented in the age group 31-50 years. No case of CLL has been reported in age less than 31 years.

Overall, statistically significant difference was observed between age and types of leukemia (p<0.05). Significant association was found between age and leukemia types among males (p<0.05), normal cytogenetics, hyperdiploidy and t (9;22) (p<0.05) and hematological parameters (p<0.05.

Conclusion: In conclusion, statistically significant association was observed between age and types of leukemia. Further more significant association was also found between age and leukemia types among males; cytogenetics; and hematological parameters.

Keywords: Acute leukemia, Acute lymphoblastic leukemia (ALL), Acute myeloid leukemia (AML), Chronic lymphocytic leukemia (CLL), Chronic myeloid leukemia (CML), Immunophenotyping.

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INTRODUCTION

Leukemias are gradual or rapidly progressing, malignant disorders, characterized by the production and propagation of immature precursor cells in the blood and bone marrow. Leukemias are sub divided into acute leukemia and chronic leukemia based on the degree of cellular maturity. Acute leukemias primarily consist of immature blast cells whereas chronic leukemias comprise of a greater number of mature cells.[1] Based on the origin of the predominant cell type (myeloid or lymphoid) and the rate of disease progression (acute or chronic), leukemia is categorized into four major subtypes: acute myelogenous leukemia (AML), chronic myelogenous leukemia (CML), acute lymphocytic leukemia,[2] and chronic lymphocytic leukemia (CLL). All these types of leukemias have different characteristics and treatment plans.[2,3] According to Globocan in 2018, Pakistan had 7139 new cases of leukemia registered and 4945 deaths were reported due to it in 2018 making it the 5th most common cancer in Pakistan.[4]

Acute leukemias are very aggressive and result in death in weeks to months if left untreated, but are potentially curable with proper treatment. They are distinguished by the rapid, unrestrained proliferation of immature hematopoietic cells at the expense of normal marrow function.[5] In Pakistan in 2019, the prevalence of acute leukemias among all leukemic patients was reported as 80% and among them ALL was present in 49.5% and AML in 31.25%.[6] The mean age of ALL in Pakistan was 15.6 years (range 1-76 years), which suggested that ALL presents mostly in the pediatric age group. The mean age of AML was 31.4 years (range 1-80 years) suggesting AML to be a disease of adult population.[7] Types of Leukemia vary with respect to age, gender, cytogenetics, and hematological abnormalities.[8-10]

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Age of presentation of CML is between 40-60 years while CLL is frequent in 60-80 years of age. In Pakistan in 2019, the prevalence of chronic leukemias among all leukemic patients was reported as 20% and among them CML was present in 10% and CLL in 9.25% of the cases.[6]

Till date, few studies are available for relationship between leukemias and age in our population. The findings on the epidemiological features of leukemias are poorly studied in Pakistan. Therefore, current research was conducted to study and evaluate the major four types of leukemias which are most prevalent and their association with different age groups and to assess differences with respect to gender, cytogenetics and hematological parameters among leukemic patients presenting at a tertiary care hospital.

METHODOLOGY

The Cross Sectional study was conducted at the Department of Medical Oncology, Jinnah Postgraduate Medical Center from October 2019 to March 2020. Sample size of 203 was estimated using Raosoft online sample size calculator by taking statistics of AML among age group 51-65 years as 13.6%.[11]

Inclusion Criteria: Patients of either gender, presenting to the Oncology Ward with confirmed diagnosis of leukemia were included in the study.

Exclusion Criteria: Patients less than 14 years of age were excluded.

The study was conducted after taking approval from ethical review board (NO.F.2-81/2019-GENL/34345/JPMC). Written informed consent was obtained from all the patients who were meeting eligibility criteria before data collection. Data regarding socio-demographics, duration of disease, family history and co-morbids were collected. The data regarding hematological parameters were also recorded. For the diagnosis of acute leukemia; bone marrow biopsy and immunophenotyping was performed, while for diagnosis of chronic myeloid leukemia bone marrow biopsy, cytogenetics and molecular test for BCR-ABL was performed and for chronic lymphocytic leukemia only immunophenotyping was done.

SPSS version 23 was used to analyze data. Descriptive analysis was performed for all numeric and categorical variables. Bivariate analysis was performed to see the association between age and type of leukemias by using chi-square/fisher exact test. The *p*-value less than and equal to 0.05 was considered as statistically significant.

RESULTS

Total 203 patients were included and the mean age was estimated as 35.46+15.14 years ranging from 14-85 years. Majority of the patients were males 129(63.5%), unemployed 114(56.2%), and belonged from urban area 120(59.1%).

Patients hailed from mixed ethnicity with majority being Sindhi speaking 86(42.4%) and Urdu speaking 71(34.9%). About 11 patients (5.4%) were diabetic, 8(3.9%) were hypertensive and only 2(1%) patients had hepatitis C virus (HCV). The median duration of disease before presenting to the hospital was 3(IQR=1-6) months. Out of 203 patients, only 7 patients (3.4%) had positive family history of cancer (Table-I).

Table-I: Descriptive Analysis of Study Sample (n=203)

Variables	Mean±SD
Age (years)	35.46±15.14
Hemoglobin (g/dl)	8.72±3.35
Median (Interquartile range)	
Duration of disease (months)	3 (1-6)
White Blood Cell (x10^9/L)	53.7(6.5-229)
Platelet (x10^9/L)	89(30-302)
	n(%)
Gender	
Male	129(63.5)
Female	74(36.5)
Occupation	
Unemployed	114(56.2)
Employed	89(43.8)
Residence	
Urban	120(59.1)
Rural	83(40.9)
Ethnicity	
Sindhi	86(42.4)
Punjabi	10(4.9)
Balochi	22(10.8)
Pathan	14(6.9)
Urdu	71(35)
Comorbid	
None	182(89.7)
Hypertension	8(3.9)
Diabetes mellitus	11(5.4)
Hepatitis C	2(1)
Family history of leukemia	
Yes	7(3.4)
No	196(96.6)

Majority of the patients had normal karyotypes 100(49.3%). In 22 patients cytogenetic analysis was not done. Among acute leukemias, 85(68.5%) had normal cytogenetics. Out of the 63 patients who had translocation(t) (9;22) 54(85.7%) were of CML while remaining 9 patients (14.2%) were of ALL. (Figure)

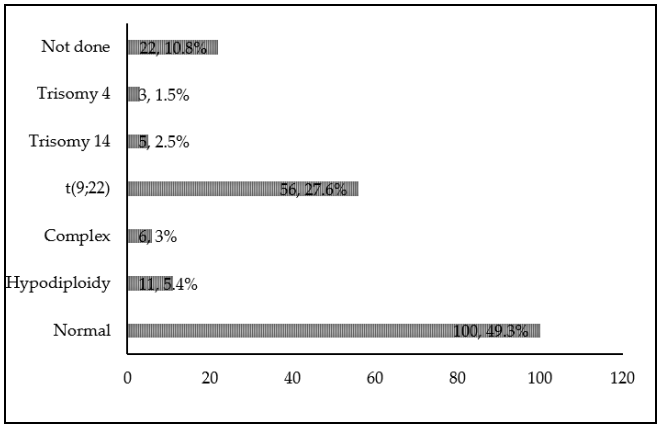

Figure: Cytogenetic Analysis of Included Patients (n=203)

Out of 203 patients, 124(61%) had acute leukemia whereas 79(39%) were diagnosed with chronic leukemias. Of 124(61%) patients, 69(34%) had AML and 55(27.1%) had ALL. Among ALL patients, B-cell type was present in 39(19.2%), while 14(6.9%) had T-cell type. 1(0.5%) patient was non-specified in terms of B or T cell type. CML was present in 61(30%) of the patients and CLL in 18(8.9%) (Table-II).

Table-II: Frequency Distribution of Leukemia Types (n=203)

Types		n(%)
Acute leukemia 124(61.1%)	Acute Myeloid Leukemia	69(34)
	Acute Lymphoblastic Leukemia	55(27.1)
	B-cell	39(19.2)
	T-Cell	14(6.9)
	Non-specified	1(0.5)
Chronic leukemia 79(38.9%)	Chronic Myeloid Leukemia	61(30)
	Chronic Lymphocytic Leukemia	18(8.9)

AML and ALL are the most frequent leukemias in the age group 19-50 years. CML is the most frequent leukemia in age group 31-50 years. No case of CLL has been reported in age less than 31 years and it is most commonly observed in age group 31-50 years. The statistically significant difference was observed between age and types of leukemia (p=0.001) (Table-III).

The stratification with respect to gender, cytogenetics and hematological parameters was performed. Significant association was found between age and leukemia types among males (p=0.001). Significant association was also found between age and normal cytogenetics; hyperdiploidy; and t (9;22) (p=0.006, p=0.015, p=0.018 values respectively).

Among all patients of acute leukemia 100 patients (95%) presented with WBC <10,000 and platelets count <150,000 and 118patients (96%) had Hemoglobin <12gm/dl. About 47 CML patients (78.3%) had WBC count >10,000 and 56 patients (93%) had Hemoglobin <12gm/dl. Significant association was found between age and leukemia types with respect to hematological parameters (p=0.001) (Table-IV).

DISCUSSION

Leukemia is a cancer of the precursor blood cells and can be categorized into acute and chronic forms. Acute leukemias are characterized by increased number of immature blast cells that are unable to carry out their normal expected functions. As a result, acute leukemias progress rapidly and require immediate treatment. In contrast to acute leukemia, chronic leukemias contains reduced number of blast cells which partially retain their normal functions. Hence, these are not as rapidly progressive and immediately life threatening.

Depending on the type of precursor cell affected, the leukemias can also be divide into lymphoblastic leukemia (arise from lymphoid precursors) and myeloid leukemias (arise from precursor cells of myeloid series).

The present study showed that acute leukemia is more common than chronic leukemia which is a similar findings in Rathee R *et al*. study.[12] Out of 203 cases of leukemia, 34% had AML, 27.1% had ALL, 30% had CML and 8.9% had CLL. In comparison to a study by Salkar AB *et al*. in 2014 of 110 leukemic patients, 71 patients had ALL followed by AML (43 cases) CML (30 cases) and then CLL (9 cases).[13]

AML can occur in any age, however, the occurrence increases with age. National

Table-III: Frequency Distribution Of Leukemia Types With Respect to Age (n=203)

Age groups (years)	Acute Myeloid Leukemia	Acute Lymphoblastic leukemia	Chronic Myeloid Leukemia	Chronic Lymphocytic Leukemia	p-value
14-18	7(10.1%)	15(27.3)	1(3.3%)	0	0.001
19-30	29(42%)	23(41.8%)	21(34.4%)	0	
31-50	22(31.9%)	16(29.1%)	28(45.9%)	8(44.4%)	
51-65	10(14.5%)	1(1.8%)	7(11.5%)	6(33.3%)	
>65	1(1.4%)	0	3(4.9%)	4(22.2%)	

Table-IV: Comaparison Age and Leukemia Types With Respect to Gender, Cytogenetic and Hematological Parameters (n=203)

	Age groups (years)	Acute Myeloid Leukemia	Acute Lymphoblastic leukemia	Chronic Myeloid Leukemia	Chronic Lymphocytic Leukemia	*p*-value
Gender						
Male	14-18	3(7.3%)	13(29.5%)	1(3.2%)	0	0.001
	19-30	18(43.9%)	19(43.2%)	10(32.3%)	0	
	31-50	14(34.1%)	11(25%)	11(35.5%)	4(30.8%)	
	51-65	6(14.6%)	1(2.3%)	6(19.4%)	6(46.2%)	
	>65	0	0	3(9.7%)	3(23.1%)	
Female	14-18	4 (14.3%)	2(18.2%)	1(3.3%)	0	0.06
	19-30	11(39.3%)	4(36.4%)	11(36.7%)	0	
	31-50	8(28.6%)	5(45.5%)	17(56.7%)	4(80%)	
	51-65	4(14.3%)	0	1(3.3%)	0	
	>65	1(3.6%)	0	0	1(20%)	
Cytogenetic						
Normal	14-18	6(13.3%)	10(25%)	0	0	0.006
	19-30	16(35.6%)	17(42.5%)	2(33.3%)	0	
	31-50	18(40%)	12(30%)	3(50%)	4(44.4%)	
	51-65	5(11.1%)	1(2.5%)	0	4(44.4%)	
	>65	0	0	1(16.7%)	1(11.1%)	
Hyperdiploidy	14-18	0	2 (33.3%)	0	0	0.015
	19-30	2(100%)	3(50%)	0	0	
	31-50	0	1(16.7%)	0	1(33.3%)	
	51-65	0	0	0	0	
	>65	0	0	0	2(66.7%)	
Complex	14-18	0	0	0	0	0.178
	19-30	3(75%)	0	0	0	
	31-50	1(25%)	1(100%)	0	1 (100%)	
	51-65	0	0	0	0	
	>65	0	0	0	0	
t(9;22)	14-18	0	4(44.4%)	2(3.7%)	0	0.018
	19-30	0	2(22.2%)	19(35.2%)	0	
	31-50	0	3(33.3%)	24(44.4%)	0	
	51-65	0	0	7(13%)	0	
	>65	0	0	2(3.7%)	0	
Hemoglobin Level						
<12 g/dl	14-18	7(10.1%)	13(26.5%)	1(1.8%)	0	0.001
	19-30	29(42%)	21(42.9%)	20(35.7%)	0	
	31-50	22(31.9%)	14(28.6%)	25(44.6%)	6(42.9%)	
	51-65	10(14.5%)	1(2%)	7(12.5%)	4(28.6%)	
	>65	1(1.4%)	0	3(5.4%)	4(28.6%)	
≥12 g/dl	14-18	0	2(33.3%)	1(20%)	0	0.022
	19-30	0	2(33.3%)	1(20%)	0	
	31-50	0	2(33.3%)	3(60%)	2(50%)	
	51-65	0	0	0	2(50%)	
	>65	0	0	0	0	
White Blood Cell						
<100(x10⁹/L)	14-18	6(10.5%)	12(27.9%)	0	0	0.01
	19-30	22(38.6%)	15(34.9%)	6(42.9%)	0	
	31-50	20(35.1%)	15(34.9%)	7(50%)	3(33.3%)	
	51-65	9(15.8%)	1(2.3%)	0	4 (44.4%)	
	>65	0	0	1(7.1%)	2(22.2%)	
≥100(x10⁹/L)	14-18	1(8.3%)	3(25%)	2(4.3%)	0	0.001
	19-30	7(58.3%)	8(66.7%)	15(31.9%)	0	
	31-50	2(16.7%)	1(8.3%)	21(44.7%)	5(55.6%)	
	51-65	1(8.3%)	0	7(14.9%)	2(22.2%)	
	>65	1(8.3%)	0	2(4.3%)	2(22.2%)	
Platelet						
<150(x10⁹/L)	14-18	7(11.9%)	9(22%)	0	0	0.001
	19-30	23(39%)	19(46.3%)	2(22.2%)	0	
	31-50	21(35.6%)	12(29.3%)	5(55.6%)	5(50%)	
	51-65	8(13.6%)	1(2.4%)	1(11.1%)	3(30%)	
	>65	0	0	1(11.1%)	2(20%)	
≥150(x10⁹/L)	14-18	0	6(42.9%)	2(3.8%)	0	0.001
	19-30	6(60%)	4(28.6%)	19(36.5%)	0	
	31-50	1(10%)	4(28.6%)	23(44.2%)	3(37.5%)	
	51-65	2(20%)	0	6(11.5%)	3(37.5%)	
	>65	1(10%)	0	2(3.8%)	2(25%)	

comprehensive cancer network (NCCN) reported that almost 50% of diagnosis of AML cases is at ≥65 years of age.[14] Majority of data from West showed that the AML was diagnosed in between 60 and 70 years and

males were more likely to be affected from AML as compare to females.[15] According to literature, there is a difference with regards to age of onset between the eastern and the western population which could be due to geographical variation or could be genetically determined.[15] The present study results demonstrate that the age of onset of AML is mostly between 19-50 years and the results are similar to other Pakistani studies reporting average age of 34.5 years.[11]

In the present study, ALL was mostly diagnosed in age group 19-30 years. A meta-analysis published in the Lancet in 2018 reported that adults with CLL were more prevalent in European and North American countries, whereas ALL in adults was prevalent in African populations, South American, Caribbean, and Asian countries.[16] Geographical differences in the age of presentation may in part be explained due to differences in the accessibility of healthcare systems between the developed and developing countries. It may also be due to different risk factors affecting particular age groups or possibly due to gene-environment interactions.[16]

Among chronic leukemic patients, CML is more common than CLL in present study. A Pakistani study conducted in Khyber Pakhtunkhwa province showed CLL is more common than CML.[17] The present study findings also reported that CML could occur at any age however, most common onset is found in between 31-50 years age. In this study, 83% of patients within the CML group were <50 years of age with male preponderance for Chronic leukemias. The mean age of CML is reported as 47.5±14.5 years and 40.9±14.5 years in two studies from Iran with male preponderance.[18,19] Similarly mean age of CML in a study from India was 37 years.[20] However the results are in contrast with the studies done in the west where the mean age of diagnosis is more than 60 years. According to American Society of Cancer, the average age at diagnosis of CML is 64 years.

CLL occurs only in older age and no cases in younger age were found in the current study. In another study, CLL is known as an older age disease and was prevalent in >60 years of age and was not found in patients <24 years of age.[17] CLL is claimed to be more prevalent in adults of Western countries whereas it is considered rare in Asian population.[21,22] The mean age of CLL is reported 60 years in one study with female pre dominance, unlike present study.[23]

In the present study, stratification with respect to hematological parameters was found statistically significant. Majority of the patients with acute leukemia presented with low hemoglobin, low WBC and low platelets making them susceptible to bleeding and life-threatening infections. This in turn leads to high mortality and worse prognosis.

CONCLUSION

In conclusion, statistically significant association was observed between age and types of leukemia. Furthermore significant association was also found between age and leukemia types among males; cytogenetics; and hematological parameters. It is recommended that more studies with larger number of patients be conducted on this topic to further consolidate these findings.

Conflict of Interest: None

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MA: & GH: Conception, study design, interperitation of data, Critically reviewed manuscript & approval for the final version to be published.

BA: & AT: Data analysis and interpretation, manuscript writing & approval for the final version to be published.

KA: & BR: Critical review, data acquisition, Drafted manuscript & approval for the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investi-gated and resolved.

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