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Comparison of NLR,LMR,PLR, RDW, and Platelet count in hematological malignancies at baseline and at intervals of 2 months in patients undergoing chemotherapy

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ABSTRACT

Blood cancer has become quite common in all age groups, worldwide. The cancer ranges from acute life-threatening leukemias to indolent chronic leukemias, Lymphoma spillovers causing morbidity and mortality to slow-growing indolent lymphomas. Since blood is present everywhere in the body hence the spread of hematological malignancies is massive. Chemotherapy is expensive and a must to treat blood cancers. However, the ancillary workups like flowcytometry etc in prognosticating and diagnosing blood cancers become quite cumbersome and heavy on the pocket for an average Indian. Therefore, the authors planned the study aimed at analyzing-

-Trend in NLR,LMR, PLR RDW, Platelet count at baseline

-Trend in NLR,LMR, PLR RDW, Platelet count 2 months post-chemotherapy

-Comparison between 2 parameters for any significant change

The study was carried out on 11 cases as a prospective case-based study of 11 cases where pre and post-values of chemotherapy cases of newly diagnosed blood cancer cases were available with the author. The baseline CBC and post-induction 1 st CBC were used to record the variables under study and latest SPSS software was used to come to a conclusion through the results.

The findings stated that there was a decline in NLR, PLR and platelet count at follow-up as compared to baseline and an increase in LMR and RDW at follow-up as compared to baseline, however, the difference was significant statistically only for PLR (p=0.028) and near significant (p=0.059) for platelet count.

Hence in view of significant findings seen only in 11 cases a larger cohort may be used to correlate these findings with follow up of such cases.

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INTRODUCTION

Blood cancer has become quite common in all age groups, worldwide. The cancer ranges from acute life-threatening leukemias to indolent chronic leukemias, Lymphoma spillovers causing morbidity and mortality to slow-growing indolent lymphomas. Since blood is present everywhere in the body the spread of hematological malignancies is massive. Chemotherapy is expensive and a must to treat blood cancers. [1]However, ancillary workups like flow cytometry, and molecular and cytogenetic workup in prognosticating and diagnosing blood cancers, become quite cumbersome and heavy on the pocket for an average Indian. The GLOBOCAN data 2020 for leukemias and lymphomas in developing countries states that there are 269,503 and 205,016 new cases of leukemia in males and females, respectively [2] while the mortality related to these leukemias and lymphomas was 176,000 and 132,000 in males and females, respectively. The diagnosis and follow-up of cases of leukemias and lymphomas is imperative, especially in cases of blood cancer. However, a drawback in the Indian subcontinent and even worldwide is the cost of investigations and treatment including the follow-ups of cases diagnosed as blood cancers. The primary or most basic investigation tools that are offered by doctors to cases of leukemia are complete blood counts and peripheral smear examinations. Based on the reports of this investigation a hematologist plans further workup of the patient.[3]Hematopoiesis is a very radio and chemo-sensitive process and hence post-therapy bone marrow suppression may occur leading to many adverse effects like, anemia, leukopenia, and thrombocytopenia can occur. Of late, many types of research have been carried out in different diseases to assess the roles of parameters derived from a simple CBC , like Neutrophil to Lymphocyte Ratio (NLR), the Lymphocyte to Monocyte Ratio (LMR) and the Platelet to Lymphocyte Ratio (PLR), as well as some CBC parameters not studied in detail initially like PDW and RDW to hypothesize course of disease progression and prognosis.[4]In hematology where chemotherapy and radiotherapy are used as a treatment modality, absolute Neutrophil count has been used as an important follow-up parameter for a long time, however in recent times the above-mentioned parameters have been studied in great detail in benign diseases like diabetes, hyperlipidemia, dengue etc. Hence the authors have attempted to analyze the variation of these parameters(NLR, LMR, PLR, RDW) in newly diagnosed cases of acute leukemias(AML and ALL) and to compare the changes in these parameters from baseline values versus the values after the first induction therapy is over to establish CBC derived parameters as effective and cheap prognostic markers aiding the more costly investigations of molecular and cytogenetics.

MATERIAL AND METHODS

The study was carried out in SMSR, Sharda University. CBC values of 11 newly diagnosed cases of acute leukemias(10 AMLs and 1 ALL)were analyzed from the department records and the derivatives of NLR,LMR,PDW,RDW were calculated from the CBC. The follow-up values were collected after 2 months of induction therapy treatment with 2 months being chosen to keep the timeline constant. The values post-chemotherapy were also analyzed for the same CBC-derived parameters. All relevant clinical information about the patient was obtained from the clinician and patient files, obtained from the medical records department.

Statistical Analysis

Data was analyzed using SPSS 21.0 software. Wilcoxon signed rank test has been used for comparison of data.An ethical waiver has been applied for.

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RESULTS

Table 1: Demographic Profile of Patients enrolled in the study

SN	Variable	Characteristic
1.	Mean age±SD (Range) in years [Median age; Interquartile range] in years	39.64±20.42 (11-65) [50; 19-59]
2.	Sex Male Female	 6 (54.5%) 5 (45.5%)

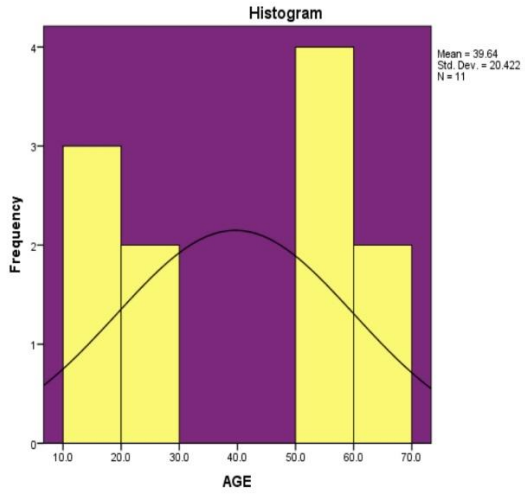

Image 2:Histogram showing age distribution of our cases

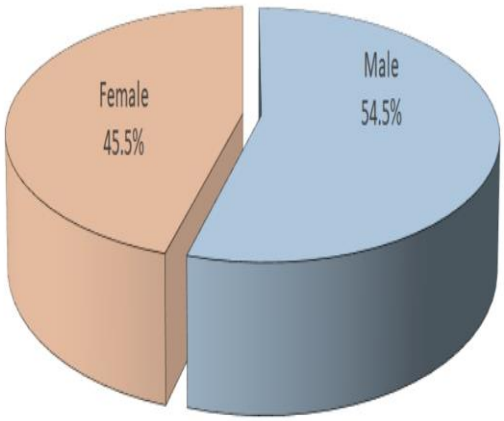

Image 2:Pie chart showing the sex distribution in our cases

There was a decline in NLR, PLR and Platelet count at follow-up as compared to baseline and an increase in LMR and RDW at follow-up as compared to baseline. However, the difference was statistically significant only for PLR (p=0.028) and near significant (p=0.059) for platelet count.(Table 2 and Image 4)

Table 2: Comparison of Blood cell parameters between baseline and follow-up (n=11)

Parameter	Baseline		Follow-up		Change		Statistical significance (Wilcxon signed rank-test)	
	Mean	SD	Mean	SD	Mean	SD	Z	P
NLR	4.72	6.08	3.53	4.99	-1.19	1.39	0.21	0.833
PLR	14.40	24.92	11.72	19.79	-2.68	1.82	2.201	**0.028**
LMR	9.70	19.71	10.17	20.16	0.47	0.60	0.536	0.592
PC	2.25	1.60	1.83	1.03	-0.41	0.21	1.89	0.059
RDW	17.82	3.42	21.59	14.44	3.77	4.04	0.271	0.786

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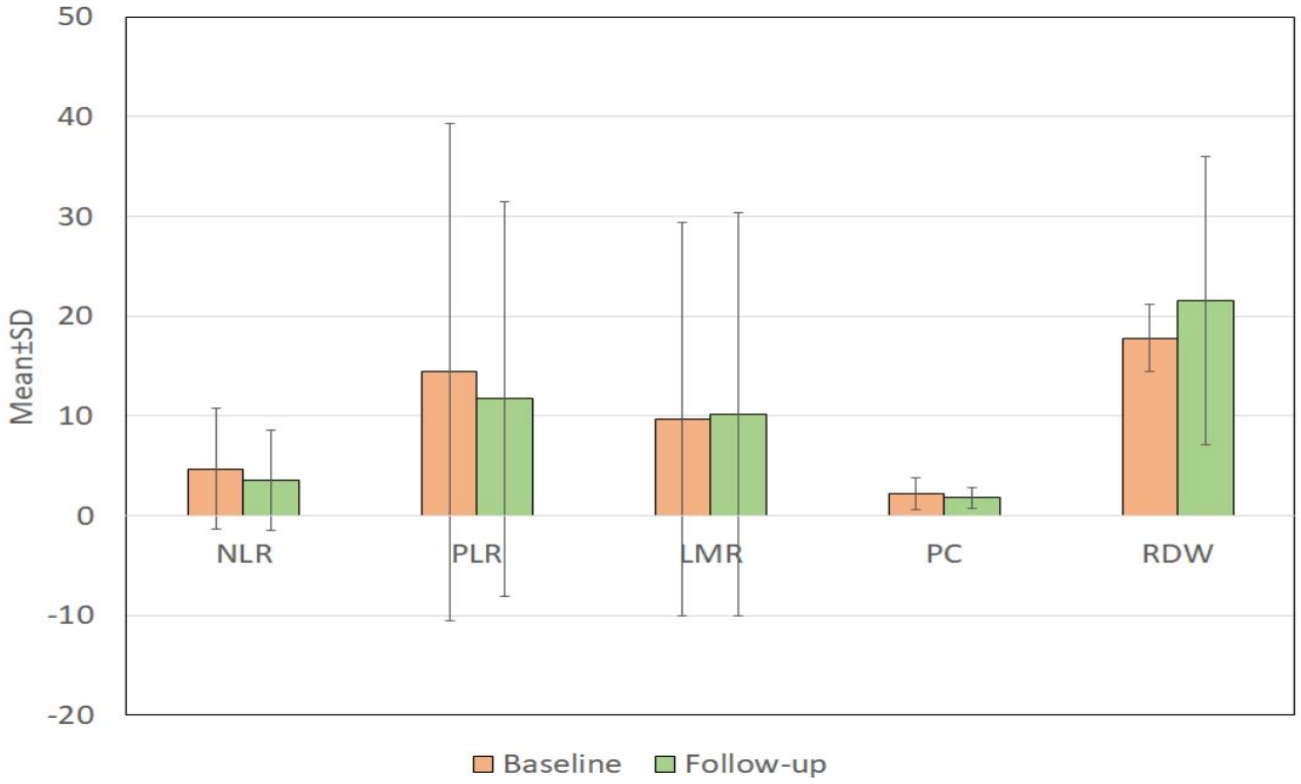

Image 4- Plot showing the mean deviation of parameters under study.

DISCUSSION

Complete blood counts are extremely useful tools for following up with patients with chemotherapy. Absolute neutrophil counts have been used for a long time now to monitor patient's responses to chemotherapy. There have been studies on RBC and related parameters , such as hemoglobin and hematocrit levels. Many studies document the development of anemia post-chemotherapy. Some studies have monitored the trends in leucocyte count and have documented changes in counts, number, size, and maturity of each of these types of blood cells and documented a deviation from normal values. There are organizations like the World Health Organization (WHO) Toxicology Grades,7 the National Cancer Institute (NCI) Common Toxicity Criteria for Adverse Events (CTCAE), and the Southwest Oncology Group (SWOG) which mention different cut-offs for some of the CBC related parameters post drug exposure.[5,6]The derived CBC parameters are NLR (total neutrophil to lymphocyte count), LMR(lymphocyte/monocyte count), and PLR(platelet lymphocyte ratio. The red blood cell

distribution width (RDW) means the variation in size and shape of RBCs seen commonly as the effect of drug therapy or in cases of hemolysis. There are two derivatives of RDW ie RDW-SD and RDWCV(calculated by the standard deviation of the mean cell size / MCV x100). RDW-SD is a measurement of the width of the red cell distribution curve (fL) [9]. These parameters are prognostically significant in many solid and blood malignancies. However, despite the reports of the prognostic significance not many studies have been performed to elucidate their importance.[7]In our study, we noted a decreasing trend in all the parameters however a statistically significant decrease was seen in PLR and a mildly significant decrease was seen in platelet counts. In a study done in cases of CLL, it was noted that post-chemotherapy, some patients experienced anemia(5%) and thrombocytopenia (15%) which was reverted by short-term treatment interruption and steroids. In another study, 40% of patients developed thrombocytopenia just after completion of the first phase of treatment of AML.[8,9]In a study done on NHLs it was noted that 3% of cases had grade 1 (WHO) toxicity, 6% had grade 2 toxicity, and one patient had extensive involvement of the bone marrow causing them to experience grade 3 thrombocytopenia. In another study on CBC parameters in relapsed NHL

cases 20% had anemia 45.7% of cases developed thrombocytopenias. There have been many clinical trials comparing radiotherapy with chemotherapy showing similar results.[10,11]In a study in preprint done on AML in 2023 which is similar to our study, they calculated NLR and LMR in cases of AML and saw that high NLR and low LMR predicted poorer outcomes in AML.[12] However, their study is on baseline parameters while we have compared baseline parameters with post-induction chemotherapy parameters and hence found relevant changes in PLR and platelet counts although other parameters show a significant decrease as well. The roles of CBC-derived parameters like NLR and LMR have been studied as prognostic markers in many hematolymphoid malignancies, for example, multiple myeloma, Hodgkin's lymphoma, etc. In a study done by Zhang et al., the authors observed that in all the cases with >50% blast in marrow as well as high NLR, the cases presented with poorer prognosis. [13]Another study done on platelet parameters shows poorer prognosis in cases of low PLR which could be the case in our cases. However since we had just a short follow-up period and few cases at our setup for acute leukemias we were unable to comment on the complete prognostic significance of our findings. [14] Some studies state that the PLR has a variation in prognostication with different treatment regimens. However thrombocytopenia was associated with poorer prognosis in most of the studies. [14,15] In studies done in the West, it has been noted that a higher PLR in pretransplant (bone marrow hematopoietic stem cells) has better overall survival and lower relapse rate and mortality after transplanting the patient with HSCs. Hence many Western studies mention the prognostically significant role of NLR, LMR, and PLR and attribute this to the tumor microenvironment and immunological interactions. [16-17]Another study showed that an RDW-CV >20.7% in the western population in cases of AML was associated with poor prognosis. In our study, there is a trend of improvement in RDW post-induction therapy rather than baseline values. Since all our cases were stable post-first treatment regimen it may be supportive of the findings of the previous study where a raised RDW was seen as a poor prognosis indicator. [18]To the best of the authors' knowledge, no such study comparing CBC parameters in baseline and post-chemotherapy phase(induction) has been done in the Indian population comparing leukemias. The study highlights the role of CBC-derived parameters-NLR, LMR, PLR, and RDW as cheap and cost-effective prognostic tools especially important in Indian scenarios where not every patient can access frequent molecular workups for prognostication of acute leukemias.[19-20]The limitation of our study is the smaller sample size and inability to follow the cases for longer time which needs to be done with larger samples to fully establish the utility and significance of CBC and CBC-derived parameters as prognostic tools. Since 90% of our cases belonged to the AML category and only 1 case was ALL we did not correlate the changes in values with different chemotherapy regimens.

CONCLUSION

Hence the authors would like to highlight the importance of CBC-derived parameters in diagnosing and prognosticating post-therapy leukemias. To the best of our knowledge, ours is the first study done in the Indian population however we advocate more such studies to be conducted to firmly cement the role of CBC and derived parameters as significant diagnostic and prognostic tools.

REFERENCES

1. Hehlmann R, Lauseker M, Saußele S, et al. Assessment of imatinib as first-line treatment of chronic myeloid leukemia: 10-year survival results of the randomized CML study IV and impact of non-CML determinants. Leukemia. 2017;31(11):2398–2406. doi:10.1038/ leu.2017.253

2. https://gco.iarc.fr/today/data/factsheets/cancers/36-Leukaemia-fact-sheet.pdf

3. Luo H, Quan X, Song XY, Zhang L, Yin Y, He Q, Cai S, Li S, Zeng J, Zhang
Q, et al. Red blood cell distribution width as a predictor of survival in
nasal-type, extranodal natural killer/T-cell lymphoma. Oncotarget.
2017;8(54):92522–35.

4. Wang J, Xie X, Cheng F, Zhou X, Xia J, Qian XF, Wang LL, Guo HF. Evaluation of pretreatment red cell distribution width in patients with multiple
myeloma. Cancer Biomarkers. 2017;20(3):267–72

5. 2. Chereda B, Melo JV. Natural course and biology of CML. Ann Hematol. 2015;94(Suppl 2):S107–S121. doi:10.1007/s00277-015-2325-z

6. Kantarjian H, O'Brien S, Jabbour E, et al. Impact of treatment end point definitions on perceived differences in long-term outcome with tyrosine kinase inhibitor therapy in chronic myeloid leukemia. J Clin Oncol. 2011;29(23):3173–3178. doi:10.1200/JCO.2010.33.4169

7. Jabbour E, Cortes J, Nazha A, et al. EUTOS score is not predictive for survival and outcome in patients with early chronic phase chronic myeloid leukemia treated with tyrosine kinase inhibitors: a single institution experience. Blood. 2012;119(19):4524–4526. doi:10.1182/ blood-2011-10-388967

8. Tiribelli M, Bonifacio M, Calistri E, et al. EUTOS score predicts long-term outcome but not optimal response to imatinib in patients with chronic myeloid leukaemia. Leuk Res. 2013;37(11):1457–1460. doi:10.1016/j.leukres.2013.07.037

9. Yamamoto E, Fujisawa S, Hagihara M, et al. European treatment and outcome study score does not predict imatinib treatment response and outcome in chronic myeloid leukemia patients. Cancer Sci. 2014;105 (1):105–109. doi:10.1111/cas.12321
10. Hoffmann VS, Baccarani M, Hasford J, et al. Treatment and outcome of 2904 CML patients from the EUTOS population-based registry. Leukemia. 2017;31(3):593–601. doi:10.1038/leu.2016.246

11. Baccarani M, Druker BJ, Branford S, et al. Long-term response to imatinib is not affected by the initial dose in patients with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase: final update from the tyrosine kinase inhibitor optimization and selectivity (TOPS) study. Int J Hematol. 2014;99(5):616–624. doi:10.1007/ s12185-014-1566-2

12. Stefanuik P, Muzyka-Kasietczuk J, Koczkodaj D, Hus M,Podhorecka M. Reading between the lines – complete blood count parameters as prognostic factors in patients with newly diagnosed acute myeloid leukemia. Research Square.2023. DOI: https://doi.org/10.21203/rs.3.rs-3210612/v1

13. Zhou XH, Zhang XY, Liang JH, et al. Low absolute NK cell counts in peripheral blood are associated with inferior survival in patients with mantle cell lymphoma. *Cancer Biomark*. 2019;24(4):439–447. doi: 10.3233/cbm-182193

14. Nteliopoulos G, Bazeos A, Claudiani S, et al. Somatic variants in epigenetic modifiers can predict failure of response to imatinib but not to second-generation tyrosine kinase inhibitors. Haematologica. 2019;104(12):2400–2409. doi:10.3324/haematol.2018.200220

15. Lauseker M, Bachl K, Turkina A, et al. Prognosis of patients with chronic myeloid leukemia presenting in advanced phase is defined mainly by blast count, but also by age, chromosomal aberrations and hemoglobin. Am J Hematol. 2019;94(11):1236–1243. doi:10.1002/ajh.25628

16. Jain P, Kantarjian HM, Ghorab A, et al. Prognostic factors and survival outcomes in patients with chronic myeloid leukemia in blast phase in the tyrosine kinase inhibitor era: cohort study of 477 patients. Cancer. 2017;123(22):4391–4402. doi:10.1002/cncr.30864
17. Radich JP, Deininger M, Abboud CN, et al. Chronic myeloid leukemia, version 1.2019, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2018;16(9):1108–1135. doi:10.6004/ jnccn.2018.0071

18. Evans TC, Jehle D. The red blood cell distribution width. J Emerg Med. 1991;9(Suppl 1):71–74. doi:10.1016/0736-4679(91)90592-4 16. Patel KV, Semba RD, Ferrucci L, et al. Red cell distribution width and mortality in older adults: a meta-analysis. J Gerontol a Biol Sci Med Sci. 2010;65(3):258–265. doi:10.1093/gerona/glp163

19. Perlstein TS, Weuve J, Pfeffer MA, Beckman JA. Red blood cell distribution width and mortality risk in a community-based prospective cohort. Arch Intern Med. 2009;169(6):588–594. doi:10.1001/ archinternmed.2009.55

20. Cavusoglu E, Chopra V, Gupta A, et al. Relation between red blood cell distribution width (RDW) and all-cause mortality at two years in an unselected population referred for coronary angiography. Int J Cardiol. 2010;141(2):141–146. doi:10.1016/j.ijcard.2008.11.187