Section: Pathology

Original Research Article

A CROSS SECTIONAL STUDY TO ASSESS THE CLINICOHEMATOLOGICAL PROFILE OF HAEMATOLOGICAL MALIGNANCIES AT A TERTIARY CARE CENTER.

Swapnil Galat[1], Keshav Pagrut[2], Farheen Tadvi[3]

[1]Assistant Professor, Department of Pathology, Shri Vasantrao Naik Government Medical College, Yavatmal, India.
[2]Associate Professor, Department of Pathology, Shri Vasantrao Naik Government Medical College, Yavatmal, India.
[3]Assistant Professor, Department of Pathology, Shri Vasantrao Naik Government Medical College, Yavatmal, India.

Received *: 17/01/2025*
Received in revised form *: 06/03/2025*
Accepted *: 22/03/2025*

Corresponding Author:
Dr. Swapnil Galat,
Associate Professor, Department of Pathology, Shri Vasantrao Naik Government Medical College, Yavatmal, India.
Email: swapnilgalat@gmail.com

DOI: 10.70034/ijmedph.2025.1.325

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (1); 1737-1743

ABSTRACT

Background: The haematological malignancies are a group of cancers that arise from a malignant transformation of cells of the bone marrow or the lymphoid tissues. The basic pathogenesis in haematological malignancies is mutation in somatic cells due to various agents like viruses, radiation exposure, and chemicals causing disturbances in cell division or lifespan of cells or precursors. These are characterized by widespread, rapid and disorderly proliferation of leukocytes and their precursor and by the presence of immature leukocytes in blood often in very large numbers. The present study was carried out to know the prevalence and the pattern of various hematological malignancies presenting at a tertiary care center including their clinical profile, hematological profile and presentation.

Materials and Methods: This was an observational prospective study carried over a period of 2 years at a tertiary care hospital. All cases of suspected haematological malignancies admitted at tertiary care centre were included in this study while already diagnosed cases were excluded. Clinical history, systemic examination details of all identified cases were recorded from patient's case records. Investigations like CBC, Peripheral Blood Smear examination were carried out and whenever necessary Bone marrow aspiration smears were analysed.

Results: 68 patients were included in this study. Age range was 3 years to 80 years with median age of 39 years. Maximum number of cases were in the age group of 31 to 45 years (26.47%) followed by 16-30 years age group (22.05). Male preponderance was noted in this with male to female ratio of 1.7:1. Majority had generalised weakness, moderate anemia, raised total leucocyte count and low platelet count. The most common haematological malignancy was Acute Myeloid Leukemia (27.94%) followed by Chronic Myeloid Leukemia (25%) and Acute Lymphoblastic Leukemia (20.58%).

Conclusion: The spectrum of haematological malignancies both in children and adults is very wide and relatively different in the developing world than the developed countries occurring at younger age with male preponderance. The present study concludes that detailed primary haematological investigations are helpful for the confirmatory diagnosis and understanding the disease process.

Keywords: Haematological malignancies, Investigations, Diagnosis.

INTRODUCTION

The haematological malignancies are a group of cancers that arise from a malignant transformation of cells of the bone marrow or the lymphoid tissues.[1] These often produce increased number of immature or abnormal leucocytes which supress the

production of normal blood cells leading to anaemia and other symptoms. These are groups of heterogenous disorders that can be distinguished from each other by various factors like origin, incidence, pathogenesis, genetic abnormalities and clinical outcomes. The basic pathogenesis in haematological malignancies is mutation in somatic cells due to various agents like viruses, radiation exposure, and chemicals causing disturbances in cell division or lifespan of cells or precursors. These are characterized by widespread, rapid and disorderly proliferation of leukocytes and their precursor and by the presence of immature leukocytes in blood often in very large numbers. They are classified into several common subtypes, generally consisting of leukemia, multiple myeloma, non-Hodgkin lymphoma, and Hodgkin lymphoma with the other hematological malignancies being polycythaemia vera, myelodysplastic syndrome, and primary myelofibrosis.[2] Hematological malignancies make up 20% of the diagnosis of cancer, a leading cause of death globally.[3]

Several classification systems have been published to subdivide haematological malignancies. In 2001 the World Health Organization (WHO) published a classification of hematopoietic and lymphoid tissues malignancies which was based on multiple information, such as clinical, morphologic, biologic, immunophenotypic and genetic features.[4,5] In 2008, the WHO published a new classification for hematopoietic and lymphoid neoplasms in conjunction with the Society for Hematopathology and the European Association of Hematopathology.[4,6] This classification was revised in 2017. The 5th edition of classification was published in 2022. This classification structure follows a lineage-based framework, flowing broadly from benign to malignant and branching down to category, family, type (disease/tumour), and subtype. Where possible, a triad of attributes was systematically applied and included: lineage + dominant clinical attribute + dominant biologic attribute.[7]

There are different patterns of distribution of these malignancies in various regions of the world, little is known about their prevalence and distribution in our environment. The present study was carried out to know the prevalence and the pattern of various hematological malignancies presenting at a tertiary care center including their clinical profile, hematological profile and presentation.

MATERIALS AND METHODS

This was an observational prospective study carried over a period of 2 years at a tertiary care hospital. All cases of suspected haematological malignancies admitted at tertiary care centre were included in this study while already diagnosed cases were excluded. Clinical history, systemic examination details of all identified cases were recorded from patient's case records. The required quantity of blood samples were collected in K3EDTA vacutainers for various investigations to be carried out. The sampled were processed on Mindray BC-6200 6 Part Blood cell counter and complete hemogram details like haemoglobin, total and differential leucocyte count, platelet count and scattergram findings were recorded. Peripheral blood smears were prepared by finger prick and stained by stains like Leishman's stain, Field Stain. The examination of peripheral blood smears were done, provisional diagnosis was prepared. Special stains like myeloperoxidase, periodic acid Schiff were done in all cases for confirmation. After taking informed consent bone marrow aspiration was done in most cases for confirmation and in cases that were presented with pancytopenia or bicytopenia. FAB classification was used for analysis of myeloid and lymphoid neoplasm. WHO classification was not used due to lack of immunophenotypic, genetic and molecular tests facilities. The data were entered into MS-excel sheet, tabulated and was analysed using percentage, means and median. The median was calculated by non-normalised data.

RESULTS

68 patients fulfilling the inclusion criteria were included in this study over a period of 2 years. Age range was 3 years to 80 years with mean age (+-SD) of 37.3 (+-20.86) years and median age of 39 years. Majority of the cases were belonging to the age group of 31 to 45 years i.e. 18(26.47%). Fig. 1 shows age-wise distribution of cases. Among 68 cases 43 cases were males and 25 were females with male to female ratio of 1.7:1.

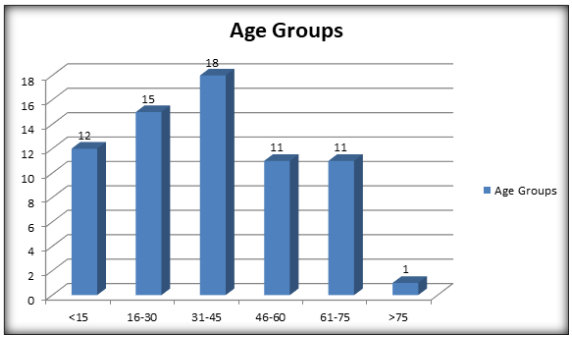


Figure 1: Age-wise distribution of cases

Out of 68 cases, maximum number of cases presented with chief complaints of generalized weakness which was seen in 45 (66.17%) cases, followed by fever and abdominal pain which constituted 37 (54.41%), 23 (33.82%) cases respectively. The most common clinical finding in this study was pallor seen in 60 (88.23%) cases followed by splenomegaly and hepatomegaly seen in 42 (61.76%) and 18 (26.47%) cases respectively. Table no. 1 shows presenting complaints and

clinical findings in cases of haematological malignancies.

Table 1: Presenting complaints and clinical findings in cases of haematological malignancies

Presenting complaints	**No. of cases**	**Percentage**
Generalized weakness	45	66.17%
Fever	37	54.41%
Abdominal Pain	23	33.82%
Anorexia and weight Loss	12	17.64%
Bone and Joint Pain	4	5.88%
Giddiness	2	2.94%
Breathlessness	2	2.94%
Bleeding tendencies	2	2.94%
Clinical findings	**No. of cases**	**Percentage**
Pallor	60	88.23%
Splenomegaly	42	61.76%
Hepatomegaly	18	26.47%
Lymphadenopathy	14	20.58%
Icterus	6	8.82%
Bleeding tendencies	2	2.94%
Oedema	1	1.47%

Out of 68 cases studied, maximum cases, [29 (48.24%)] had moderate anaemia [Hb 6.1-8 gm%]. Haemoglobin ranged from 3.4 gm% to 19.6 gm% (Median: 7 gm %) (Mean:7.04 gm %). In Total Leucocyte Count (TLC) 34 (50%) cases had count of >50001/cumm. TLC ranged from 1000 – 298000/cumm, (Median: 50200/cumm) (Mean: 72542.64cumm). Lowest TLC was 1000/cumm seen in a case of multiple myeloma. Out of 68 cases studied, maximum number of cases, i.e. 20 (29.41 %) cases had Platelet count >150000/cumm. Platelet count ranged from 10000- 616000/cumm. Table no. 2 shows distribution of cases according to CBC parameters values.

Table 2: Distribution of cases according to CBC parameters values

CBC Parameter	**No. of cases**	**Percentage**
Hemoglobin (gm/dl)		
<6.0	21	30.88%
6.1-8	29	42.64%
8.1-11	17	25%
>11	1	1.47%
Total Leucocyte Count (/cmm)		
<4000	14	20.58%
4001-11000	4	5.88%
11001-50000	16	23.52%
>50000	34	50%
Platelet Count (/cmm)		
<25000	9	13.23%
25001-50000	15	22.05%
50001-75000	11	16.17%
75001-100000	8	11.76%
100001-150000	5	7.35%
>150001	20	29.41%

Peripheral blood smears were examined in all cases where most common RBC morphology seen was normocytic normochromic in 29 (42.64%) cases followed by microcytic hypochromic picture in 27 (39.70%) cases. Other morphologies obtained were anisopoikilocytosis in 11(16.17%), dimorphic blood picture in 10(14.70%), Rouleaux formation in 4(5.88%), Macrocytic in 2(2.94%) cases.

Out of 68 cases studied, haematological malignancies were diagnosed on Peripheral blood smears in 36 (52.94%) cases while in 30 (44.11%) cases haematological malignancies were diagnosed on bone marrow aspiration smears and 2 cases required bone marrow biopsy due to hypocellularity and dry tap on bone marrow aspiration. Bone marrow aspirate was hypercellular in 30 cases, hypocellular in 1 and dry tap in 1 case.

The most common haematological malignancy found in this study was Acute Myeloid Leukemia found in 19 (27.94%) cases followed by Chronic Myeloid Leukemia in 17 (25%) cases and Acute Lymphoblastic Leukemia in 14 (20.58%) cases. Fig. no. 2 shows distribution of study subjects according to the type of malignancy.

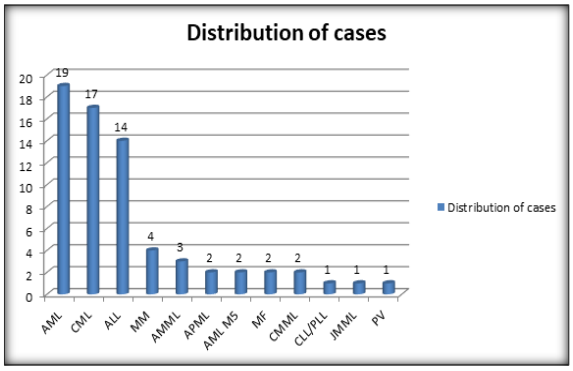


Figure 2: Distribution of study subjects according to the type of malignancy

Abbreviations in figure 2 are as Acute myeloid leukemia (AML), Chronic myeloid leukemia (CML), Acute Lymphoblastic leukemia (ALL), Multiple myeloma (MM), Acute myelomonocytic leukemia (AMML), Acute promyelocytic leukemia (APML), Myelofibrosis (MF), Chronic myelomonocytic leukemia (CMML), CLL/PLL (Chronic lymphocytic leukemia/prolymphocytic leukemia), Juvenile myelomonocytic leukemia (JMML), Polycythemia Vera (PV)

We have found 19 cases of AML M1 and M2 from which maximum i.e. 7 cases were in 31-40 yrs age group and male to female ratio was 1.1:1. There were 17 cases of CML from which maximum (12) cases were observed after 40 years of age with median age of 52 years and male to female ratio of 1.8:1, one case was in blastic crisis phase with blast count of 45% while remaining 16 cases were having chronic phase. Out of 14 cases of ALL maximum (10) cases were observed in <10 years age group, median age was 7.5 years and male to female ratio of 3.6:1, there were 12 cases of ALL L1 and 2 cases of ALL L2. Table no.3 shows the association between the type of malignancy, age group and sex.

Table 3: Association between the type of malignancy, age group and sex

Sr. No.	Type of malignancy	Age group in years								Total	Sex	
		<10	11-20	21-30	31-40	41-50	51-60	61-70	71-80		Male	Female
1	AML (M1 & M2)	0	3	4	7	3	1	1	0	19	11	10
2	ALL (L1 & L2)	10	1	1	1	1	0	0	0	14	11	3
3	AMML	0	1	1	0	0	0	1	0	3	3	0
4	APML	0	0	1	0	0	1	0	0	2	2	0
5	AML M5	0	0	0	0	0	2	0	0	2	0	2
6	CML	0	1	2	2	3	4	5	0	17	11	6
7	CMML	0	0	0	1	0	1	0	0	2	2	0
8	JMML	1	0	0	0	0	0	0	0	1	0	1
9	CLL	0	0	0	0	0	0	1	0	1	1	0
10	MF	0	0	1	1	0	0	0	0	2	1	1
11	PV	0	0	0	0	0	0	1	0	1	1	0
12	MM	0	0	0	0	1	0	2	1	4	1	3

Bone marrow aspiration was done in 32 cases in which there was decreased or slightly increased total leucocyte count with abnormal WBC flag on CBC report and atypical cells were seen on peripheral blood smear. Out of 32 cases, 9 cases of AML, 7 cases of ALL, 4 cases of multiple myeloma, 3 cases of AMML, 2 cases of APML, 2 cases of CMML, 1 case each of AML M5, JMML and PV were diagnosed on bone marrow aspirate while 2 cases of myelofibrosis were diagnosed on bone marrow biopsy due to hypocellularity and dry tap on bone marrow aspirate. Special staining was done in 61 cases where MPO positivity was seen in 38 cases, PAS positivity in 11 cases and PAS negativity in 4 cases.

Table 4: Shows bone marrow aspirate findings in various haematological malignancies

BM aspiration finding	Cellularity	M:E ratio	Erythroid series	Myeloid/Lymphoid series	Megakaryocyte series
AML	Hypercellular	Increased	Supressed	Hyperplastic, myeloblasts	Normal
ALL	Hyper-cellular	Increas-ed	Supressed	Hyperplastic, lymphoblasts	Suppressed
MM	Hypercellular	Normal	Supressed	Supressed with presence of >20% plasma cells.	Supressed
AMML	Hypercellular	Increased	Supressed	Hyperplastic with myeloblasts, monoblasts, promonocytes, monocytes	Normal
APML	Hypercellular	Increased	Supressed	Hyperplastic with hypergranular promyelocytes	Normal
CMML	Hypercellular	Increased	Normal	Hyperplastic with myeloid and monocytic proliferation	Hyperplastic, Dysmegakaryo-poiesis
AML M5	Hypercellular	Increased	Supressed	Hyperplastic, monoblasts	Supressed
JMML	Hypercellular	Increased	Supressed	Hyperplastic with myeloid and monocytic proliferation	Supressed
PV	Hypercellular	Increased	Hyperplastic with micronormoblastic maturation	Hyperplastic with all cell lineages	Normal

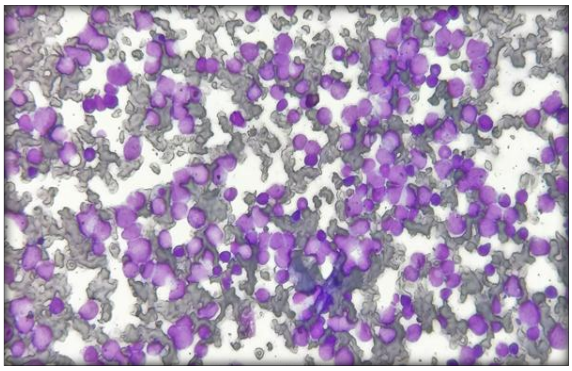
DISCUSSION

Haematological malignancies incidence rate is increasing in our country due to improvement in statistics. They have varied presentation according to geographical regions, life styles, economic conditions and poverty rate8. According to 2019 data leukemia is the most common haematological malignancies with higher mortality rate.[9] There are various studies conducted on various aspects of haematological malignancies. In our study total 68 cases with haematological malignancies were studied. Mean age in our study was 37.3 years with median age of 39 years which is comparable with studies done by Amina Ismaeel et.al,[10] and Hossain MS et.al,[11] Age range in our study was 3 years to 80 years which is in concordance with study done by Suganthi Venkatesan et.al. (2 to 70 years).[12] The patients in the age group of 31–45 years were most common followed by the 16–30 years group. In the study done by Vinayak Pai et.al,[13] most cases belonged to the age group 36–65 years while in study by Ahirwar R.et.al,[14] out of 73 cases 21 cases (28.77%) were of age group 16 to 30 years, 19 cases (26.03%) were of age group 31 to 45 years. The difference observed could be due to geographical variation of cases. Most of the patients in our study were males (63.23%) and females were 36.76% with male to female ratio of 1.7:1. The studies done by Vinayak Pai et.al,[13] Radha Rathee et.al,[3] Shafaq Maqsood et.al,[15] found male preponderance. The incidence of malignancies in males is increasing due more exposure to occupational and environmental hazards.

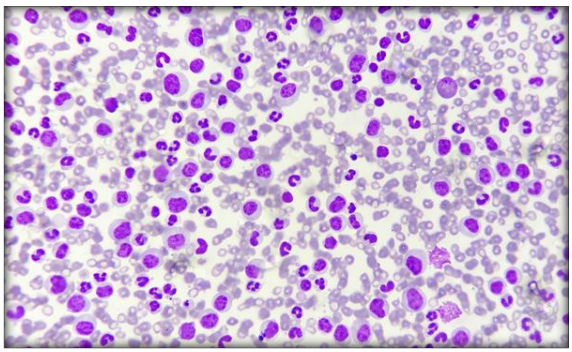
The most common presenting complaint in this study was generalized weakness (66.17%) followed by fever (54.41%) and abdominal pain (33.82%). Fatigue was the most common presenting complaint followed by fever in study done by Suganthi Venkatesan et.al,[12] and Vinayak Pai et.al.[13] In this study pallor (88.23%) was the most common clinical finding followed by splenomegly (61.76%) and hepatomegaly (26.47%) which is similar to studies done by Suganthi Venkatesan et.al,[12] Vinayak Pai et.al,[13] and Radha Rathee et.al.[3]

After analysis of CBC reports, majority of the cases (98.52%) had Hb <11 gm/dl while increased Hb (19.7 gm/dl) was seen in case of PV. TLC was increased (>11000/cmm) in 73.52% cases and low platelet count (<150000/cmm) was seen in 70.58% cases. These findings are consistent with other studies.

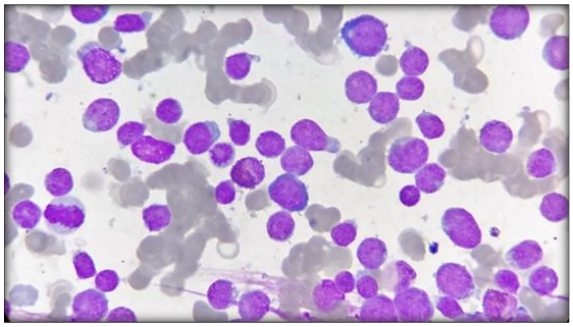
AML (27.94%) was the most common haematological malignancy found in this study followed by CML (25%) and ALL (20.58%). This is in concordance with the studies by Amina Ismaeel et.al,[10] and Sansiya BS et.al,[16] while in the study done by Ahirwar R.et.al,[14] CMlL was the most common followed by ALL and AML. The other cases were of Multiple Myeloma (5.88%), AMML (4.41%), APML (2.94%), AML M5 (2.94%), Myelofibrosis (2.94%), CMML (2.94%), CLL/PLL (1.47%), JMML (1.47%) and Polycythemia Vera (1.47%). In the study by Vinayak Pai et.al,[13] 2 cases of APML, 3 cases of CLL and 8 cases of MM were reported. MM was the fourth most common haematological malignancy in the study by Elidrissi Errahhali et. al.[17] Kumar R et al,[18] found myelofibrosis as cause of pancytopenia in their study in 1.2% of cases. Khunger JM et al,[19] found myelofibrosis as cause of pancytopenia in 1% of cases in their study. Nigam R et al. (2014),[20] in their study found 1 case of polycythemia vera while Bashir N et al (2018),[21] found 4 cases of polycythemia vera in their study. 6.1% cases of AMML were reported in the study by Sansiya BS et.al,[16] while 2 cases of AML M5 were reported in study by Suganthi Venkatesan et.al.[12] We did not find any study reporting JMML and CMML. Among ALL cases, ALL-L1 was most common in children and ALL-L2 was seen in adults. Confirmation of diagnosis by flow cytometry, immunohistochemical and cytogenetics studies could not be done due to unavailability of these facilities and there was no follow up of patient to monitor prognosis.



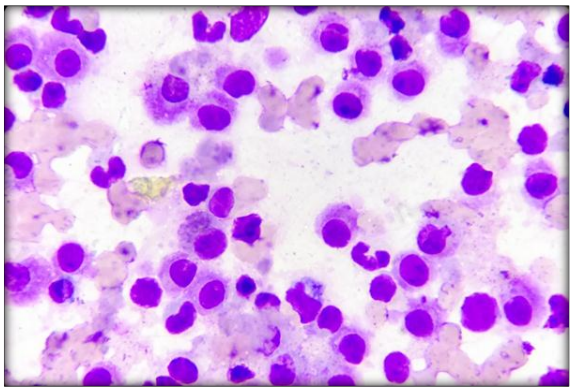
Bone marrow aspiration smear showing hypercellularity with myeloblasts– AML - M1. (Leishman's stain, 40x).



Peripheral blood smear showing all maturation stages of myeloid series CML-CP. (Leishman's stain, 40x).



Bone marrow aspiration smear showing lymphoblast– ALL-L1. (Leishman's stain, 100x).



Bone marrow aspiration smear showing increased number of plasma cells- Multiple Myeloma. (Leishman's stain,100x).

CONCLUSION

Haematological malignancies occur in relatively younger age with median age at diagnosis of 39 years. Male were more affected than females with male to female ratio of 1.7:1. Age and sex distribution of patients in this study was consistent with findings in other studies. The majority of patients had lower haemoglobin, high leukocyte count and lower platelet count, fever, pallor, generalized weakness and bodyaches. AML was the most common reported primary hematologic malignancy, followed by CML; whereas CLL/PLL, JMML, PV was the least common type. The incidence of AML and myeloproliferative neoplasms was more common in adults while that of ALL was more common in children. The present study concludes that detailed primary haematological investigations like CBC reports, Peripheral Blood Smear along with bone marrow aspiration and special staining are helpful for understanding the disease process. It is an important step to arrive at the confirmatory diagnosis of broad-spectrum haematological malignancies. Further studies in peripheral parts of India are needed to understand the epidemiology and identify risk factors of these neoplasms for implementing tailored preventive strategies more effectively.

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