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Clinicopathological Study of Leukaemia in Gauhati Medical College & Hospital, Assam, India: A One Year Retrospective Study

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Abstract: ***Introduction: Leukemias are neoplastic proliferations of haematopoietic stem cells and form a major proportion of haematopoietic neoplasms that are diagnosed worldwide. Typing of leukemia is essential for effective therapy because prognosis and survival rate are different for each type and sub-type Aims: To carry out the incidence of acute and chronic leukemias presenting in various departments of GMCH, Guwahati, Assam. Methods: It was a retrospective study of 182 patients carried out in the department of Pathology over a period of one year between February 2017 and January 2018. Diagnosis was based on peripheral blood count, peripheral blood smear and bone marrow examination (as on when available- marrow sample) for morphology along with cytochemical study whenever possible. Results: In the present study, commonest leukemia was Acute myeloid leukemia (AML) followed by Acute lymphoid leukemia (ALL), chronic myeloid leukemia (CML) and chronic lymphoid leukemia (CLL). Out of total 182 cases, 96 were male and 82 were females with Male: Female ratio is 1.11: 1. Acute lymphoid leukemia was the most common type of leukaemia in the children and adolescents. Myeloid neoplasms were most common in adults. Conclusion: Detailed hematological analysis including peripheral blood and bone marrow aspiration smears examination with cytochemical stains and cytogentic analysis are necessary for early and definite diagnosis and effective management of hematological malignancies.***

Keywords: Acute and Chronic leukaemia, Tertiary care hospital.

1. Introduction

Leukemias are a group of hematological malignancies in which there is unregulated and rapid proliferation of leukemic progenitor cells. This results in replacements of normal hematopoietic precursor cells of erythroid, megakaryocytic, myeloid or lymphoid lineage by proliferating leukemic cells in bone marrow manifesting in the form of anemia and/or thrombocytopenia with leukocytosis or in form of pancytopenia with presence of immature leukocytes in peripheral blood. Leukemia is the eleventh most common cancer worldwide with about 257, 000 new cases each year [1]. Leukaemias form a significant percentage of haematological disorders and affects individuals of all age groups throughout the world, but the incidence of disease and the frequency of various morphological types and sub-types have been found to be differing in different countries.[2] Leukemia are of two types; acute and chronic. Acute leukemias are; acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). In childhood, ALL is most common type than AML. In India, the incidence of ALL and AML are 35% and 15% of all hematological malignancies respectively. Chronic leukemias are classified into chronic myeloid leukemia (CML) and chronic lypmphocytic leukemia (CLL). [3, 4]A number of recurrent genetic abnormalities play an important role in malignant transformation of leukemic cells. Diagnosis of different leukemia now depends on cellular morphological details and assessment of genetic changes in subtypes. French American British (FAB) morphologic classification of leukemia has been used since many years. Morphological assessment usually requires blood and bone marrow aspiration smears and marrow trephine biopsy sections with special cytochemical stains. [5, 6, 7] If not treated, leukemia results in death within a few weeks or months. Therefore it is important that leukemia must be diagnosed as soon as possible so that the treatment can be started in early stage of disease when leukemic burden is low. The objectives of the present study were to determine the presenting clinical sign and symptoms and broadly categorize different types of leukaemia attending the outpatient department of Gauhati Medical College.

2. Literature Survey

Gajender Singh et al [8] in their study at PGIMS, Rohtak, Haryana, India diagnosed a total of 356 patients over a period of 5years. In their study, 66.8% of patients had acute leukemia while 33.2% had chronic leukemia Acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) were found in 29.7% and 37.3% of the patients respectively. Of chronic type leukemia, 28.3% patients had chronic myeloid leukemia (CML) and only 4.7% had chronic lymphocytic leukemia (CLL).Overall male preponderance was found in the study with a percentage of 56.46% of total cases and 43.54% in females. Male to female ratio was 1.5:1.

Nighat Nasim et al[9] in their study conducted over a period of 2years in PGMI, Lahore found 45 cases of leukaemia and observed that acute leukemia was more prevalent than chronic leukaemia. The ratio of acute (80%) and chronic leukaemias (20%) was 4:1. Male to female ratio was 1.3: 1. Most of the patients (42%) were below the age of 15 years.

ALL (49%) was more common than AML (31%). Among chronic leukaemias, CML (16%) was more common than CLL (2%) and CMML (2%).

Jaya Bhaskar Baviskar et al[10] in her study at Pravara Institute of Medical Sciences, Loni, Maharashtra diagnosed 156 cases of leukaemia over a period of 5 years and observed that the commonest leukemia was chronic myeloid leukemia (CML) (33.97%) followed by Acute lymphoid leukemia (ALL) (26.28%), Acute myeloid leukemia (AML) (23.07%) and then chronic lymphoid leukemia (CLL) (15.38%). Out of total 156 cases, 90 were male and 66 were females with Male: Female ratio is 1.36:1. Acute lymphoid leukemia was the most common type of leukaemia in the children and adolescents. Myeloid neoplasms were most common in adults.

Jagannath Jatav et al[11] in their study at Gajra Raja Medical College, Gwalior found acute leukaemia in 83cases over a period of one year. Of these 83 cases, 46 (55.4%) were AML and 37 (44.6%) were ALL. 53 cases (63.85%) were male whereas 30 cases (36.15%) were female. Male-female ratio was 1.76:1. Highest number of cases which comprising 25.3% (83/21) of total cases belonged to 11-20 years of age group followed by 20.28% and 19.27% belonged to 21-30 years and 0-10 years of age group respectively.

Sadia Sultan et al [12] in their study at Liaquat National Hospital, Pakistan diagnosed a total of 125 patients with de novo AML during a period of 5 years. There were 76 males and 49 females (ratio 1.5:1), with an age range between 15 and 85 years and a mean age of 38.8±20.1 years. The major complaints were fever (72.8%), generalized weakness (60%), bleeding (37.6%) and dyspnea (12%). Physical examination revealed pallor in 56.8%, splenomegaly and hepatomegaly in 16% and 12.8%, respectively, and lymphodenopathy in 10.4%. The mean hemoglobin was 8.19±2.12g/dl, a mean total leukocyte count of 43.1±68.5x109/l and a mean platelet count of 62.3±78.6x109/l.

3. Materials and Methods

The present study was a retrospective study for a period of one year (February 2016 to January 2017). During this period, records of all patients attending the OPD and casualty of Gauhati Medical College & Hospital with a history of short duration of clinical features like pallor, fatigue, bleeding in the form of bruising, petechiae or ecchymotic spots, persistent fever, bone or joint pains with or without organomegaly and/or lymphadenopathy and who were later diagnosed as leukaemia were taken up for the study. A detailed clinical history regarding nature and duration of illness, loss of weight, significant family history and drug history, if any, was taken. This was followed by detailed general physical and systemic examination. Other primary hematological malignancies like lymphomas and plasma cells disorders and metastatic deposits in marrow were also excluded.

Inclusion criteria: Patients presenting with a history of short duration of clinical features like pallor, fatigue, bleeding in the form of bruising, petechiae or ecchymotic spots, persistent fever, bone or joint pains with or without organomegaly and/or lymphadenopathy which were later diagnosed as leukaemia in peripheral blood examination were included in the study. Only newly diagnosed cases were included in the study.

Exclusion criteria: Known cases of leukaemia or who were previously on treatment for leukaemia were excluded from the study

A total of 182 patients with acute and chronic leukemia reported during the study period were included in the study. These patients were evaluated especially regarding age, gender and chief complaints. Diagnosis was made on findings of Complete blood count (i.e. Haemoglobin, Total leucocyte count and Platelet count) which was done by automated cell counter; peripheral blood smear stained by Leishman stain and bone marrow aspiration smear (in selected cases)stained by Geimsa stain. Cytochemistry studies like myeloperoxidase (MPO), Periodic acid schiff stain (PAS) and Sudan black B (SBB) were done to differentiate myeloid and lymphoid leukemia. These stains were prepared and used as per the guidelines endorsed in Practical Haematology Dacie and Lewis 11th edition. Then all cases were diagnosed and classified, as acute myeloid leukemia, acute lymphoid leukemia, chronic myeloid leukemia and chronic lymphoid leukemias.

4. Results

In our study, 78.57% of patients had acute leukemia while 21.43 % had chronic leukemia.

Table 1: Percentage of acute/ chronic leukemias

Type of leukemia	Total no. of cases	Percentage
Acute leukemia	143	78.57
Chronic leukemia	39	21.43
Total	182	100

Acute myeloid leukemia (AML) and Acute lymphoblastic leukemia (ALL) and were found in 53.85% and 24.72% of the patients respectively. Of chronic type leukemia, 18.68 % patients had chronic myeloid leukemia (CML) and only 2.75 % had chronic lymphocytic leukemia (CLL) (Table 2).

Table 2: Prevalence of different types of acute/ chronic leukemias

Type of leukemia	Total no. of cases	Percentage (%)
AML	98	53.85
ALL	45	24.72
CML	34	18.68
CLL	5	2.75

Overall male (n=96) preponderance was found in our study with a percentage of 53.84% of total cases and 46.16% in females (n= 86). Male to female ratio was 1.11: 1. Male preponderance was observed in AML (56%), ALL (57.78%) and CLL (60%) whereas female preponderance was observed in CML (55.88%)

Table 3: Gender wise distribution of different types of leukaemia

	Male	%	Female	%	Total
AML	55	56	43	44	98
ALL	26	57.78	19	42.22	45
CML	15	44.12	19	55.88	34
CLL	3	60	2	40	05
					182

It was observed from table 4 that, age group found to be most vulnerable for the various leukemias is 0-9 years followed by 30-39 years. AML was commonest in age group of 30-39 years, ALL between 0-9 years of age group. CML were evenly distributed from the age group of 30-49years and peak incidence was found in between 30-39 years followed by 40-49 years, while CLL were more common in the age group of 50-69 years.

Table 4: Age wise distribution for each type of leukaemia

Age	AML	ALL	CML	CLL	TOTAL	%
0-9	10	21	0	0	31	17.03
10-19	13	14	0	0	27	14.8
20-29	20	05	0	0	25	13.7
30-39	22	05	2	0	29	15.19
40-49	18	0	4	0	22	12.17
50-59	12	0	14	2	28	15.14
60-69	01	0	6	2	9	4.9
70-79	01	0	8	1	10	5.5
80-89	01	0	0	0	1	0.5
TOTAL	98	45	45	5	182	

Table 5 depicts the prominent clinical presentations of all the 182 patients of leukaemia. The symptom of patients suffering from leukaemia is variable but by analyzing the cases a common spectrum of presentation was noted. Fever and Generalized weakness were the most common presenting symptoms followed by loss of appetite, bleeding manifestations and bone pain respectively. Pallor was the most frequently observed sign along with bony tenderness, lymphadenopathy and splenomegaly. In AML, the most common presenting clinical feature was fever followed by pallor, generalized weakness, bleeding manifestations, lymphadenopathy, spenomegaly and bone pains. Similarly, fever, generalized weakness and lymphadenopathy were the most common presenting clinical features of patients with ALL. CML patients mostly presented with generalized weakness, splenomegaly, loss of appetite and pallor, whereas most of the patients of CLL were incidentally diagnosed and complained of mostly generalized weakness and loss of appetite and pallor was a common presenting sign followed by lymphadenopathy, splenomegaly and bleeding manifestations in these patients.

Table 5: Frequency of Clinical Features

Types	AML	%	ALL	%	CML	%	CLL	%	Total	%
Fever	85	86.7	37	82.2	18	53	1	20	141	77.47
Gen. Weakness	62	53	31	68.8	30	88.2	4	80	128	70.32
Pallor	72	83.7	28	84.4	20	82.3	3	60	123	67.58
Loss of Appetite	36	36.7	12	26.6	22	64.7	3	60	109	59.89
Bleeding manifestations	66	77.5	26	57.8	3	8.8	1	20	96	52.74
Lymphadenopathy	44	44.9	30	66.6	11	32.3	2	40	87	47.8
Splenomegaly	36	36.7	21	46.6	26	76.5	2	40	85	46.7
Bony Tenderness	36	36.7	29	64.4	10	29.4	0	0	75	41.2

Table-6 shows the laboratory indices in different leukaemias. Out of the total of 182 cases total, 8 cases (4.4%) showed leucopenia (total count< 4000/ cumm), 28 cases (15.38%) had leucocyte count within normal range (4000-11, 000/cumm), 30 cases (16.4%) had leucocyte count between 11, 000-25, 000/cumm. 46 cases (25.2 %) between 25, 000- 50, 000 /cumm, 34 (18.7%) cases had total leucocyte count between 50, 000-1, 00, 000 /cumm whereas 36 cases (19.7%) had total count > 1, 00, 000/cumm. Anaemia was detected in almost 100% of the leukaemic patients. There was severe degree of anemia in 38.40% (n=70) of cases (Hb <6 g/dl), and 43.9 % (n = 80) had moderate degree of anaemia (Hb: 6.1-9 g/dl) while 17.5 % n=32) cases had mild anaemia. No case showed Hb% more than 12gm%. Amongst the leukaemia cases, 20 cases (10.9%) showed platelet count above 1, 00, 000/cumm and another 20 cases (10.9%) showed platelet count between 50, 000-100, 00020/cumm, whereas 62 cases (34%) showed platelet count between 25, 000-50, 000/ cumm and 80 cases (43.9%) showed severe thrombocytopenia with platelet count < 20, 000/ cumm. Amongst the leukaemia cases 30 cases (16.4%) showed blast percentage <20%, 62 cases (34%) showed blast percentage between 20-50%, 53 cases (29.1%) showed blast percentage between 50 -80% and 37 cases (20.3%) had blast percentage of >80%.

Table 6: Frequency of Laboratory indices on reporting

Parameter	Range	No of cases	%
Total count (cells/cubic mm)	<4000	8	4.4
	4000-11, 000	28	15.38
	11, 110-25, 000	30	16.4
	25, 100 -50, 000	46	25.2
	50, 000-1, 00, 000	34	18.7
	>1, 00, 000	36	19.7
Hb (gm%)	<6	70	38.4
	6.1-9	80	43.9
	9.1-12	32	17.5
Platelet (per cubic microlitre)	<20, 000	80	43.9
	20, 001- 50, 000	62	34
	50, 001-1 lakh	20	10.9
	>1 lakhs	20	10.9
% blast	<20%	30	16.4
	20-50%	62	34
	51-80%	53	29.1
	>80%	37	20.3

5. Discussion

In the year of 1857, Virchow probably was the first to classify leukemia. On the pathologic distribution of tumor he distinguished splenic and lymphatic forms of leukemia. (18) The incidence of leukemia has increased considerably and this rise is noticeable because of improved statistics, better case findings with novel technologies which lead to better diagnosis and treatment methods. The incidence of leukemia found to be varying from different geographical areas according to their life styles, economic conditions, and poverty rate. (19)

Majority of the leukaemic cases were Acute leukaemias (78.57%) as per morphological classification. Chronic leukaemias accounted for only 21.43% of leukaemic cases. Similar findings were observed in the study of Singh G et al from Rohtak, Haryana. They reported 66.8% cases of Acute leukaemias and 33.2% cases of chronic leukaemia. Nasim et al found 80% acute leukaemia cases and Humayan et al showed 90% of acute leukaemia cases.

Acute Myeloid leukaemia accounted for 53.85% cases of all leukaemias. While there were only 2.75% cases of Chronic lymphocytic leukaemias.Singh G et al from Rohtak also reported maximum number of cases as AML and CLL accounted for only 4.7% cases. Jatav et al from Gwalior, Madhya Pradesh also reported 55.4% cases of AML. Similar were the findings of Khalid Hassan et al, Laishram et al etc.

When cases were distributed according to gender wise, Male preponderance was seen in all forms of leukaemia except Chronic myelogenous leukaemia. Male: Female ratio was 1.1:1.Similar findings were also observed in the study of Singh G et al who also found a female preponderance in CML cases. Ullah K, Harani MS, Jmili NB et al also found male preponderance in leukaemic cases.

When distributed age wise, Paediatric age group of 0-9 years accounted for maximum number of leukaemia cases (17.03%).Acute lymphoblastic leukaemia was most prevalent in 0-9 years of age group while Acute myeloid leukaemia was most prevalent in 30-39 years of age group. ALL was also the most common subtype in under 15 years of age group in the study of Singh G et al from Rohtak. Similar findings were also seen in the study of Nasim N et al and Gupta R et al. Out of132 cases of AML, Singh G et found 102 cases in adult as compared to pediatric population (30cases).Paul B et al, Nasim N et al also reported similar findings in their study.

Chronic lymphocytic leukaemia was exclusively reported in patients above 50 years. Singh G et also reported all CLL cases in elderly patients. They reported all of the CLL cases in the age group of 41-90 years of age group. A study from AIIMS, New Delhi reported 68.42% of CLL cases in patients of more than 55 years of age.CLL is the most common form of leukaemia affecting adults in western countries. However the incidence of CLL is lower in India (1.95-8.8%). In the present study there were only 5 cases of CLL.

Considering the presenting complaints, Fever, generalized weakness, Pallor were invariably seen in majority of the cases. Bleeding manifestations, splenomegaly, lymphadenopathy were seen in half of the leukaemia cases. Similar symptoms were observed by prior studies conducted in the Indian subcontinent. Khalid et al, Sadia Sultan et al from Lahore, Kakepoto et al from India also found similar presenting complaints. However bleeding manifestations were reported in a higher proportion in Pakistani study (80.4%) of Asif and Hasan et al.

In acute leukaemias extramedullary infiltration of leukaemic cells produces visceromegaly and lymphadenopathy. It was observed in 46.7% of our cases. However Hamid and Nabhi et al reported only 20% of such signs.

Hyperleucocytosis was seen in 19.7% of the cases. Asif and Hasan reported hyperleucocytosis in 11% cases. It is well known that hyperleucocytosis carries a poor prognosis in leukaemia cases. Thrombocytopenia was seen in about 90% of cases. It is a well known manifestation of Acute leukaemias. A Pakistani study found thrombocytopenia in 84% of their cases. Similar finding was seen in another study by Naseem et al.

6. Images

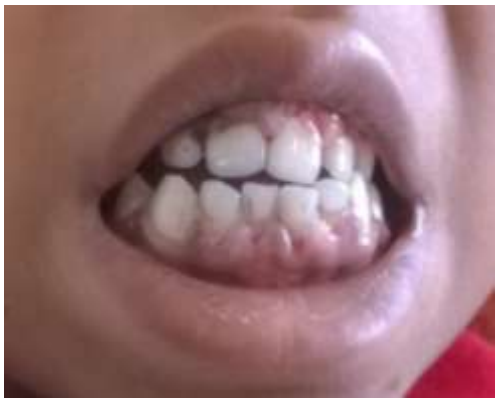

Figure 1: A case of Monoblastic leukaemia (M5) presenting with gum hypertrophy and bleeding manifestation

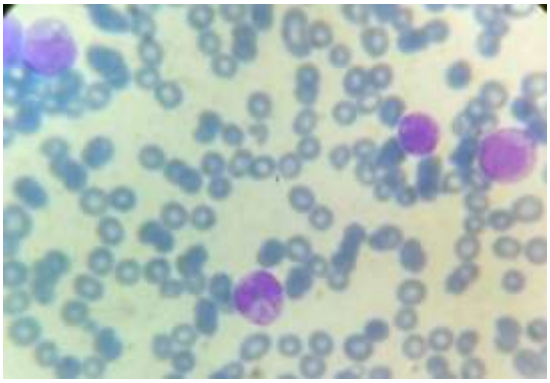

Figure 2: Photomicrograph of a case of Acute Promyelocytic leukaemia (M3) showing a faggot cell and atypical promyelocytes.Leishman 100x10

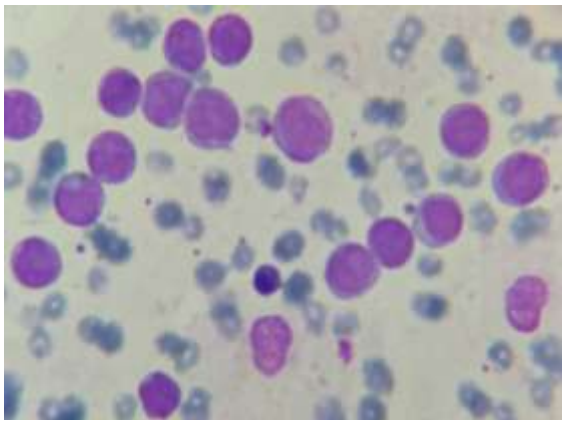

Figure 3: Photomicrograph of a case of Acute Monoblastic leukaemia (M5) showing monoblast, immature as well as mature monocytic forms. Leishman 100x10

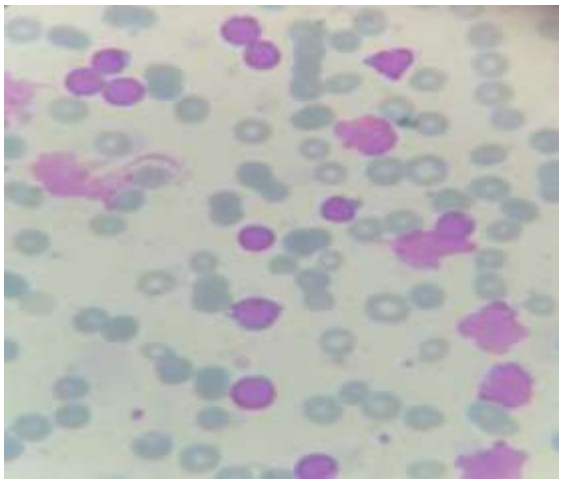

Figure 4: Photomicrograph of a case of Chronic Lymphocytic Leukaemia (CLL) showing mature lymphocytes with many smudge cells. Leishman 100x10

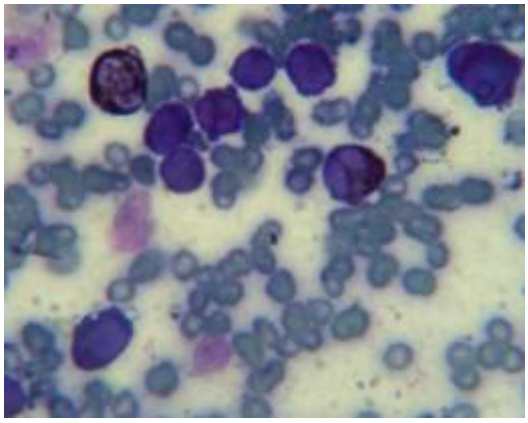

Figure 5: Photomicrograph of a case of Acute Promyelocytic Leukaemia (APML) showing abnormal promyelocytes showing strong positivity for Sudan Black B

7. Conclusion

In India, under the existing circumstances, population screening for the study of leukemia is extremely difficult due to lack of diagnostic and specialized services in periphery. Therefore, we have to depend largely on the hospital based data. Keeping in view the increased amount of morbidity and mortality associated with leukemia, early recognition of signs and symptoms of leukemia can ensure that the disease is diagnosed or at least suspected quite early in its course. This will also ensure timely referral of such patients from primary and secondary health care centers for detailed hematological analysis at a tertiary care center like our institution, where clinicians and hematopathologists can play a vital role in its effective management.

8. Conflict interest

None

9. Declaration of Author

We declared that the study was conducted in GMCH, Guwahati and all liabilities pertaining to claims relating to the content of the article will be borne by the author.

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