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Research Article

PATTERN OF AGE PRESENTATION IN PATIENTS DIAGNOSED WITH CHRONIC MYELOID LEUKEMIA AT JPMC KARACHI

AmnaMasood Bhutto[1]., GhulamHaider[2]., Adnan Anwar[3]., AmjadHakro[4]., SummaiyaIqbal[5]., Muhammad Ejaz Khan[6] and ZarghoonaWajid[7]

[1,6]Resident Medical Oncology Oncology ward, Jinnah Postgraduate Medical Center, Karachi
[2]Incharge Medical Oncology ward, Jinnah Postgraduate Medical Center, Karachi
[3]Department of Physiology Altibri Medical College Karachi
[4] Consultant Psychiatrist, Depot Line Clinics, Pakistan Association of Mental Health, Karachi
[5]Hamdard College of Medicine and Dentistry Hamdard University Hospital
[7]Medical Assistant, Musavvir Stem Cell Clinic and Pathology Laboratory Karachi

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A B S T R A C T

Objective: To identify the age presentation of Chronic Myeloid Leukemia and its association with haematological parameters in patients at in Medical Oncology JPMC, Karachi, Pakistan.

Material and methods: This was a cross sectional observational study through convenient sampling technique conducted from April 2016 to September 2017 in Oncology ward of JPMC, Karachi after ethical approval. Total 94 admitted patients in haematology oncology unit diagnosed with CML were included. Patients were divided into two groups on the basis of median age value. SPSS version 20.0 was used and Mann Whitney test was applied to assess the significance.

Results: A total of 94 patients were included having median age of 40.49 years. The median and mean rank of variables was recorded in 2 age groups of below and above 40 years. Haemoglobin level was 8.6 gm/dl in patient with age below 40 years with mean rank 47.74 and above 40 was 9.1 gm/dl and 47.25 (p=0.93), total leukocyte count was 229 x103cells/mm3 and 51.46 below 40 years and 177 x103cells/mm3and 43.37 above 40 years (p=0.15), platelets below 40 years was 502 x103cells/mm3and 52.85 and above 40 years was 377 x103cells/mm3and 41.91 (p=0.05), respectively.

Conclusion: Our study predicted the median age of 40.49 years in chronic myeloid leukemia patients. No significant difference existed in hematological parameters. However, there was substantial difference observed in platelet count of these patients.

INTRODUCTION

Chronic Myeloid Leukaemia (CML) is a blood can cerarising from a molecular mutation in a single pluripotent haematopoietic stem cell which results in uninhibited production of the myeloid progeny.(1)CML has been studied extensively which makes it the first cancer to have constant identification of mutation that is applicable for diagnosing. After the cutting-edge finding by Nowell and Hungerford in 1960, CML was declared as the primary cancer linked with a precise chromosomal abnormality- the Philadelphia chromosome- which is shortened chromosome 22 formed by balanced translocation between chromosome 9 and 22.(2,3) The translocation has involvement of the breakpoint cluster region (BCR) of chromosome 22 as well as the Abelson (ABL) oncogene on chromosome 9.

Corresponding author:* **AmnaMasood Bhutto
Resident Medical Oncology Oncology ward, Jinnah Postgraduate Medical Center, Karachi

BCR-ABL mutation makes a fusion gene that forms a protein having increased tyrosine kinase activity.(4) According to the 2008 World Health Organization classification of myeloid malignancies, CML shouldn't be diagnosed without it's molecular studies.(5,6) Median age of patients with CML in Arab countriesis between 50-65 years including males being relatively more affected as compared to females.(7,8) Patients might be asymptomatic at the time of presentation in which CML is diagnosed after an abnormal full blood cell count. A tri-phasic or bi-phasic CML disease comprises a majority of symptomatic patients present in the chronic phase. Other phases include accelerated or blast phase.(9) The usual clinical symptoms includefever, anemia, excessive sweating, spleenomegaly, anorexia, early satiety, weight loss and fatigue.(10) Some patients have, features of hyperviscosity, spontaneous bruising or bleeding. Gout, priapism, vertigo and hearing loss might be present. (11). Examination of blood film shows neutrophilia, with a left shift and frequently

eosinophilia and basophilia. Cytogenetic studies disclose the Philadelphia chromosome in approximately 90 – 95% of patients and in around half of the Philadelphia chromosome negative patients, BCR-ABL mutation (which can be major, minor or micro depending on the breakpoint on BCR) couldyet be reported using molecular techniques.(12) 2 prognostic scoring systems, are available for risk differentiation of patients with CML. Onescore was laid in chemotherapy era and is centered on patient age, spleen size, platelet count, and the percentage of blasts in the peripheral blood.(13) Another model is related to patients treated with interferon which include seosinophils and basophils in peripheral blood.(14) Both the scoring systems classify patients into 3 risk groups: low, intermediate, and high.. On the other hand, gene expression profiling has reported a near connection of gene expressions amongst the accelerated and the blast phase. Almost all of the genetic alterations in progression take place in the transition from chronic to accelerated phase.(3) Untreated chronic phase CML (CP-CML) ultimately progresses to advanced-phase disease in approximately 3 to 5 years.(4) Activation of beta-catenin–signaling pathway in CML granulocyte-macrophage progenitors (that improves the self-renewal activity and leukemic potential of the cells) might similarly be a key patho-biologic occurrence in advancement to blast phase CML. (15)

The objective of this study was to determine the presentation of age in patients diagnosed withCML and its association with different hematological parameters.

MATERIAL AND METHODS

This was a cross sectional observational study through convenient sampling technique conducted for duration of one and half year from April 2016 to September 2017 in Oncology ward of Jinnah Postgraduate Medical Centre, Karachi. Ethical approval was taken from the Institutional review board of JPMC, Karachi.

The total of 94 patients who were admitted in haematology oncology unit were selected for the study. On their first presentation, all CML patients diagnosed on blood complete picture and bone marrow trephine examination, aged 18 years or above, were included. Any case of CML who received prior chemotherapy and patients not consenting to participate or having incomplete datawere excluded from the study. Informed consent was taken from the patients with complete concealment of the data. The demographic data including age, gender and ethnicity of the patients was documented. Complete blood picture was performed in laboratory of Jinnah Hospital, which included haemoglobin, total leukocyte count, haematocrit, mean corpuscular volume, neutrophils, reticulocytes, basophils, eosinophil, lymphocytes, promyelocytes, myelocytes, metamyelocytes, blast cells, platelets and plasma cells. Patients were divided into two groups on the basis of median age value of 40 years.

The statistical software SPSS version 20.0 was used for data analysis. The quantitative data was expressed as median and inter-quartile range. Shapiro Wilk test was used to check the normal distribution. Mann-Whitney test was applied to assess the significance set at 0.05 level. Pie chart was used to show the frequency of age presentation in CML patients.

RESULTS

In the total of 94 patients included in the study the median age of the patients was 40.49±12.7 years. The frequency of age in CML was represented as age groups of 10-30 years in 26(28%), 31-40 years in 22(23%), 41-50 years in 28(30%), 51-60 years in 13(14%) and 61-80 in 5(5%) patients.(Figure: 1) The median and interquartile range (IQR) were reported in comparison to below and above 40 years. Median and IQR of haemoglobin levels below 40 years and below was 8.6 g/dl and 7.4-10.7 g/dl, while above 41 years was 9.1 g/dl and 7.5-9.9 g/dl. The haematocrit below 40 years was 32.1% and 30.3-34.8% while above 41 years was 32.3% and 30-35%.

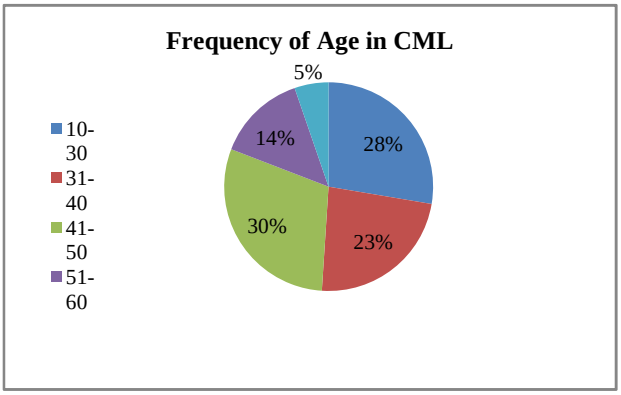

Figure 1 Frequency of Age in CML

MCV below 40 years was 95.5fl and 83.3-100fl while above 41 years was 92fl and 80-100fl. Total leukocyte count (TLC) below 40 years were 229 $x10^3$ cells/ mm^3 and 132.4-335.7 $x10^3$ cells/ mm^3while above 41 years was 177.8$x10^3$ cells/ mm^3 and 69.3-286.1$x10^3$ cells/ mm^3. Neutrophils below 40 years were 55% and 45-65% while above 41 years was 59.5%and 50.3-67.8%. Reticulocytes below 40 years was 2.5% and 1.6-3.18% while above 41 years was 2.6% and 1.9-3.0%. Basophils below 40 years were 4%and 2-6% while above 41 years was 4.5% and 2-6%. Eosinophil below 40 years was 3% and 7.4-2-4% while above 41 years was 3% and 2-4%. Lymphocytes below 40 years were 3% and 2-5%while above 41 years was 5% and 2.8-8.2%. Median and IQR of promyelocytes below 40 years were 5% and 2.3-7.0 while above 41 years was 3% and 2-5. Median and IQR of myelocytes below 40 years was 17% and 9.3-21.9 while above 41 years was 17% and 9.8-21.3. Median and IQR of monocytes below 40 years was 3% and 2-4% while above 41 years was 2.8%and 1.8-4.0%. Metamyelocytes below 40 years was 8% and 6.0-10.8% while above 41 years was 8% and 3.8-12%. Blast cells below 40 years were 3% and 2-4% while above 41 years was 4% and 2-5%. Platelets below 40 years were 502$x10^3$ cells/ mm^3 and 331.5-622.5 $x10^3$ cells/ mm^3 while above 41 years was 377$x10^3$ cells/ mm^3 and 238-575.3$x10^3$ cells/ mm^3. Plasma cells were same in both the age groups with median of 3% and IQR of 2-5%. (Table 1)

The mean rank was also recorded in comparison to below and above 40 years of age. Mean rank of hemoglobin in patients below 40 years was 47.74 while in above 41 years was 47.25. (p-value=0.93) Mean rank of hematocrit in patients below 40 years was 47.57 while in above 41 years was 47.42. (p-value=0.97) Mean rank of MCV in patients below 40 years was 49.56 while in above 41 years was 45.35. (p-value=0.45) Mean rank of TLC in patients below 40 years was 51.46 while in above 41 years was 43.37. (p-value=0.15) Mean rank of

neutrophil in patients below 40 years was 42.71 while in above 41 years was 52.50. (p-value=0.08) Mean rank of reticulocytes in patients below 40 years was 46.79 while in above 41 years was 48.24. (p-value=0.79) Mean rank of basophil in patients below 40 years was 46.89 while in above 41 years was 48.14. (p-value=0.82) Mean rank of eosinophil in patients below 40 years was 47.11 while in above 41 years was 47.90. (p-value=0.88) Mean rank of lymphocytes in patients below 40 years was 42.21 while in above 41 years was 53.02. (p-value=0.05) Mean rank of promyelocytes in patients below 40 years was 52.41 while in above 41 years was 42.38. (p-value=0.07) Mean rank of myelocytes in patients below 40 years was 46.80 while in above 41 years was 48.23. (p-value=0.80) Mean rank of monocytes in patients below 40 years was 48.88 while in above 41 years was 46.07. (p-value=0.61) Mean rank of metamyelocytes in patients below 40 years was 48.99 while in above 41 years was 45.95. (p-value=0.59) Mean rank of blast cells in patients below 40 years was 44.57 while in above 41 years was 50.55. (P-value=0.28) Mean rank of platelets in patients below 40 years was 52.85 while in above 41 years was 41.91. (p-value=0.05) Mean rank of plasma in patients below 40 years was 47.65 while in above 41 years was 47.35. (p-value=0.96)(Table 2)

DISCUSSION

The median age presentation of CML patients in our study was 40.49 which was less than the median a of age presentation reported in a study by O'Brien *et al*., in which the mean age was 67 years. (16) One of the study predicted, the median age in patients with chronic myeloid leukemia as 43.4 years. (13) The above age finding is in line with our study in which median age was similar. In another study by Hasford *et al*., the median age presentation of CML was reported to be 50 years. (14) In an alternative study, the median age presentation recorded was 36.5 years with a mean haemoglobin concentration of 8.5g/dl ±2.5 and mean TLC of $293x10^9$/L. (17) The median age mentioned above is less than the median age presentation in our study, i.e. while median haemoglobin and TLC were 8.85 g/dl and $229x10^9$/L respectively. Bansal S *et al*., reported that the median age presentation was found to be ranging from 32 to 42 years with a median haemoglobin range from 9 g/dl to 11 g/dl.(18). The median age found in our study tends to fall within the above said range while median haemoglobin was found to be 8.85 g/dl. European data from a study by Tardieu S *et al*., suggested the median age presentation to be 55 years. (19) In a Pakistani study by Ahmed R *et al*, the mean age of CML patients presented with was 37.87 years.

Table 1 Median and IQR of haematological parameters in different age groups

Variables	40 years and below (n=48)		41 years and above (n=46)	
	Median	IQR	Median	IQR
Hemoglobin (gm/dl)	8.6	7.4-10.7	9.1	7.5-9.9
Hematocrit (%)	32.1	30.3-34.8	32.3	30-35
Mean corpuscular volume (fl)	95.5	83.3-100	92	80-100
Total leucocyte count ($x10^3$cells/mm^3)	229	132.4-335.7	177.8	69.3-286.1
Neutrophils (%)	55	45-65	59.5	50.3-67.8
Reticulocytes (%)	2.5	1.6-3.18	2.6	1.9-3.0
Basophil (%)	4	2-6	4.5	2-6
Eosinophil (%)	3	2-4	3	2-4
Lymphocytes (%)	3	2-5	5	2.8-8.2
Promyelocytes (%)	5	2.3-7.0	3	2-5
Myelocytes (%)	17	9.3-21.9	17	9.8-21.3
Monocytes (%)	3	2-4	2.8	1.8-4.0
Metamyelocytes (%)	8	6.0-10.8	8	3.8-12
Blast cells (%)	3	2-4	4	2-5
Platelets ($x10^3$cells/mm^3)	502	331.5-622.5	377	238-575.3
Plasma cells (%)	3	2-5	3	2-5

Table 2 Association of different variables with age groups

Variable	Age Groups				p-value
	40 years and below (n=48)		41 years andabove (n=46)		
	Mean Rank	Sum of Ranks	Mean Rank	Sum of Ranks	
Hemoglobin	47.74	2291.5	47.25	2173.5	0.931
Hematocrit	47.57	2283.5	47.42	2181.5	0.979
Mean corpuscular volume	49.56	2379	45.35	2086	0.454
Total leucocyte count	51.46	2470	43.37	1995	0.151
Neutrophils	42.71	2050	52.50	2415	0.082
Reticulocytes	46.79	2246	48.24	2219	0.797
Basophil	46.89	2250	48.14	2214.5	0.822
Eosinophil	47.11	2261.5	47.90	2203.5	0.887
Lymphocytes	42.21	2026	53.02	2439	0.052
Promyelocytes	52.41	2515.5	42.38	1949.5	0.072
Myelocytes	46.80	2246.5	48.23	2218.5	0.800
Monocytes	48.88	2346	46.07	2119	0.612
Metamyelocytes	48.99	2351.5	45.95	2113.5	0.588
Blast cells	44.57	2139.5	50.55	2325.5	0.277
Platelets	52.85	2537	41.91	1928	0.05
Plasma	47.65	2287	47.35	2178	0.956

Mean haemoglobin was 9.94 g/dl ± 1.8 while mean TLC, platelets, blood and marrow blasts were $214.3x10^9$/L, $551.4x10^9$/L, 3.4% and 9.3% respectively (20) Although, there was no identifiable contributing factor that would explain the occurrence of CML at young age in this population. The increase in the age of patients in our study might be due to the fact that the incidence of CML has risen over the years. In another Indian study by Chavan *et al*., the mean age of presentation of CML reported was 42.76 years. (21) This study provides the basis for future research, exploring the risk factors leading to early onset of CML. Fortunately, the impact of new therapies on CML has significantly increased long-term survival in young patients.

The quantitative approach of our study has assured that we have sampled the extensive range of patients suffering from chronic myeloid leukemia. However, the study might not be immune from observer and selection bias. Considering the observations of our study and to what range, these age groups are consistent with the clinical features of the disease would be revealing to discover more facts about the disease.

CONCLUSION

The present study predicted the median age of 40.49 years in patients suffering from chronic myeloid leukemia. Furthermore, no significant difference existed in various hematological parameters. However, there was substantial difference observed in platelet count of these patients.

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