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Clinico Pathological Profile of Chronic Myeloid Leukemia (CML)

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Abstract
Chronic myeloid leukemia (CML) is one of the chronic myeloproliferative disorders and it is characterized by having certain hematological and cytogenetic markers. It is very common blood neoplasm in India that often need basic clinical history, examination and routine blood workup to establish a diagnosis. It has got good cure rate if diagnosed early. The present study was conducted to find clinico-hematological parameters in Indian population at a tertiary care center.

Keywords: CML, Hematological parameter, Clinical feature

Introduction
Chronic myeloid leukemia (CML) is a clonal malignant neoplasm of pleuripotent hematopoietic stem cell characterized by the excessive proliferation of mature granulocytes and their precursors in the bone marrow and peripheral blood and in 90% of cases; it is due to the presence of Philadelphia chromosome (Ph). The Philadelphia (Ph) chromosome is characterized by a translocation between chromosome 9 and 22 {(9; 22) (q34; q11)}. This translocation leads to the formation of Break-point Cluster Region and Abelson's (BCR-ABL), a new hybrid fusion gene that encodes for an oncoprotein (p210) located in the cytoplasm that has a strong capacity to activate tyrosine kinase resulting in the activation of several downstream signals that transform hematopoietic stem cells into leukemic cells. Thus, currently, tyrosine kinase activity is thought to play a central role in the pathogenesis of CML [1]. Besides leukemia induced factors, other risk factors contribute to the CML including lower socioeconomic status, occupational exposure to benzene, formaldehyde, high doses of ionizing radiation among the atomic bomb survivors, other risk factors such as alcohol abuse, obesity, weight gain during adulthood and effects of preservatives or pesticides used in the food industry causes CML [2, 3]. Clinically 50% of CML patients are asymptomatic but remaining present with anemia, splenomegaly, fever, bleeding tendency, hepatomegaly, lymphadenopathy, and complications such as renal failure, hearing loss, and priapism. Laboratory diagnosis includes complete blood count, peripheral blood examination, and bone marrow examination, and it shows low hemoglobin, increased total WBC count, thrombocytopenia, or normal platelet count or thrombocytosis. The peripheral blood smear shows an increasing number of mature and immature granulocytes (myelocytes, metamyelocytes, and band cells) [4, 5]. The CML being the commonest leukemia in Asia needs proper clinico-hematological profiling and early diagnosis and treatment to improve survival rate in CML [6]. The present study was conducted to evaluate the clinico-hematological parameters, clinical presentations, and frequencies of three phases of CML.

Material and methods
This study was conducted in the Department of Pathology, Gajra Raja Medical College, and Jayarogya Hospital, Gwalior for one-year duration. The cases were selected from patients visiting the In and Outpatient department with the provisional diagnosis of chronic myeloid leukemia. In this study, all newly diagnosed CML patients (based on the hematological ground) were included. In all the cases detailed history was taken and clinical findings were noted and the following investigations were done. Complete blood counts (by Mindray BC 5000), was done using EDTA blood. A peripheral blood smear was made on clear glass slides with a fresh finger-prick blood sample. Smears were fixed and stain by Leishman's.

stain. After completion of the investigation, patients were categorized into various CML phases based on the World Health Organization (WHO) criteria. The chronic phase (CP) was defined as myeloid blasts less than 10% in peripheral blood smear or bone marrow. The accelerated phase (AP) was defined as blast 10%-19 of white blood cells: persistent thrombocytopenia (<1 lac/cumm) unrelated to therapy; or persistent thrombocytosis (>1 lac/cumm) unresponsive to therapy. The blast crisis (BC) phase was defined as peripheral blood blasts (≥20%) in peripheral white blood cells or nucleated bone marrow cells.

Results

In our study total, 41 cases of CML were identified, including 23 (56.09%) male and 18 (43.90%) female (Table 1) with male to female ratio of 1.27:1 and age of patients ranged from 14 years to 66 years (Table 2). The first and major presenting clinical feature observed was anemia that was evident in 39 patients (95.12%) followed by splenomegaly in 35 patients (85.36%) and finally loss of weight was encountered in 21 (52.21%) patients as the first clinical feature (Table 3). The hemoglobin values are shown in (Table 4). In CML, a total 20 cases (48.78%) showed hemoglobin between 9.1-12 mg/dl, 18 patients (43.90%) between 6.1-9 mg/dl. Peripheral blood examination in most of these patients showed normocytic normochromic RBCs with occasional nucleated RBCs (nRBCs) while two cases showed dimorphic blood pictures. In the patients of CML, 20 (48.75%) cases showed total leukocyte count between 101 $x10^9$- 200 $x10^9$ /cumm and 10 (24.39%) patients had total leukocyte count between 50 $x10^9$-100 $x10^9$/cumm (Table 5). Total 28 cases (68.29%) presented with platelet count > 150 $x10^9$ /cumm. (Table 6) There were 38 cases (92.68%) in the chronic phase and 03 (7.31%) cases in the accelerated phase. No case was found in the blast crisis phase of CML.

Table 1: Sex-wise distribution of chronic myeloid leukemia (n=41)

S.N.	Male	Female
1	23 (56.09%)	18 (43.90%)

Table 2: Age-wise distribution of chronic myeloid leukemia (n=41)

S.N.	Age in years	CML (n=41)	Percentage (%)
1	0-15	1	2.43
2	16-30	7	17.07
3	31-45	24	58.53
4	>45	9	21.95

Table 3: first presenting clinical features in patients of CML (n=41)

S.N.	First presenting clinical feature	CML (n=41)
1	Symptoms due to anemia (pallor, fatigue, lethargy, dizziness, body aches)	39 (95.12%)
2	Splenomegaly	35 (85.36%)
3	Loss of weight	21 (52.21%)
4	Fever	08 (19.51%)
5	Abdominal discomfort	06 (14.63%)
6	Difficulty in breathing	06 (14.63%)
7	Asymptomatic (Diagnosed during routine checkup)	03 (07.31%)

Table 4: Hb% in patients of chronic myeloid leukemia (n=41)

S.N.	Hb (gm/dl)	Patients of CML (n=41)
1	<6	19 (2.43%)
2	6.1 - 9	18 (43.90%)
3	9.1 - 12	20 (48.78%)
4	>12	02 (4.87%)

Table 5: Total leukocyte count in chronic myeloid leukemia (n=41)

S.N.	TLC /cumm ($x10^9$)	CML (n=41)
1	11-50	04 (9.75%)
2	51-100	10 (24.39%)
3	101-200	20 (48.75%)
4	>200	07 (17.07%)

Table 6: Platelet counts in chronic myeloid leukemia (n=41)

S.N.	Platelet count /cumm ($x10^9$)	CML (n=41)
1	< 50	02 (4.87%)
2	51-100	02 (4.87%)
3	101-150	09 (21.95%)
4	>150	28 (68.29%)

Table 7: Phase wise distribution of CML based on Blast cell count (n=41)

S.N.	Blasts cells (%)	Phases	CML (n=41)
1	<10	Chronic	38 (92.69%)
2	10-19	Accelerated	03 (7.31%)
3	>20	Blastic	00

Discussion

In the present study, most of the patients 24/41 (58.53%) were in 31- 45 years of age group. Ganesan P *et al.,* so found the median age of CML patients in India to be 35 years [7]. Male preponderance was seen with the male-female ratio being 1.27:1. Similar findings were observed in the study conducted by R *et al*. [8]. In our study majority of cases presented with signs and symptoms of anemia, weight loss, and fever. Similar features were also observed by Bhutani M *et al.,* and Prasad RR *et al.,* [9, 10]. The frequency of chronic phase and accelerated phase was 92.68% and 7.21% respectively in the total 41 cases suffering from CML. Similar finding was observed by Chang F *et al*. [11].

Limitation

No, follow up with confirmatory tests like cytogenetic or flow cytometry could be done due to the unavailability of resources and poor affordability.

Conclusion

Chronic myeloid leukemia is a common neoplasm of hematopoietic cells in India and diagnosis is almost always certain on clinical and peripheral blood examination and in most instances it does not require any advanced technique for diagnosis.

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