



STUDY OF LEUCOCYTE ALKALINE PHOSPHATASE SCORE IN LEUKEMOID REACTION AND CHRONIC MYELOID LEUKEMIA CASES.

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ABSTRACT:

INTRODUCTION: Hematologic conditions such as myeloproliferative disorders and a variety of non-hematologic conditions such as infections, inflammatory states, advanced malignancies, drugs (mainly corticosteroids and recombinant hematopoietic growth factors), severe hemorrhage, splenectomy and tissue ischemia may result in very high white blood cell counts (WBCs).¹ Infection is the most common cause of an elevated WBC, commonly between 10,000 and 20,000/ μ L commonly points to an infectious or it may be due to a reactive process. A very high white blood cell counts (generally $>50 \times 10^9/\mu$ L) may produce a peripheral blood film appearance similar to leukemia (in those patients who do not have leukemia), termed as a leukemoid reaction.²

METHOD: The present study "Study of leucocyte alkaline phosphatase score in leukemoid reaction and chronic myeloid leukemia cases" was conducted in our institution.

Total 50 cases of patients that presented with high WBC count in OPD and admitted in wards were studied.

RESULT: The present study was undertaken to evaluate the significance of peripheral smear and leukocyte alkaline phosphatase score to differentiate leukemoid reaction and chronic myeloid leukemia. Total fifty cases of high WBC count who met the inclusion criteria were included in the study. There were 27 males and 23 females, and their age ranged from 3 days to 85 years. Of the fifty cases, the cases of leukemoid reaction and CML were thirty five and fifteen respectively.

CONCLUSION: Amongst the patients presenting with high WBC count, 35(70%) patients had leukemoid reaction and, 15 (30%) patients had chronic myeloid leukemia. Most common cause of leukemoid reaction was infection (74.28%) followed by alcoholic liver disease (17.14%), diabetic ketoacidosis (2.85%), bleeding (2.85%) and stress (angina) (2.85%).

In present study, most common age group affected was 21-40 years in case of leukemoid reaction and 41-60 year in case of CML. In present study, 32% of affected patients were males, and 38% patients were female in case of leukemoid reaction and 22% of affected patient were males, and 8% were female in case of CML.

KEY WORDS: Leukemoid reaction, Chronic myeloid leukemia

Introduction:

Hematologic conditions such as myeloproliferative disorders and a variety of non-hematologic conditions such as infections, inflammatory states, advanced malignancies, drugs (mainly corticosteroids and recombinant hematopoietic growth factors), severe hemorrhage, splenectomy and tissue ischemia may result in very high white blood cell counts (WBCs).¹

Infection is the most common cause of an elevated WBC, commonly between 10,000 and 20,000/ μ L commonly points to an infectious or it may be due to a reactive process.

A very high white blood cell counts (generally $>50 \times 10^9/\mu$ L) may produce a peripheral blood film appearance similar to leukemia (in those patients who do not have leukemia), termed as a leukemoid reaction.²

Most leukemoid reactions are granulocytic, although lymphocytic reactions may also occur.

In granulocytic leukemoid reaction, there is significant increase in mature neutrophils in peripheral smear and differential count showing marked shift to left as evidence by the presence of myelocytes and metamyelocytes.

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm and a clonal neoplastic hematopoietic stem cell disorder as evidenced by involvement of all hematopoietic cell lines, characterized by predominant proliferation of granulocytic cells.³

On peripheral smear examination of CML, there are more immature cells, basophils and eosinophils. The diagnosis of leukemoid reaction is based on the exclusion of chronic myeloid leukemia (CML).

Leukemoid reaction should be differentiated from myeloproliferative condition because it affects patient disease management and prognosis significantly.

Peripheral smear study is helpful in differentiating both the conditions, but at times, it does produce diagnosis dilemmas. Whereas qualitative assay of LAP in neutrophils can be an important tool in differentiating LR from CML. Leukocyte alkaline phosphatase is an enzyme present in the cytoplasmic microsomes of neutrophils, band, metamyelocytes and myelocytes but not in lymphocytes and monocytes.

LAP (leukocyte alkaline phosphatase) activity helps to differentiate leukemoid reactions from CML. In leukemoid reaction, the LAP score is high whereas in CML it is very low.⁴

High level of LAP score is seen in physiological response, the leukemoid reaction, and the pathology that include mature white blood cells, such as polycythemia vera (PV), essential thrombocytosis (ET), and in primary myelofibrosis (PMF).

Lower level of LAP score is seen in CML, paroxysmal nocturnal hemoglobinuria (PNH) and acute myeloid leukemia (AML).

Other investigation which can help to differentiate LR and CML is cytogenetic study of the bone marrow cells and even peripheral blood should reveal the typical Ph1 chromosome, which is reciprocal translocation of chromosome 9 and 22. This is hallmark of CML, found in almost all patients with the disease and present throughout the entire clinical course of CML.

The present study conducted in hospitalized patient with high neutrophil count to differentiate between neutrophilic leukemoid reaction and chronic myeloid leukemia.

AIMS AND OBJECTIVES:

- To study LAP score in patient with LR and CML and correlate with normal subjects.
- To study LAP score in patient with LR and CML and correlate with diagnosis.
- To determine LAP activity in patient with CML in our center and compare the result of our study with those in published literature.

MATERIAL AND METHODS:

The present study "Study of leucocyte alkaline phosphatase score in leukemoid reaction and chronic myeloid leukemia cases" was conducted in our institution.

Total 50 cases of patients that presented with high WBC count in OPD and admitted in wards were studied.

Type of study: Prospective study

Inclusion criteria: Patients of any age and either gender having total leucocyte count more than 50000 cells/cumm, with predominance of neutrophils were included in the study.

Exclusion criteria: Patients with high WBC count with lymphocytosis were excluded from the study..

Statistical analysis: Data collected was analysed statistically using percentage and frequency distribution and was presented in the form of tables, charts and graphs.

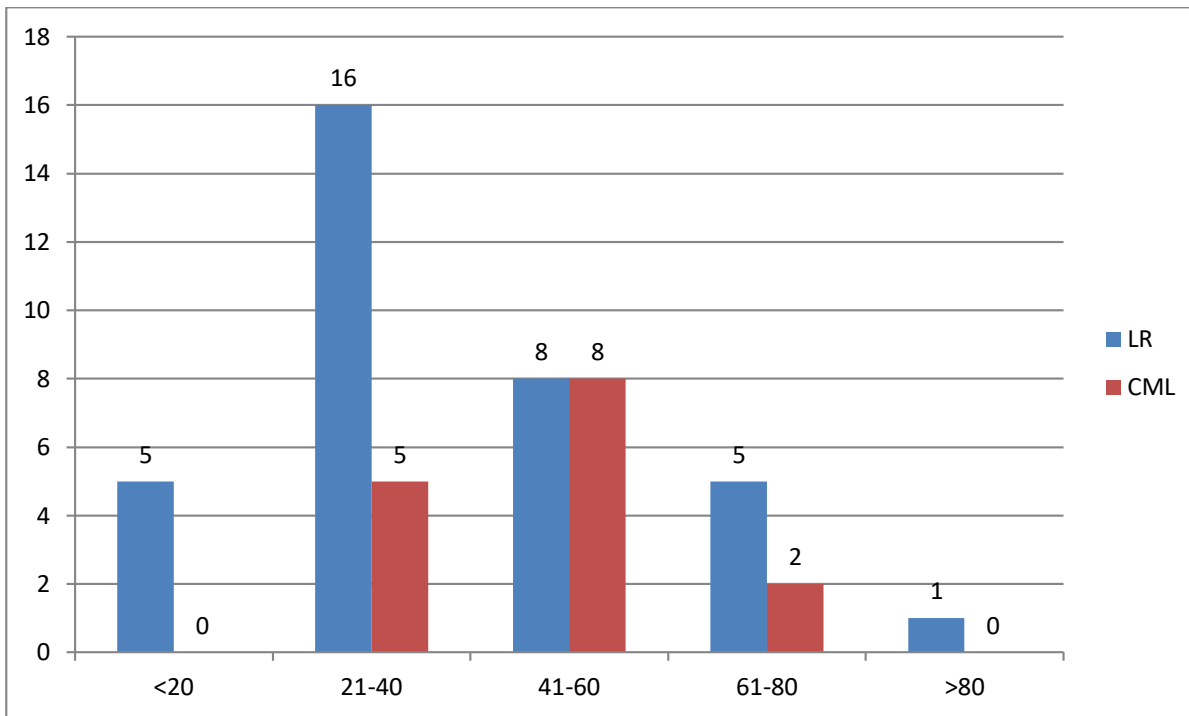
For sake of convenience in analysis, patients were divided in following age groups: below 20 years, 21 to 40 years, 41 to 60 years and 61 to 80 years.

OBSERVATIONS AND RESULTS:

The present study was undertaken to evaluate the significance of peripheral smear and leukocyte alkaline phosphatase score to differentiate leukemoid reaction and chronic myeloid leukemia. Total fifty cases of high WBC count who met the inclusion criteria were included in the study. There were 27 males and 23 females, and their age ranged from 3 days to 85 years. Of the fifty cases, the cases of leukemoid reaction and CML were thirty five and fifteen respectively.

Table 1: Age distribution of cases

Age (years)	Leukemoid reaction	Percentage	Chronic myeloid leukemia	Percentage
<20	5	14.28%	0	0%
21-40	16	45.71%	5	33.33%
41-60	8	22.85%	8	53.33%
61-80	5	14.28%	2	13.33%
>80	1	2.85%	0	0%

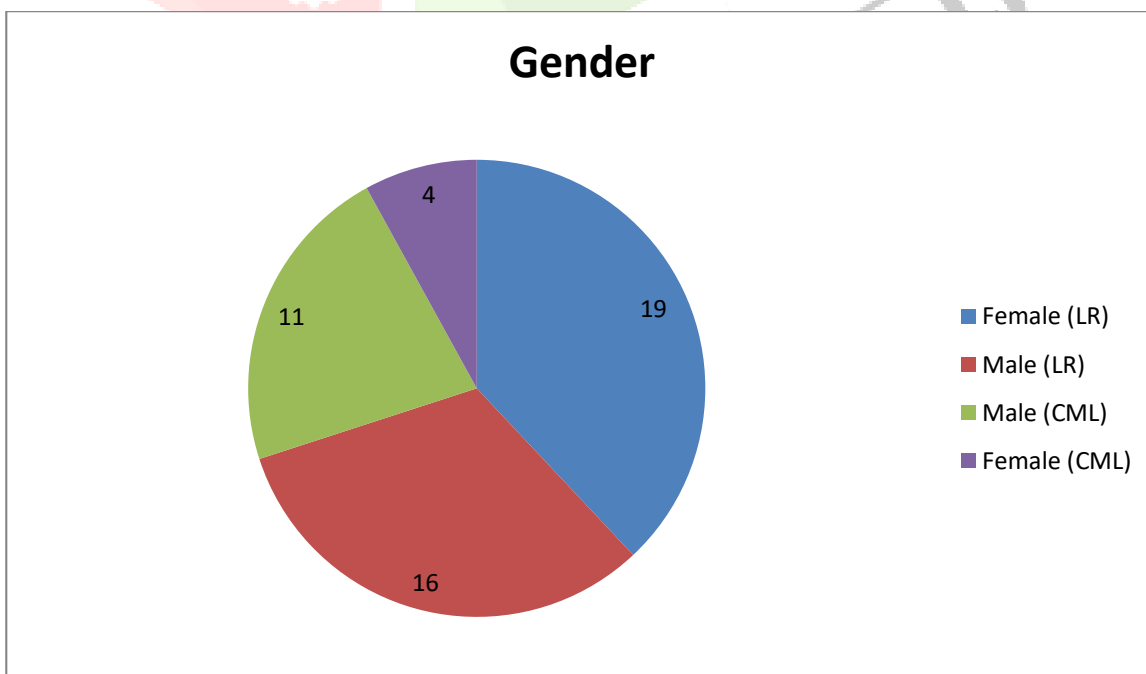


Maximum cases of leukemoid reaction were seen in the age group of 21-40 years.

Age group of 41-60 years was affected by maximum cases of CML.

Table 2: Distribution of study cases according to gender

Gender	No. of cases of Leukemoid reaction	No. of cases of CML
Male	16 (32%)	11 (22%)
Female	19 (38%)	4 (8%)
Total (50)	35 (70%)	15 (30%)



In this study out of 35 cases of leukemoid reaction, 16 cases (32%) were male while 19 (38%) were female.

In cases of CML, out of total 15 cases, 11 (22%) were male and 4 (8%) were female.

Table 3: Showing cause of leukemoid reaction

Disease	No. of patients
Infection	26 (74.28%)
Alcoholic liver disease (ALD)	6 (17.14%)
Diabetic ketoacidosis (DKA)	1 (2.85%)
Bleeding	1(2.85%)
Stress (angina)	1(2.85%)

In our study, infection is most common cause of leukemoid reaction. Other causes are alcoholic liver disease, diabetic ketoacidosis, bleeding and stress.

Table 4: LAP score in leukemoid reaction

Sr. No.	WBC count (/cumm)	LAP score
1	51000	276
2	52000	284
3	57000	254
4	54000	270
5	53000	290
6	74000	302
7	80000	280
8	55600	298
9	51500	275
10	52700	285
11	54000	290
12	86200	294
13	58000	302
14	53300	291
15	56000	302
16	53000	293
17	52000	282
18	56400	304
19	57900	308
20	88000	280
21	51000	274
22	60000	318
23	52800	287
24	51200	278
25	97000	385
26	59500	311
27	58000	312
28	53600	295
29	50500	304
30	88000	294
31	56400	307
32	52000	284
33	51400	279
34	64000	320
35	52000	275

In our study, maximum LAP score was 385 and minimum score was 254 in case of leukemoid reaction. Patient with LAP score 385 had WBC count of 97000/cumm and patient with LAP score 254 had WBC count of 57000/cumm.

Table 5: LAP score in CML

Sr. No.	WBC count (/cumm)	LAP score
1	2.61 lakh	0
2	1.26 lakh	1
3	2.81 lakh	2
4	3.18 lakh	1
5	2.87 lakh	1
6	3.22 lakh	1
7	1.21 lakh	0
8	1.38 lakh	1
9	1.11 lakh	2
10	3.25 lakh	1
11	1.19 lakh	1
12	2.50 lakh	1
13	5 lakh	0
14	3.70 lakh	0
15	3.16 lakh	1

In present study, maximum LAP score in case of CML was 2 and minimum was 0. Out of 15 cases, 2 patients had score 2 and 4 patients has score 0.

DISCUSSION:

Table 6: Comparison of different studies for gender distribution in leukemoid reaction

Sr. No.	Author Name	Gender distribution
1	Israel et al	88/85
2	Y.R. Lawrence et al	33/21
3	AbdelGhafar et al	18/17
4	Our study	19/16

Israel et al⁶ studied 173 patients with LR and found that LR was seen evenly in both genders (female/male = 88/85). Similar study conducted by Y.R. Lawrence et al⁵ shows out of total 54 cases, 33 (61.1%) were female.

Study done by AbdelGhafaret al⁷ shows number of females affected are 18 out of 35 cases of leukemoid reaction.

Table 7: Comparison of LAP score and WBC count with other study

Sr. no.	Author name	WBC count (/cumm)	LAP score
1	Zafar et al	31000	220
		45000	115
2	Our study	97000	385
		57000	254

In our study, maximum LAP score was 385 with WBC count of 97,000/cumm and minimum score was 254 with WBC count of 57,000/cumm, while study done by Zafar et al⁸ shows maximum LAP score of 220 in case of myeloid leukemoid reaction with WBC count of 31,000/cumm and minimum LAP score was 115 with WBC count of 45,000/cumm.

Table 8: Comparative study of most commonly affected age group in CML

Sr. no.	Author name	Age group (years)
1	F.H. Algahtni et al	41-60
2	Kumar et al	31-40
3	Our study	41-60

In our study, maximum affected age group are 41-60 years in CML. Similar study conducted by F.H. Algahtni et al¹⁰ shows maximum patients of CML are from 41-60 years age group. Study conducted by Kumar et al⁹ shows maximum patients of CML are from 31-40 years age group.

Table 9: Comparison of CML and LAP score with other study

Sr. no.	Author name	Score 0	Score 1	Score 2
1	Zafar et al	-	1	2
2	Our study	4	9	2

In case of CML, in our study 9 cases had score 1, 4 had score 0, 2 had score 2 out of total 15 cases, while study conducted by Zafar et al⁸ shows 2 patients with score 2 and 1 had score 1 out of 7 cases.

SUMMARY AND CONCLUSION:

The present study was conducted to differentiate CML and leukemoid reaction by LAP score by special stain: leukocyte alkaline phosphatase stain. Total 50 cases of patients that presented with high WBC count in OPD and admitted in wards were studied.

Results of the present study showed that the commonest cause of leukemoid reaction was infection. Various other causes of leukemoid reaction were alcoholic liver disease, diabetic ketoacidosis, bleeding and stress (angina).

LAP score is simple, easy and relatively less costly test which does not require any special conditions to test blood samples with markedly elevated WBC count. It helps to differentiate between leukemoid reaction and CML on peripheral smear but their management strategies and prognosis are poles apart.

Amongst the patients presenting with high WBC count, 35 (70%) patients had leukemoid reaction and, 15 (30%) patients had chronic myeloid leukemia. Most common cause of leukemoid reaction was infection (74.28%) followed by alcoholic liver disease (17.14%), diabetic ketoacidosis (2.85%), bleeding (2.85%) and stress (angina) (2.85%).

In present study, most common age group affected was 21-40 years in case of leukemoid reaction and 41-60 year in case of CML. In present study, 32% of affected patients were males, and 38% patients were female in case of leukemoid reaction and 22% of affected patient were males, and 8% were female in case of CML.

Patients with leukemoid reaction had high LAP score while patient with CML had low LAP score.

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