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Exploring the Relationship between CD66c Expression and Clinico-Haematological Parameters in Pediatric B-Cell Acute Lymphoblastic Leukemia (ALL)

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Abstract:-

- ***Background:***

Pediatric B-cell Acute Lymphoblastic Leukemia presents with diverse clinical and hematological manifestations. Understanding these characteristics is crucial for effective management and prognostication.

- ***Methods:***

This study conducted as prospective observational study at Lady Hardinge Medical College and Kalawati Saran Children Hospital, New Delhi, from November 2017 to March 2019. This study enrolled 30 pediatric patients with B-cell ALL who underwent comprehensive evaluations including routine and specialized hematological tests, bone marrow aspiration (BMA), cytochemistry, and immunophenotyping. Clinical features, hematological parameters, and CD66c expression on lymphoblasts were assessed.

- ***Results:***

Immunophenotyping revealed that 28 cases (93.3%) were CALLA positive (CD10 positive), while 2 cases (6.7%) were CALLA negative (CD10 negative). The age ranged from 1.5 to 12 years, with a 2:1 male to female ratio. The mean age was 4.8 years.. Common presenting complaints included fever (93.3%) and pallor (60.0%). Hepato-splenomegaly (60.0%) and lymphadenopathy (60.0%) were the most frequent clinical findings. Hematological findings showed moderate to severe anemia (mean hemoglobin 7.19 g/dL), with 56.7% of patients having hemoglobin levels between 4.0-7.9 g/dL. Leukocytosis (>10,000/cumm) was observed in 53.3% of cases, with 20% having total leukocyte counts >50,000/cumm. Thrombocytopenia (platelet count ≤ 25,000/cumm) was noted in 56.7% of patients. Immunophenotyping revealed CD66c expression >20% gated in 46.7% of cases, correlating with more severe clinical features and poorer hematological parameters.

- ***Conclusion:***

Pediatric B-cell ALL exhibits a spectrum of clinical and hematological features. Elevated CD66c expression correlates with aggressive disease presentation and worse clinical outcomes, suggesting its potential utility as a prognostic marker. Early identification of these parameters can aid in risk stratification and tailored therapeutic approaches.

Keywords:- *Pediatric Leukemia, B-Cell ALL, CD66c Expression, Clinical Features, Hematological Parameters.*

I. INTRODUCTION

One of the most common subtypes of juvenile leukaemia is paediatric B-cell acute lymphoblastic leukaemia (ALL), which is defined by the clonal proliferation of immature B-cell precursors in the bone marrow and peripheral blood. This malignancy represents a significant portion of pediatric cancers, accounting for nearly one-quarter of all cases, with the highest incidence occurring between 2 to 5 years of age [1]. The clinical presentation of B-cell ALL is diverse, encompassing symptoms such as fever, pallor, hepatosplenomegaly, and lymphadenopathy, underscoring its systemic impact on young patients [2].

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In recent years, advances in diagnostic and prognostic tools, especially immunophenotyping using flow cytometry have changed the understanding and application of ALL [3]. Immunophenotyping enables accurate classification of leukemia a based on surface antigen markers expressed on blood cells such as CD10 (CALLA). CD66c has gained attention for its potential as a biomarker associated with disease aggressiveness and poor prognosis in both adult and pediatric ALL [4] Latest research indicates that the carcinoembryonic antigen-related cell fusion molecule family's CD66c (CEACAM6), a cell adhesion molecule, is a key player in the pathophysiology of ALL.[4]

From hematologic perspective, B-cell ALL is characterized by spontaneous leukemia hemodynamic dysfunction occurs in different lineages of blood products. Anemia is a common finding, often severe, with a significant proportion of patients exhibiting low hemoglobin levels (< 8 g/dL). Leukocytosis, an increased number of white blood cells, is common and can vary widely in severity, sometimes reaching extreme levels (> 100,000 cells/mm3) as opposed to thrombocytopenia, platelets decreased numbers are also common, seen in some patients It contributes to the tendency to bleed [5] These clinico-hematological parameters are crucial for the initial diagnosis and ongoing management of pediatric B-cell ALL. They provide insights into disease progression, response to therapy, and overall prognosis.

In order to investigate the potential prognostic significance and clinical implications of CD66c expression in lymphoblasts, the study evaluates the frequency and intensity of this expression in lymphoblasts at the time of diagnosis among paediatric patients with B-cell acute lymphoblastic leukaemia (ALL). Additionally, it correlates these expression levels with clinico-haematological parameters.

II. METHODOLOGY

➢ *Study Design*

This follow-up prospective observational study was carried out in hospitals from November 2017 to March 2019 at the Department of Pathology, Lady Hardinge Medical College, and the Department of Paediatrics, Kalawati Saran Children Hospital, New Delhi. Thirty newly diagnosed B-cell Acute Lymphoblastic Leukaemia (ALL) patients under the age of eighteen who were registered and consented to treatment at the aforementioned facilities were included in the study.

➢ *Selection Criteria:*

- *Inclusion Criteria:*

✓ Patients under 18 years of age newly diagnosed with B-cell ALL.
✓ Patients prepared to receive care at Kalawati Saran Children Hospital and Lady Hardinge Medical College.

- *Exclusion Criteria:*

✓ Patients with relapsed B-cell ALL.
✓ Patients who had received corticosteroids for ≥8 days prior to enrolment.

➢ *Diagnostic Procedure:*

- Complete Hemogram including Hemoglobin (Hb), Total Leucocyte Count (TLC), Differential Leucocyte Count (DLC), Platelet count, and Peripheral Smear using Sysmex XN-1000.
- Peripheral smear examination for morphological analysis.
- Bone Marrow Aspiration (BMA) to assess cellularity and morphology, stained with Wright stain.

➢ *Special Investigations:*

- *Immunophenotyping:*

✓ Flow cytometry analysis using Beckman Coulter FC500 to determine immunophenotypic markers on lymphoblasts.

- *Cytochemistry:*

✓ Myeloperoxidase (MPO), Sudan Black B (SBB), and Periodic acid Schiff (PAS) staining performed to identify specific cytoplasmic characteristics in blasts.

- **Data Collection:** Peripheral blood and bone marrow samples were collected and processed promptly for analysis. Flow cytometry data were analysed to identify abnormal antigen expressions indicative of B-cell ALL.
- **Data analysis**: Analysis was conducted to explore CD66c expression levels and clinico-haematological parameters using appropriate statistical test in percent value.

III. RESULTS

Within the study, thirty paediatric patients diagnosed with B-cell Acute Lymphoblastic Leukaemia (ALL) had extensive investigations that included cytochemistry, immunophenotyping, bone marrow aspiration (BMA) studies, and regular and specialty haematological assays. Immunophenotyping revealed that out of 30 cases, 28 were CALLA positive (CD 10 positive), and 2 were CALLA negative (CD 10 negative). The age range of the patients was 1.5–12 years, with a standard deviation of 2.83 and a mean age of 4.8 years. The highest number of patients (11 out of 30) fell within the 2 to 4-year age group. No cases were reported in children younger than 1 year or older than 12 years. The study found a male-to-female ratio of 2:1, with 20 male cases (66.7%) and 10 female cases (33.3%). Among the two CALLA negative cases, one was male, and one was female.

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Table 1 Presenting Complaints in B Cell all Cases (N=30)

Complaint	Frequency	Percentage
Fever	28	93.3%
Joint Swelling	1	3.3%
Pallor	18	60.0%
Pain Abdomen	5	16.7%
Bodyache	3	10.0%
Bleeding	3	10.0%
Weakness	2	6.7%
Neck Swelling	2	6.7%

In this table 1& Figure 1 common presenting complaints in B-cell ALL cases were fever (93.3%), followed by pallor (60%), pain abdomen (16.7%), bodyache and bleeding (10% each), weakness and neck swelling (6.7% each), and joint swelling (3.3%).

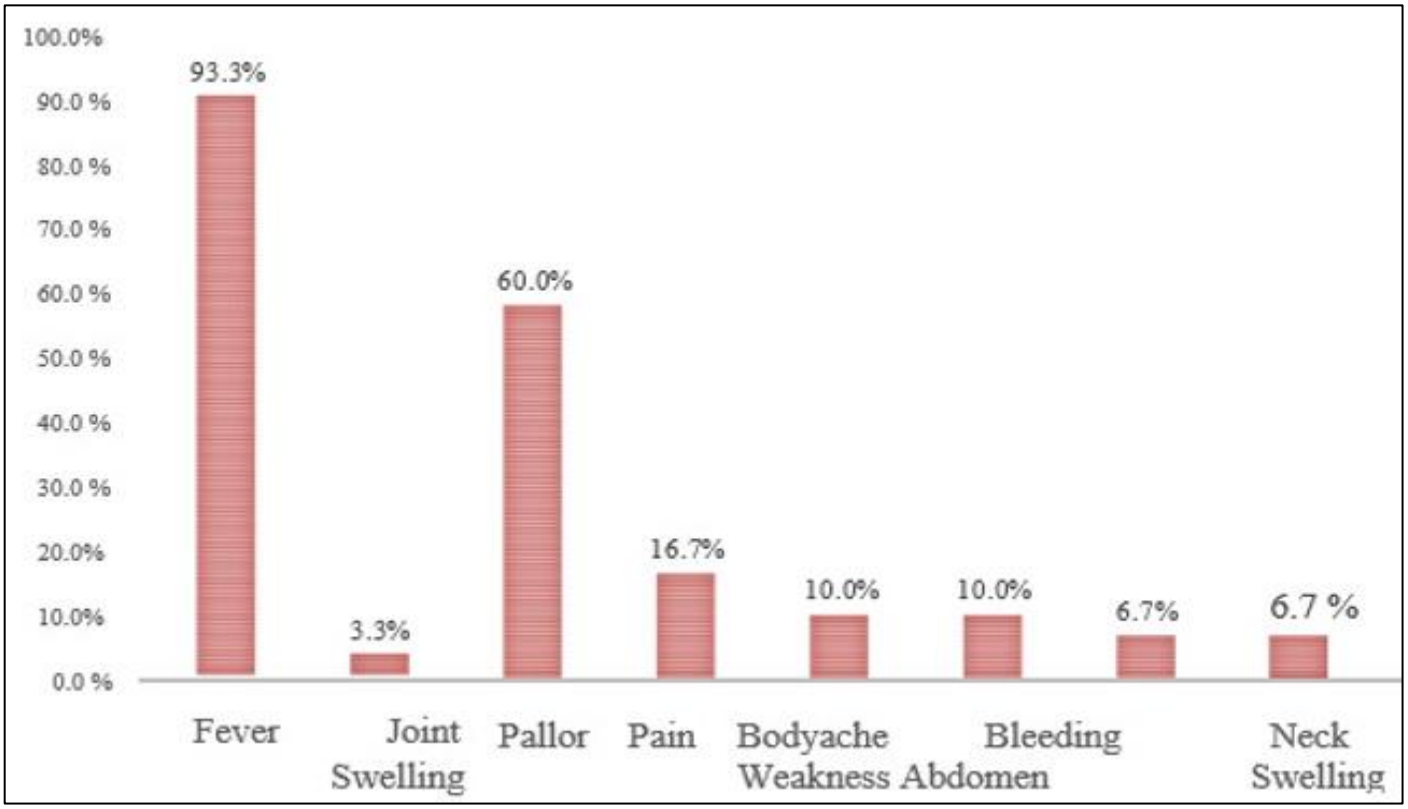

Fig 1 Presenting Complaints in B Cell all Cass (N=30)

Table 2 Salient Clinical Features of B Cell all (N=30)

Feature	Frequency	Percentage
Hepato-splenomegaly	18	60.0%
Hepatomegaly	6	20.0%
Lymphadenopathy	18	60.0%
Bone Pain	3	10.0%
Edema	3	10.0%
Petechiae	2	6.7%

In table 2 and figure 2 observation suggest that in B-cell ALL cases included hepato-splenomegaly (60%), lymphadenopathy (60%), hepatomegaly (20%), bone pain (10%), edema (10%), and petechiae (6.7%).

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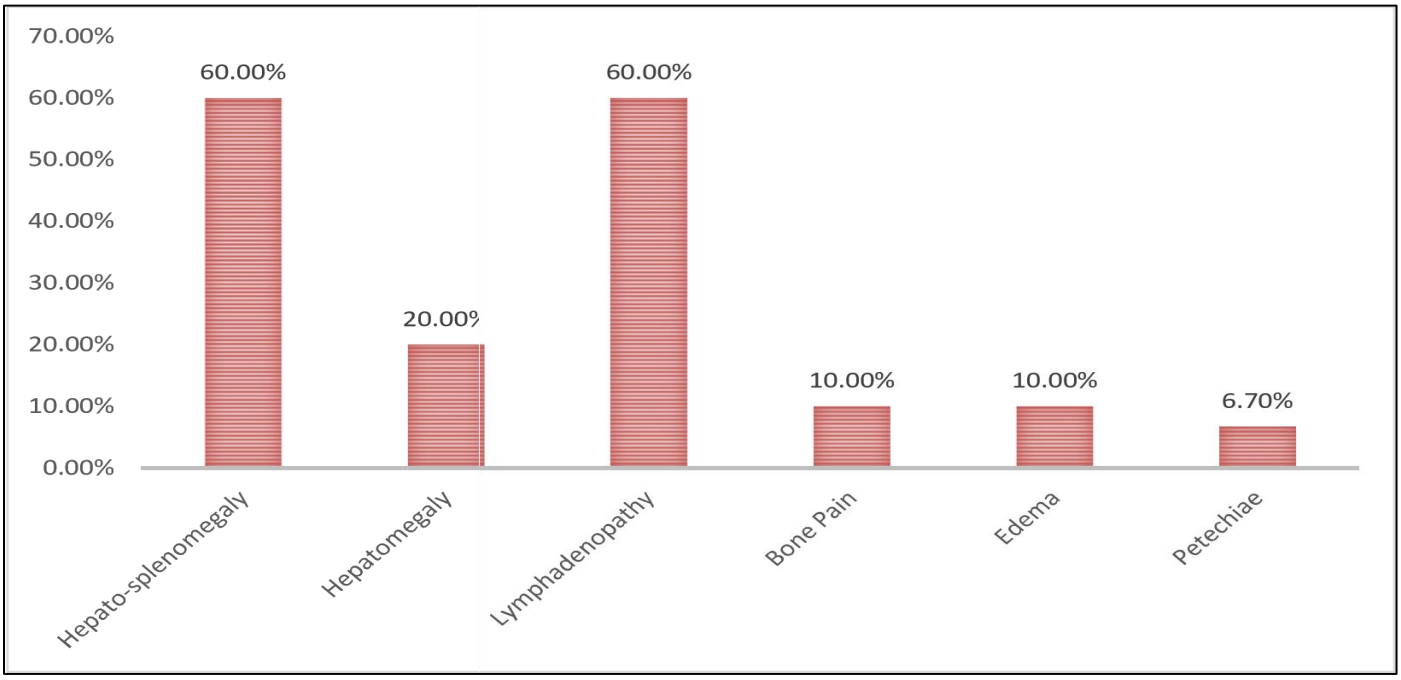

Fig 2 Salient Clinical Features of B Cell all (N=30) Hematological Findings

Table 3 Hemoglobin Levels (N=30)

Hemoglobin (gm/dL)	**Frequency**		**Percentage**		
< 4.0	1		3.3%		
4.0 - 7.9	17		56.7%		
8.0 - 11.9	12		40.0%		
	Mean	SD	Median	Minimum	Maximum
Haemoglobin (gm/dL)	7.19	2.03	7.10	3.9	11.7

B-cell ALL patients frequently had anaemia, leucocytosis, and thrombocytopenia; as a result, table 3 predicts a mean haemoglobin concentration of 7.1 g/dL with a standard deviation of 2.03. As illustrated in Figure 3, the 30 patients' distribution of haemoglobin levels was as follows: 3.3% had levels below 4.0 g/dL, 56.7% had levels between 4.0 and 7.9 g/dL, and 40.0% had levels between 8.0 and 11.9 g/dL. With a range of 3.9 to 11.7 g/dL, the median haemoglobin level was 7.10 g/dL.

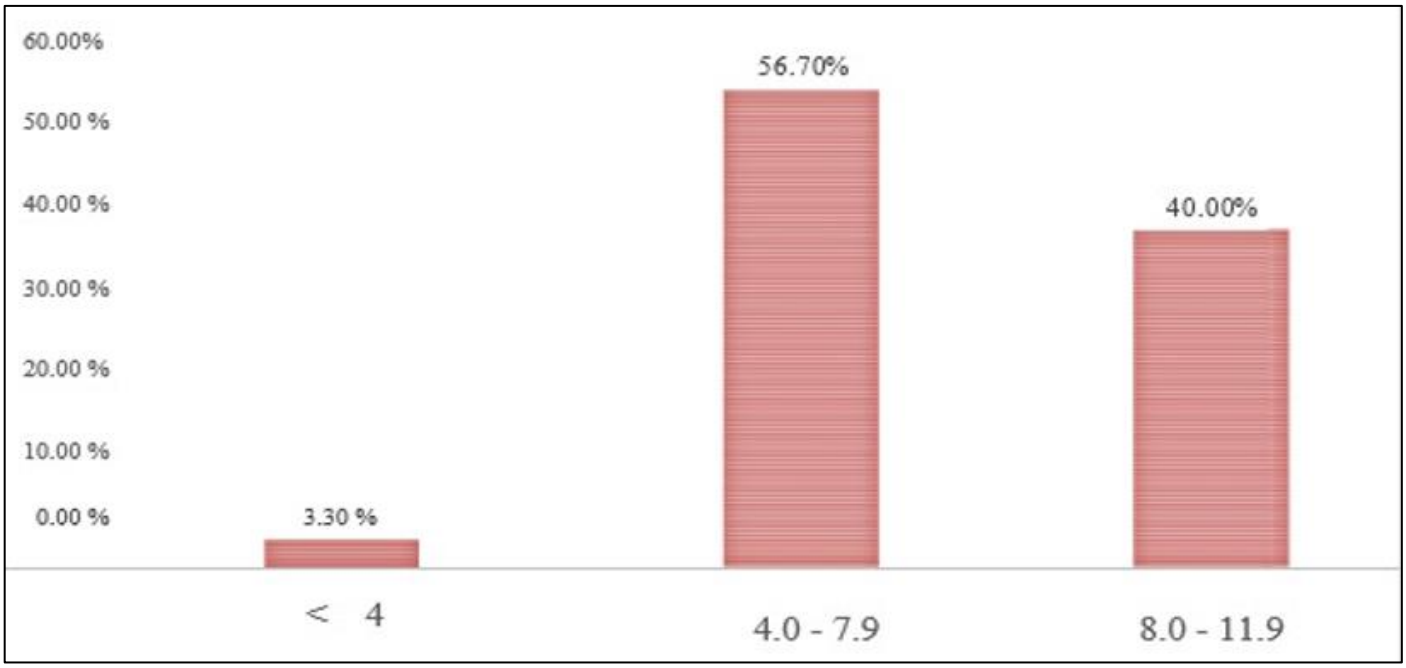

Fig 3 Hemoglobin Levels (N=30)

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Table 4 Total Leucocyte Count (N=30)

Total Leukocyte Count (/cumm)	Frequency			Percentage	
<= 10,000	14			46.7%	
10,001 - 20,000	3			10.0%	
20,001 - 30,000	2			6.7%	
30,001 - 40,000	2			6.7%	
40,001 - 50,000	3			10.0%	
50,001 - 60,000	1			3.3%	
60,001 - 70,000	0			0.0%	
70,001 - 80,000	0			0.0%	
80,001 - 90,000	2			6.7%	
90,001 – 1,00,000	1			3.3%	
> 1,00,000	2			6.7%	
	Mean	SD	Media	Minimum	Maximum
Total Leukocyte Count (/cumm)	37,448	56,409	12,295	1,560	2,46,450

Out of the 30 cases, in Table 4 and Figure 4 16 (53.3%) showed leucocytosis (>10,000/cumm), with 6 cases (20%) having markedly elevated total leukocyte count (TLC) (>50,000/cumm). The distribution of total leukocyte count (TLC) among the patients was as follows: 46.7% had TLC ≤ 10,000/cumm, 10.0% had TLC between 10,001-20,000/cumm, 6.7% each had TLC between 20,001-30,000/cumm and 30,001-40,000/cumm, 10.0% had TLC between 40,001-50,000/cumm, and smaller percentages had higher counts. At a minimum of 1,560 and a maximum of 2,46,450/cumm, the mean TLC was measured at 37,448/cumm, with a standard deviation of 56,409.

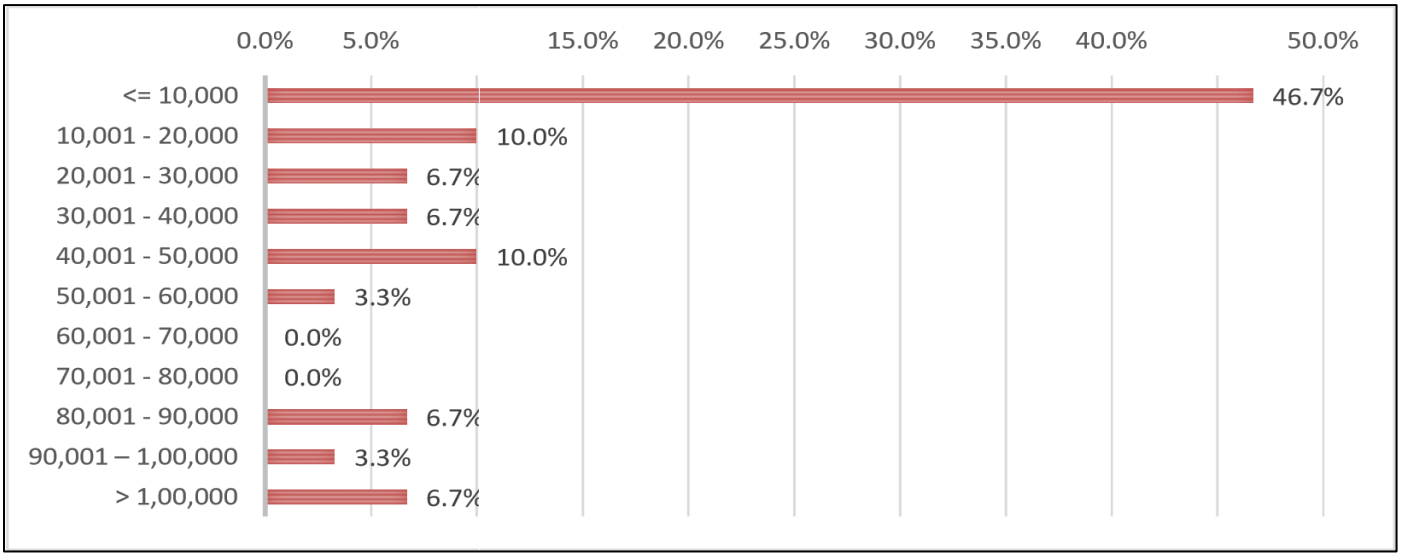

Fig 4 Total Leucocyte Count (N=30)

Table 5 Platelet Count (N=30)

Platelet Count (/cumm)	Frequency			Percentage	
<= 25,000	17			56.7%	
25,001 – 50,000	6			20.0%	
50,001 – 75,000	2			6.7%	
75,001 – 1,00,000	4			13.3%	
1,00,001 – 1,25,000	1			3.3%	
1,25,001 – 1,50,000	0			0.0%	
>1,50,001	0			0.0%	
	Mean	SD	Median	Minimum	Maximum
Platelet Count (/cumm)	36,000	32,527	24,000	4,000	1,18,000

Among the 30 cases, in Table 5 and Figure 5 , 56.7% had a platelet count ≤ 25,000/cumm, 20.0% had counts between 25,001-50,000/cumm, 6.7% had counts between 50,001-75,000/cumm, 13.3% had counts between 75,001-100,000/cumm, and 3.3% had counts between 100,001-125,000/cumm. No cases had platelet counts above 125,000/cumm. The platelet count ranged from 4,000 to 118,000/cumm, with a mean of 36,000/cumm, a standard deviation of 32,527, and a median of 24,000.

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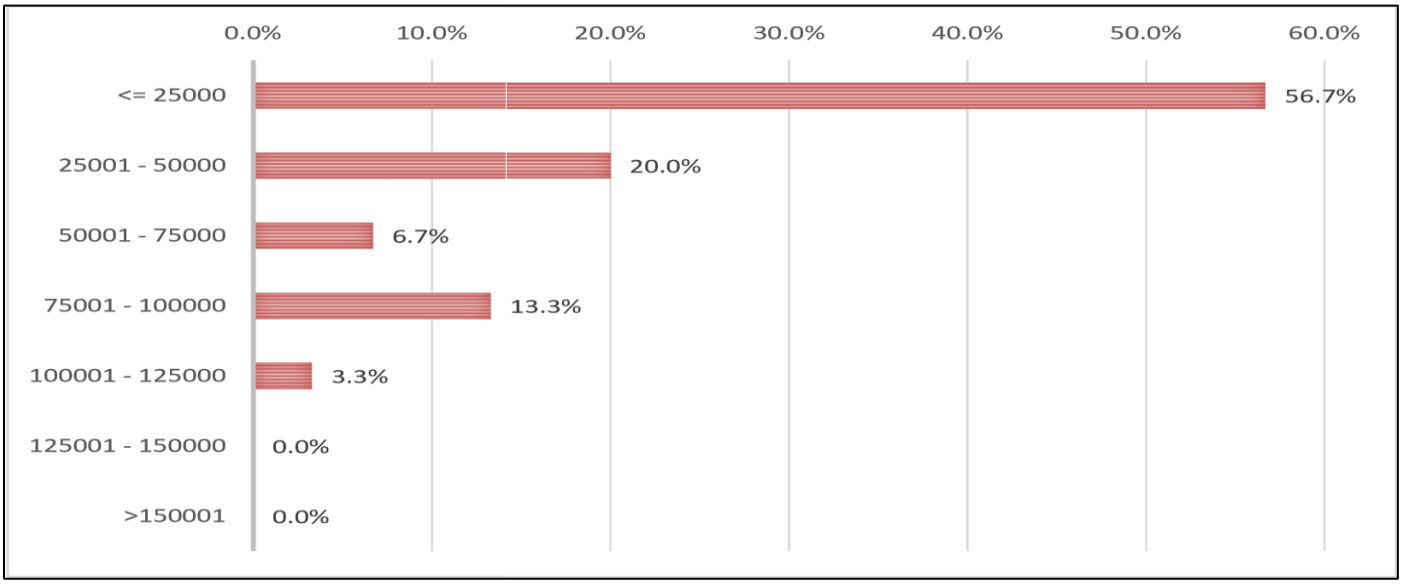

Fig 5 Platelet Count (N=30) Cytochemistry

Table 6 CD66c Expression in Lymphoblasts at Diagnosis (n=30)

CD66c: % Gated	**Frequency**	**Percentage**
<5%	13	43.3%
5 – 10%	2	6.7%
10 – 15%	1	3.3%
15 – 20%	0	0.0%
>20%	14	46.7%
CD66c Expression	Frequency	Percentage
Dim	18	60.0%
Moderate	12	40.0%
Bright	0	0.0%

At diagnosis, as shown in Table 6 , CD66c expression in lymphoblasts showed that 43.3% of cases had <5% gated, 6.7% had 5-10%, 3.3% had 10-15%, and 46.7% had >20% gated. Regarding expression intensity, 60.0% were dim, 40.0% were moderate, and none were bright. According to the study, more severe clinical and haematological characteristics were linked to paediatric B-cell Acute Lymphoblastic Leukaemia (ALL) cases with higher CD66c expression (>20% gated). Patients with elevated CD66c expression tended to have higher rates of complications such as hepato-splenomegaly and lymphadenopathy. Hematologically, these patients often exhibited more severe anemia, with lower hemoglobin levels, higher total leukocyte counts (TLC), and lower platelet counts. Overall, elevated CD66c expression in lymphoblasts at diagnosis correlated with a more aggressive disease presentation and worse clinical and hematological outcomes in pediatric B-cell ALL patient.

IV. DISCUSSION

The present study intended to evaluate the clinical and hematological factors linked with CD66c expression in pediatric patients diagnosed with B-cell Acute Lymphoblastic Leukemia (ALL). Our findings provide valuable insights into the prognostic implications of CD66c expression and its correlation with disease severity markers.

The majority of patients presented with fever (93.3%), followed by pallor (60.0%) and hepatosplenomegaly (60.0%), consistent with typical symptoms of ALL in pediatric populations. These findings align with previous literature highlighting fever and pallor as common initial complaints in pediatric ALL [5]. The study discovered that fever, which occurred in 28 cases (93.3%) and pallor in 18 cases (60%) of the study group, was the most frequent clinical symptom among paediatric patients with B-cell acute lymphoblastic leukaemia (ALL). Additionally, pain abdomen (16.7%), bodyache (10%), bleeding (10%), weakness (6.7%), neck swelling (6.7%), and joint swelling (3.3%) were also noted. These findings are consistent with established literature that identifies fever and pallor as frequently reported initial symptoms in pediatric ALL [6].

Specifically, Menon et al.,(2024)[7] reported fever in 84% of acute leukemia cases and pallor in 76% of total acute leukemia cases among children. Our findings align closely with these results, underscoring the typical clinical presentation of pediatric ALL.

Furthermore, we observed hepatosplenomegaly in 60% of our cases, with hepatomegaly noted in 80% and splenomegaly in 60%. Lymphadenopathy was also a prevalent feature (60%), alongside less frequent occurrences of bone pain (10%), edema (10%), and petechiae (6.7%).

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These clinical findings are similarly documented in studies by Li ,(2022)[8] who reported splenomegaly in 64% of B-ALL cases, where hepatomegaly was noted in 70% of acute leukemia cases.Collectively, these consistent observations across different studies highlight the reliability and significance of fever, pallor, hepatosplenomegaly, and other associated clinical features as hallmark indicators in the diagnosis and clinical management of pediatric B-cell ALL.

The haematological results we obtained demonstrated notable anomalies in paediatric B-cell acute lymphoblastic leukaemia (ALL). Anemia was prevalent, with a mean hemoglobin level of 7.19 g/dL, indicating moderate to severe anemia. In another study by Karai et al.,(2021)[9] majority of patients (56.7%) fell within the 4.0-7.9 g/dL range, underscoring the high frequency of anemia in this cohort . Additionally, leukocytosis (>10,000/cumm) was observed in 53.3% of cases, with some patients showing markedly elevated total leukocyte counts (>50,000/cumm), reflecting the aggressive nature of the disease and its potential impact on prognosis [3]. Other study by Kulis et al.,(2022)[10] suggested that thrombocytopenia was also prominent, with 56.7% of patients presenting with platelet counts ≤ 25,000/cumm, consistent with the bone marrow suppression typical of ALL [4]. Our immunophenotyping revealed that 46.7% of patients had >20% CD66c expression on lymphoblasts at diagnosis, correlating with severe clinical manifestations like hepatosplenomegaly and lymphadenopathy. This suggests CD66c as a marker for disease aggressiveness in pediatric B-cell ALL. These findings align with Pierzyna et al.,(2021) [11] which reported CD66c as a frequently expressed aberrant myeloid antigen in B-cell precursor ALL. In our study, 60.0% showed dim expression and 40.0% moderate expression, both linked to poorer clinical outcomes. Monitoring CD66c at diagnosis could aid in risk stratification and treatment planning, with higher expression indicating the need for intensified treatment. Elevated CD66c correlates with severe clinical presentations and adverse hematological profiles, underscoring its potential as a prognostic marker to guide therapeutic strategies and improve patient outcomes.

V. CONCLUSION

Our study underscores the significant association between elevated CD66c expression (>20% gated) and the severity of clinical and hematological parameters in pediatric B-cell Acute Lymphoblastic Leukemia. Patients with higher CD66c expression demonstrated increased rates of complications, notably hepato-splenomegaly and lymphadenopathy, indicative of a more aggressive disease phenotype. Hematologically, these patients exhibited severe anemia, higher total leukocyte counts (TLC), and lower platelet counts. These findings suggest that CD66c expression serves as a potential prognostic marker, predicting disease aggressiveness and clinical outcomes in pediatric B-cell ALL. Incorporating CD66c expression assessment into routine diagnostic protocols may aid in stratifying patients for tailored therapeutic interventions and monitoring disease progression. To corroborate these results and investigate the potential therapeutic target and prognostic value of CD66c in paediatric ALL therapy, more long-term research is necessary.

REFERENCES

[1]. Sethy S, Sahoo SS, Jena RK, Das S,. Clinico-Haematological Profile of patients with Mixed Phenotype Acute Leukemia: In a Tertiary Care Centre.
[2]. Khan F, Malik HS, Bozdar M, Mahmood R,. Clinico-haematological Profile and Post-Induction Remission Status of Newly Diagnosed Paediatric Acute Lymphoblastic Leukaemia Patients with ETV6:: RUNX1 Gene Rearrangement. Journal of Haematology and Stem Cell Research. 2023;3(2):68-73.
[3]. Rushin Patel et al; Glob Acad J Med Sci; Vol-6, Iss-2 (Mar-Apr, 2024): 83-97
[4]. Meena R, Nangia A, Sharma S, Chandra J. Serum levels of vascular endothelial growth factor and its receptor in newly diagnosed paediatric acute lymphoblastic leukemia. Indian Journal of Hematology and Blood Transfusion. 2021 Oct;37(4):586-92.
[5]. Onoja AM, Otene SA, Onoja AT, Ibrahim IN,. Prevalence and nature of adult hematological malignancies using bone marrow aspiration cytology in a tertiary health facility: a seven year retrospective review. Western Journal of Medical and Biomedical Sciences. 2021 Apr 12;2(1):43-9.
[6]. El Achi H, Dupont E, Paul S, Khoury JD. CD123 as a biomarker in hematolymphoid malignancies: principles of detection and targeted therapies. Cancers. 2020 Oct 23;12(11):3087
[7]. Menon H, Singh PK, Bagal B, Dolai T,. Minimal Residual Disease in the Management of B-Cell Acute Lymphoblastic Leukemia: A Systematic Review of Studies from Indian Settings. Indian Journal of Hematology and Blood Transfusion. 2024 Jan;40(1):1-1.
[8]. Li W. Measurable Residual Disease Testing in Acute Leukemia: Technology and Clinical Significance. Exon Publications. 2022 Oct 16:79-100.
[9]. Kárai B, Tisza K, Eperjesi O, Nagy AC,. A Novel Method for the Evaluation of Bone Marrow Samples from Patients with Pediatric B-Cell Acute Lymphoblastic Leukemia—Multidimensional Flow Cytometry. Cancers. 2021 Oct 9;13(20):5044.
[10]. Kulis J, Wawrowski Ł, Sędek Ł, Wróbel Ł. Machine learning based analysis of relations between antigen expression and genetic aberrations in childhood B-cell precursor acute lymphoblastic leukaemia. Journal of Clinical Medicine. 2022 Apr 19;11(9):2281.
[11]. Pierzyna-Świtała M, Sędek Ł, Kulis J,. Multicolor flow cytometry immunophenotyping and characterization of aneuploidy in pediatric B-cell precursor acute lymphoblastic leukemia. Central European Journal of Immunology. 2021 Jul 1;46(3):365-74.