ORIGINAL ARTICLE

ACUTE MYELOID LEUKEMIA, EPIDEMIOLOGY AND SEASONALITY, A SINGLE CENTER EXPERIENCE

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ABSTRACT

Background and Objectives: In this study we retrospectively evaluated data of acute myeloid leukemia (AML) patients diagnosed at our center over a span of 7 years. The data was categorized according to FAB classification and then studied for demographic features and for any evidence of seasonality.

Methods: This was a cross sectional study conducted at Shaikh Zayed Medical Complex (SZMC), Lahore. In this study we retrospectively evaluated data of AML patients diagnosed over a span of 7 years from 1st July 2001 to 30th June 2008. The data was categorized according to FAB classification and studied for demographic features. We also analysed the cohort for number of acute myeloid leukemias presenting in each month of the year to assess for any evidence of seasonality.

Results: Ninety eight patients of AML were studied, 55 males and 43 females. Eleven patients belonged to the paediatric age group with a male to female ratio of 1.2:1; and 87 were adults, male to female ratio of 1.28:1. The mean age of the entire cohort was 37.08 ± 21.63 years. For adult cases the mean age came to 40.93 ± 19.91 years and for paediatric group the mean age was 7.33 ± 4.05 years. M2 category was most common (38 cases) and collectively M2 and M4 contributed 57% of the entire cohort. Monthly distribution of cases showed a prominent peak (30 cases, 30.5%) in the months of September and October. M2 and M4 collectively contributed 22 out of these 30 cases (p value < 0.05).

Conclusion: AML M2 and M4 were the most common categories of FAB classification at our Centre. There was a significant increase in the presentation of AML M2 and M4 cases in the months of September and October.

Key words: Acute myeloid leukemia, AML, epidemiology, seasonality.

INTRODUCTION

Acute leukemias show geographical variations in occurrence, age and sex distribution as well as French – American – British (FAB) classification subtypes, possibly due to ethnic and environmental factors.[1] Regional variations have been described for AML. FAB-M2 is the most common type of AML in Japan and its frequency is higher in children than in adults,[2] a fact that was not observed in Australia.[3] Promyelocytic leukemia (FAB-M3) shows a remarkably high frequency among Hispanics in the United States [4] and in several countries in South America including Brazil.[1] From Pakistan single centre studies report maximum patients in either M2 or M4 category,[5-7] but no population based records are available. However, cancer registry from a single centre in Lahore determines leukemia to be the most common cancer in males.[8]

Etiology of acute leukemias have been in focus since long and infection is a proposed aetiology for many haematological malignancies. Evidence suggests antigenic stimulation consequent to community – acquired infections may contribute to the risk of AML.[9] Therefore seasonal changes in incidence of AML have been studied extensively over the last 2 decades for supportive evidence with mixed results.[10-12] To our knowledge seasonality has not been reported in any study from Pakistan, but we did come across a few studies from Asia.[13-15]

In this study we retrospectively evaluated data of AML patients diagnosed at our center over a span of 7 years. SZMC is a large tertiary care facility in the city of Lahore. The data was categorized according to FAB classification and then studied for demographic features. We also analysed the cohort for number of acute myeloid leukemias diagnosed in each month of the year for any evidence of seasonality.

MATERIALS AND METHODS

This cross – sectional descriptive study was carried out at the Department of Haematology Shaikh Zayed Hospital (SZH) Lahore. The bone marrow records of AML patients were retrospectively evaluated for patient data

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from 1st July 2001 to 30th June 2008. All 98 patients diagnosed with acute myeloid leukemia according to FAB criteria during this period were studied. The data collected included findings in history, examination, blood counts and bone marrow findings. The history of fever, bleeding from any site, weight loss, easy fatiguability; examination findings included pallor; fever; bleeding manifestations in the skin (e.g. bruises and purpura), signs of bleeding from the nose, oral cavity, vagina, anal canal; accessible lymph adenopathy in the cervical, axillary and inguinal region, hepatomegaly and splenomegaly. Complete blood counts at presentation and peripheral smear findings were also recorded. Bone marrow aspirate records were reviewed for cellularity, evidence of dysplasia, erythropoiesis, myelopoiesis and megakaryopoiesis and cytochemical stains including myeloperoxidase, non specific esterase and Periodic Acid Schiff stain. The collected data was entered into SPSS version 19.0 for analysis. Nominal data of variables including pallor, fever, bleeding, weight loss, splenomegaly. hepatomegaly, lymphadenopathy; were recorded as frequency / percentages. The cohort was divided into 2 groups on the basis of age above and below 14 years. The mean age of the paediatric group and the adult group was calculated separately. The variables in CBC including haemoglobin (Hb), Total leucocyte count (TLC), Platelet count were recorded as mean ± standard deviation for each group. The groups were further analysed separately for gender distribution. The cohort was classified according to FAB classification and each FAB class was individually evaluated for mean age of presentation, gender distribution, mean Hb, TLC and Platelet count. The entire cohort was then analysed for distribution of AML cases diagnosed in each month. The cases were stratified by month of presentation and FAB subtype. The chi square test was applied to assess for significance and p-value of ≤ 0.05 was taken as statistically significant.

Table 1: *Frequency and percentage of 98 cases of AML cases according to FAB classification according to age and gender stratification.*

Patient Cohort	*Paeds*	*Adult*	*Male*	*Female*	*Total*
M0	0	2 (2%)	1 (1%)	1 (1%)	2 (2%)
M1	1 (1%)	12 (12.2%)	3 (3%)	9 (9.1%)	13 (13.2%)
M2	4 (4%)	34 (34.7%)	23 (23.5%)	11 (11.2%)	38 (38.8%)
M3	1 (1%)	9 (9.1%)	7 (7.1%)	2 (2%)	10 (9.8%)
M4	2 (2%)	16 (16.3%)	7 (7.1%)	9 (9.1%)	18 (1.84%)
M5	3 (3%)	7 (7.1%)	4 (4%)	3 (3%)	10 (9.8%)
M6	0	7 (7.1%)	4 (4%)	3 (3%)	7 (7.1%)
M7	0	0	0	0	0
Total	11 (11.2%)	87 (88.8%)	49 (0.5%)	38 (38.8%)	98 (100%)

Table 2: *The mean age, Hb, TLC and Platelet count of 98 cases of AML.*

Patient Cohort	*Age In Years*	*Haemoglobin g/dl*	*WBC × 10^9/l*	*Platelet × 10^9/l*
Paediatric group	7.33+/-4.05	7.72+/-3.34	41.92+/-63.86	19.55+/-15.35
Adult group	40.93+/-19.91	7.16+/-2.55	47.76+/-4.38	28.52+/-21.78
Males	41.48+/-22.01	7.24+/-2.44	44.46+/-63.89	30.42+/-23.14
Females	40.22+/-17.07	7.07+/-2.71	51.68+/-65.64	26.21+/-20.08
Total	37.08+/-21.63	7.22+/-2.62	47.17+/-64	27.63+/-1.34

Table 3: *Distribution of 98 cases of AML according to the month of presentation.*

Month	*No. of AML Cases Reported*	*Percentage*	*Cumulative Percentage*
Jan	4	4.1	4.1
Feb	1	1.0	5.1
Mar	11	11.2	16.3
Apr	9	9.2	25.5
May	5	5.1	30.6
Jun	12	12.2	42.9
Jul	5	5.1	48.0
Aug	7	7.1	55.1
Sep	12	12.1	67.3
Oct	18	18.4	85.7
Nov	6	6.1	91.8
Dec	8	8.2	100

RESULTS

Ninety eight patients of AML were included in the study. There were 55 males and 43 females. Eleven were children less than or equal to 14 years of age with a male to female ratio of 1.2:1 (6 males, 5 females); and 87 were adults, male to female ratio of 1.28:1 (49 males, 38 females). The distribution pattern of FAB categories of AML segregated on the basis of age/ gender are detailed in Table 1.

The mean age, CBC findings are elaborated in Table II. The mean age in years for M0 was 62.5, M1 was 50.54, M2 was 41.32, M3 was 23.89, M4 was 28.21, M5 was 30.3, M6 was 30 years.

The commonest complaint of the patients was pallor and easy fatiguability affecting all the cases. Fever was seen in 60 cases, followed by complaints of bleeding which were present in 21 cases. Hepatomegaly (34 cases), Splenomegaly (30 cases), Lymphadenopathy (16 cases) were relatively infrequent.

Monthly distribution of cases reported over a span of 7 years showed a small peak in March and April of 20 cases (20.4%), a small peak in June of 12 cases (12.2%) and a prominent peak of 30 cases (30.5%) in the months of September and October as seen in Table III. When the data was cross examined for month of presentation and the FAB subcategory we found 22 of these 30 cases falling in the M2, M4 category (p-value < 0.05).

Table 4: *Comparison of FAB subtypes of AML with studies from within Pakistan.*

Study	1	2	3	4	5	6
No of cases in each study	143	32	98	116	74	62
M0	0	12.5%	2.0	7.7	0	1.6
M1	20.27	6.3%	18.36	8.7	8.1	22.5
M2	47.55	50%	38.77	30.25	16	32.2
M3	11.18	9.4%	10.2	10.4	15	9.1
M4	13.28	15.6%	18.36	36.2	46	22.5
M5	3.49	3.1%	10.2	6	9.5	8.6
M6	4.19	3.1%	7.1	0.8	0	1.6
M7	0	0	0	0	2.7	1.6

Key:

1. KEMU (Lahore) 17
2. SZMC (Lahore) 23
3. SZMC (present study)
4. AKUH(Karachi) Harani 6
5. AKUH (Karachi)Kakepoto 7
6. RMC(Rawalpindi) Hassan 24

DISCUSSION

This study consisted of 98 patients of acute myeloid leukemia diagnosed by FAB criteria over a span of 7 years in a single tertiary care hospital of Lahore. M2 category was most common (38 cases) and collectively M2 and M4 contributed 56 cases (57%) of the entire cohort. Comparison of this study with other studies from Pakistan is presented in Table IV. Together M2 and M4 contribute more than 55% of all AML patients in these studies. M2 has been reported as the most common AML subtype in Nepal,[14] Oman,[15] Japan.[2]

The ages ranged from 1 year to 90 years. The paediatric mean age of 7.55 ± compares well with another Pakistani study which report a mean age of 8 ± 5 years.[16] In the present study 51% cases were seen in the 2nd to 4th decade which is similar to a study from Lahore which report a maximum number of patients were in the 15 – 25 years age group.[17] Male preponderance for AML has been reported in nearly all large studies, and we also found the same result. In general it has long been known that myeloid neoplasms affect males more frequently.[18,19] This male excess is seen in both children and adults therefore an underlying genetic predisposition to malignancy is most likely which is triggered secondarily by environmental factors.[20]

We reported an increased diagnosis of AML in the months of September and October i.e. 30 cases (30.5%). M2 and M4 categories collectively contributed 22 out of these 30 cases i.e. a 73% (p value < 0.05). This data suggests that the September, October peak was primarily due to the increased number of M2 and M4 cases. In Lahore a 10 year average temperature of 34°C (day), 25°C (night) is reported in September and 32°C (day), 20°C (night) in October. These 2 months follow a long summer which is hot and dry in May – June; hot and wet with monsoon rains in July-August and early September. This season has a spectrum of infectious disease associated with it including viral infections causing diarrhea, dengue and flu. It has been suggested that peak incidence of leukemia occurs when pathogens are present in a susceptible population and other important immunological factors act in concert. Subsequently, acute infection or reactivated chronic infection could be responsible for induction of leukaemia, symptoms, and incident diagnosis.[21]

Seasonal variation in AML has been reported by Drapkin et al in under 50-years-old with de novo AML, where they found a 44% increase in incidence between October and December. His study was carried out on combined data of 3000 cases thus providing strong evidence of a non-uniform distribution of cases diagnosed by month.[10] Eatough reported a peak presentation in months of February and March and trough

months of August and September for monocytic leukaemia diagnosis.[23] In our centre we found an increase in the presentation of AML M2 and M4 in the post monsoon season. However we were unable to compare these results with regional reports as we could not find any in the literature.

It is ***concluded*** that AML M2 and M4 were the most common categories of FAB classification at our centre. There was an increase in the presentation of AML M2 and M4 cases in the months of September and October.

ACKNOWLEDGEMENTS

We are very thankful to Dr. Bilal Basit, Dr. Ahmed Mustafa, Dr. Huma Mazhar who helped in the compilation of the data of these patients.

Authors Contribution

(Author 1, 2, 3 and 4 were involved in the conceptualization of the study, collection of data, analysis and writing of the manuscript, Author 5 and 6 were involved in review of cases and proof reading / corrections of the manuscript).

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