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Original Article

Diagnostic utility of leukocyte volume, conductivity, and scatter (VCS) parameters in febrile neutropenia among pediatric oncology patients: A prospective observational study

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ABSTRACT

Objectives: Early identification of infection is crucial for reducing morbidity and mortality in febrile neutropenia (FN). Conventional biomarkers, including C-reactive protein (CRP) and procalcitonin (PCT), have limitations in availability and additional cost. A complete blood count (CBC) performed by automated hematology analyzers provides volume, conductivity, and scatter (VCS) parameters for leukocytes, reflecting cellular morphometric and structural changes that may serve as rapid adjunctive markers for infection.

Material and Methods: In this prospective observational study, 35 pediatric oncology patients (<18 years) with 50 FN episodes were analyzed at a tertiary cancer care center. VCS parameters of neutrophils and monocytes—mean neutrophil volume (MN-V-NE), conductivity (MN-C-NE), scatter (MN-S-NE), mean monocyte volume (MN-V-MO), and conductivity (MN-C-MO)—were recorded at a non-febrile state and during FN episodes. Correlations with blood culture, CRP, PCT, and clinical outcomes were assessed. Diagnostic accuracy was determined using receiver operating characteristic (ROC) analysis.

Results: Significant elevations were observed during FN for MN-V-NE ($p = 0.001$), MN-V-MO ($p = 0.009$), and MN-C-MO ($p = 0.028$) compared to baseline. Blood cultures were positive in 28% of episodes, with equal proportions of Gram-positive and Gram-negative organisms, and 28.6% fungal isolates. CRP and PCT levels were significantly higher in culture-positive cases ($p < 0.01$). ROC analysis showed MN-V-NE had the highest diagnostic accuracy for FN (AUC = 0.78; sensitivity 94% at cutoff >142.5), followed by MN-C-MO [area under curve (AUC) = 0.63; specificity 84% at cutoff >117.5]. No VCS parameters correlated with mortality or discharge status.

Conclusion: VCS parameters, particularly MN-V-NE and MN-C-MO, are rapid, cost-effective adjuncts for FN diagnosis in pediatric oncology patients but lack prognostic significance.

Keywords: Febrile neutropenia, Hematology analyzer, Pediatric oncology, Sepsis biomarkers, VCS parameters

INTRODUCTION

Globally, approximately 400,000 children are diagnosed with cancer every year, while 76805 new cases of malignancy are estimated in India annually.[1,2] Chemotherapy remains a cornerstone of pediatric cancer management but is frequently associated with prolonged neutropenia, predisposing patients to febrile neutropenia (FN), a medical emergency with a reported mortality of 2–13% varying based on prompt treatment versus delayed treatment.[3-6] FN not only increases the risk of sepsis and multi-organ failure but also prolongs hospitalization, delays chemotherapy, and adds to treatment costs.

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The Infectious Diseases Society of America (IDSA) defines FN as an oral or axillary temperature >38.3°C or two consecutive readings >38.0°C within 12 hours, lasting at least 1 hour, in the presence of an absolute neutrophil count (ANC) <500/mm³ or <1000/mm³ with an anticipated decline.[7] Both hematological malignancies and solid tumors (e.g., high-risk neuroblastoma, osteosarcoma, Ewing sarcoma) carry FN risk, although incidence is higher in leukemia and post-hematopoietic stem cell transplant settings.[8-10]

Blood cultures remain the diagnostic gold standard but have a positivity rate of only 10–20% in FN episodes.[9-11] Common biomarkers such as C-reactive protein (CRP) and procalcitonin (PCT) demonstrate variable sensitivity and specificity and are influenced by non-infectious inflammatory conditions. Therefore, there is an unmet need for inexpensive, widely available, and rapid biomarkers to aid early diagnosis and therapeutic decision-making in FN.

Modern automated hematology analyzers, beyond enumerating blood cells, provide morphometric and structural data through volume, conductivity, and scatter (VCS) parameters, collectively termed cell population data (CPD).[12-14] The Coulter LH system measures:

Volume (V): Via electrical impedance

Conductivity (C): Using radiofrequency opacity (reflecting nuclear-cytoplasmic ratio and internal composition)

Scatter (S): Based on laser light diffraction (indicative of granularity and cytoplasmic complexity)

Previous studies indicate that VCS parameters, particularly mean neutrophil volume (MNV), increase significantly in septic patients, even in those with leukopenia, and may outperform conventional markers like white blood cells (WBC) count, CRP, and PCT for early sepsis detection.[15-18] However, data on their role in pediatric FN is limited.

Objective

This study aimed to assess variations in VCS parameters during FN episodes compared to baseline in pediatric oncology patients and evaluate their diagnostic accuracy, correlation with conventional biomarkers, and prognostic utility.

MATERIAL AND METHODS

This was a prospective observational study carried out at a tertiary care cancer center affiliated with a medical teaching institution in North India. The study formed part of a postgraduate research project and received prior approval from the Institutional Research Committee (SRHU/HIMS/ETHICS/2025/81)

Study population

A total of 35 pediatric patients (aged <18 years) with a confirmed diagnosis of malignancy and undergoing chemotherapy were enrolled. Children receiving leukocyte transfusions for sepsis were excluded. Informed consent was obtained from parents or legal guardians before inclusion in the study.

Data collection

Clinical and laboratory data were retrieved from the hospital's electronic medical record system after confirming the diagnosis and chemotherapy protocol. Baseline measurements were recorded when the child was clinically stable and a febrile, with no evidence of infection.

Volume, conductivity, and scatter (VCS) parameters were extracted from the complete blood count (CBC) performed during routine follow-up or chemotherapy visit immediately before the febrile episode. Further data collection points were at the time of admission for febrile neutropenia (FN) and every 48 hours thereafter until discharge or death.

The VCS parameters included mean neutrophil volume (MN-V-NE), mean neutrophil conductivity (MN-C-NE), mean neutrophil scatter (MN-N-S), mean monocyte volume (MN-V-MC), mean monocyte conductivity (MN-C-MC), mean monocyte scatter (MN-S-MC).

These values were extracted from CBC reports generated by the automated Coulter analyzer.

Study protocol

On presentation with FN, patients underwent evaluation as per institutional protocol, which included CBC, C-reactive protein (CRP), procalcitonin, and blood culture. VCS data from Day 1 of admission were retrieved, followed by alternate-day readings during hospitalization. For comparison, VCS values from the most recent prior visit (either outpatient or inpatient for chemotherapy) when the child was clinically well were considered as baseline values.

Data management and statistical analysis

All data were compiled in Microsoft Excel and analyzed using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA). Categorical variables were compared using the Chi-square test or Fisher's exact test where appropriate. A p-value <0.05 was considered statistically significant. Continuous variables were expressed as mean ± standard deviation (SD). Correlation between variables was assessed using Pearson correlation and the Mann-Whitney U test. Receiver operating characteristic (ROC) curves were plotted to determine optimal cut-off values for VCS parameters, and their sensitivity and specificity for predicting FN episodes were calculated.

RESULTS

During the study period, 50 episodes of febrile neutropenia (FN) were recorded among 34 pediatric oncology patients. Of these, 29% (n = 10) occurred in children aged <5 years, 39% (n = 13) in those aged 6–10 years, and 32% (n = 12) in children >10 years. The study cohort comprised 61% males (n = 21) and 39% females (n = 13).

Distribution of underlying malignancies

Leukemia constituted the predominant diagnosis. Acute lymphoblastic leukemia (ALL) accounted for the majority, with 28 cases, while acute myeloid leukemia (AML) was observed in 3 cases, and solid organ malignancies in another 3 cases. The low representation of solid tumors likely reflects the reduced incidence of FN in this group.

Comparison of VCS Parameters at Baseline and FN Onset

Table 1 summarizes the comparison of Volume, Conductivity, and Scatter (VCS) parameters between baseline (afebrile state) and at the onset of FN episodes. Mean Neutrophil Volume (MN-V-NE) showed a significant rise from a median of 144.50 (IQR: 138.75–154.25) at baseline to 165.00 (IQR: 148.00–180.25) during FN (P = 0.001). Mean Monocyte Volume (MN-V-MO) and Mean Monocyte Conductivity (MN-C-MO) also demonstrated significant increases (P = 0.009 and P = 0.028, respectively). Other parameters, including MN-C-NE, MN-MALS-NE, MN-UMALS-NE, MN-LMALS-NE, and MN-LALS-NE, did not show statistically significant changes (P > 0.05).

Table 1: VCS value – Baseline vs febrile neutropenia at onset

VCS Parameters	Baseline (Median/IQR)	Sensitivity (Median/IQR)	P Value
MN-V-NE	144.50 (138.75-154.25)	165 (148.00-180.25)	0.001
MN-C-NE	144 (139.00-146.25)	145 (140.00-148.25)	0.548
MN-MALS-NE	132 (126.75-138.00)	131.50 (126.00-136.25)	0.841
MN-UMALS-NE	130.50 (123.00-135.00)	130 (126.00-136.00)	1.000
MN-LMALS-NE	129 (122.00-135.25)	130 (122.00-132.25)	0.841
MN-LALS-NE	156 (140.75-164.75)	153 (140.50-165.25)	0.689
MN-V-MO	178 (163.00-184.00)	183.50 (176.50-198.75)	0.009
MN-C-MO	121 (119.00-125.00)	123 (120.00-129.00)	0.028

Of the 50 episodes, 28% (n = 14) showed positive blood cultures, while 60% (n = 36) were sterile. VCS: Volume, conductivity, scatter; IQR: Inter quartile range , MN-V-NE: Mean neutrophil volume, MN-C-NE: Mean neutrophil conductivity, MN-MALS-NE: , MN-UMALS-NE:, MN-LMALS-NE: ,MN-LALS-NE: , MN-V-MO: Mean monocyte volume, MN-C-MO: Mean monocyte conductivity, p value significant for <0.05

Blood culture positivity and VCS parameters

Among the 50 FN episodes, 28% (n = 14) yielded positive blood cultures, while 72% (n = 36) were sterile. The distribution of isolated organisms is illustrated in Figure 1.

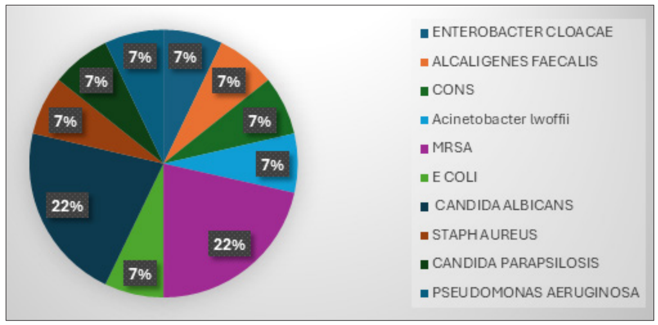

Figure 1: Presents the spectrum of organisms identified in febrile neutropenia (FN) episodes that showed positive blood cultures

When comparing VCS parameters between culture-positive and culture-negative cases, no statistically significant differences were observed. For instance MN-V-NE median was 169.50 (IQR: 152.75–180.50) in culture-positive cases versus 162.50 (IQR: 148.00–180.50) in sterile cases (P = 0.753). MN-C-NE medians were identical (145) in both groups (P = 0.829).

Comparison by procalcitonin and CRP status

Similarly, there were no significant differences in VCS parameters between procalcitonin-positive and procalcitonin-negative FN episodes. MN-V-NE was higher in procalcitonin-positive cases (median: 173.00) than in negative cases (median: 157.00), but the difference was not statistically significant (P = 0.247). Other VCS indices (MN-C-NE, MN-MALS-NE, MN-V-MO, MN-C-MO) also showed P > 0.05 across groups. No significant variations were found in VCS parameters based on CRP positivity. MN-V-NE medians were 165.50 for CRP-positive cases and 159.00 for CRP-negative cases (P = 0.850).

Fatal outcomes and VCS patterns

Fatality was documented in 4 cases (11.7%) during FN episodes. Comparison of VCS values on Day 1 of FN between patients who were discharged and those who succumbed revealed no significant differences. MN-V-NE was 159.00 (IQR: 104.50–165.00) in fatal cases and 166.00 (IQR: 148.50–180.50) in survivors (P = 1.000). MN-V-MO was 160.00 in fatal cases versus 184.00 in survivors (P = 0.234).

Predictive value of VCS parameters for FN

ROC curve analysis demonstrated that certain VCS parameters—particularly MN-V-NE, MN-V-MO, and MN-C-MO—showed good predictive value for FN [Figure 2 and Table 2]. The predictive value of VCS parameters for culture-proven sepsis or outcome was not significant.

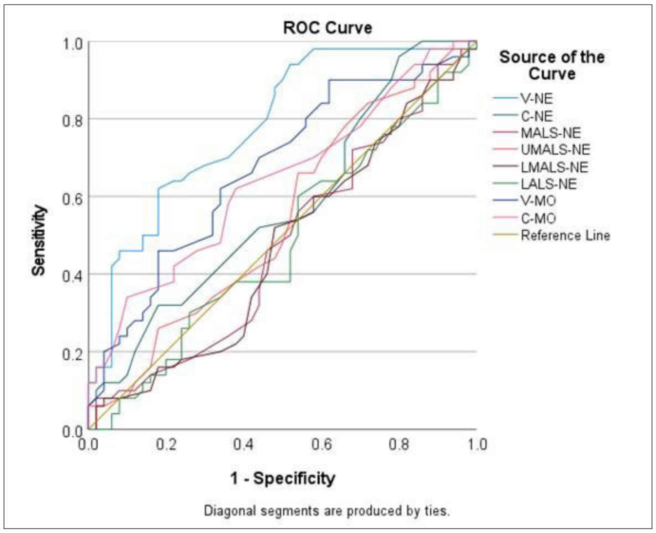

Figure 2: ROC curve- to determine predictive value of VCS parameters for febrile neutropenia. ROC: Receiver operating characteristics, VCS: Volume, conductivity, scatter, V-NE: Volume neutrophil, C-NE: Conductivity neutrophil, MALS: Mean axila light scatter, LMALS: Low-angle MALS, UMALS- Upper-angle MALS, LALS: Low-ngle light scatter, V-MO: Volume monocytes, C-MO: conductivity monocytes

Table 2: VCS parameters ROC cut-off for FN episode

VCS Parameters	Cutoff	Sensitivity	Specificity	AUC	P Value
MN-V-NE	142.50	0.94	0.54	0.78	0.000
MN-V-MO	166.50	0.90	0.62	0.67	0.003
MN-C-MO	117.50	0.94	0.84	0.63	0.017

VCS: Volume, conductivity, scatter, ROC: Receiver operating characteristic, FN: Febrile neutropenia, MN-V-NE: Mean neutrophil volume, MN-V-MO: Mean monocyte volume, MN-C-MO: Mean monocyte conductivity, AUC: Area under curve, P value significance <0.05

Trend analysis over time

Evaluation of VCS parameter trends on Days 1, 3, and 5 of FN episodes indicated dynamic changes. MN-V-NE increased markedly at FN onset (Day 1), showed a slight decline by Day 3, and stabilized by Day 5. A similar pattern was observed for MN-V-MO, whereas MN-C-NE remained relatively stable throughout the course.

DISCUSSION

This study evaluated changes in VCS parameters from baseline to the onset of febrile neutropenia (FN) in pediatric oncology patients. We observed a significant increase in mean neutrophil volume (MN-V-NE; p = 0.001), mean monocyte volume (MN-V-MO; p = 0.009), and mean monocyte conductivity (MN-C-MO; p = 0.028) during FN episodes. These findings suggest that specific VCS parameters, particularly those reflecting cellular volume and conductivity, may serve as early indicators of FN. Other parameters, including scatter-related metrics, did not demonstrate statistically significant changes, indicating limited diagnostic relevance in this context.

The potential diagnostic utility of VCS parameters in FN prediction has been previously suggested in the literature, though data remains scarce. Our results are consistent with the hypothesis that neutrophil and monocyte activation during infectious or inflammatory states contributes to changes in cell volume and conductivity, which are measurable through automated hematology analyzers.[12,15,18]

When comparing blood culture-positive episodes to sterile cases, no statistically significant differences were observed in any VCS parameter. This suggests that while VCS parameters change during FN, they may not differentiate between microbiologically confirmed infections and culture-negative episodes. Similar findings were reported by Bharti A *et al.*, who found limited utility of certain VCS parameters in diagnosing sepsis.[15] In contrast, Sudhakar et al. reported that specific VCS indices could predict bacterial infection and its severity, and Zhou *et al.* demonstrated that a combined panel of VCS parameters improved diagnostic accuracy for bacterial infections in chemotherapy recipients.[16,17] This discrepancy underscores the need for larger, multicentric studies to validate these observations.

Furthermore, no significant correlations were found between VCS parameters and established inflammatory markers such as C-reactive protein (CRP) or procalcitonin (PCT). While CRP and PCT remain established biomarkers for sepsis, their lack of association with VCS parameters in our study suggests that morphological changes detected by VCS may represent a distinct biological phenomenon, potentially reflecting early cellular activation rather than systemic inflammatory responses. Previous studies reported significant but variable associations between VCS indices and sepsis biomarkers, highlighting possible differences in patient populations or study methodologies.[18,19]

Importantly, baseline VCS parameters did not correlate with clinical outcomes, such as survival versus mortality. This finding suggests that while VCS parameters may be useful for early detection of FN, they are not reliable prognostic indicators in pediatric oncology patients. Their inability to predict adverse outcomes limits their role in risk stratification or therapeutic decision-making at present.

Receiver Operating Characteristic (ROC) curve analysis demonstrated that MN-V-NE exhibited the highest discriminative ability for FN diagnosis, with an area under the curve (AUC) of 0.78, indicating good diagnostic performance. Monocyte-related parameters, including MN-C-MO and MN-V-MO, also showed moderate diagnostic accuracy. A review of literature has found variable ROC analysis results. While Kannan & Selvam noted poor specificity of MN-V-NE and poor sensitivity of MN-V-MO (40% and 42.29% respectively), Mardi et al noted a better sensitivity and specificity of MN-V-NE (76%, 63%) and for MN-V-MO (86%, 40%).[20,21]A Recent study by Nesagri et al showed unusually high sensitivity and specificity of MN-V-NE (97%, 96%) and MN-V-MO (95%,86%) for FN.[22] These observations are clinically relevant, as they point to the possibility of using automated cell analyzer-derived indices as adjunct tools for FN diagnosis, particularly in resource-limited settings where advanced biomarkers may not be readily available.

CONCLUSION

Overall, the study highlights the potential of VCS parameters as rapid, cost-effective markers for identifying FN episodes. However, their lack of correlation with infection severity, culture positivity, or outcomes indicates that they should be interpreted cautiously and in conjunction with clinical findings and standard biomarkers.

Author contributions: SP,NA, MD, AB, KD: Conceptualized the study; SP, NA, MD, KD: Drafted methodology and worked for data collection; SP, AB, KD: Drafted manuscript and all authors reviewed and finalized the draft.

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REFERENCES

1. Ward ZJ, Yeh JM, Bhakta N, Frazier AL, Girardi F, Atun R. Estimating the total incidence of global childhood cancer: A simulation-based analysis. Lancet Oncol 2019;20:483–493.
2. Arora RS, Bagai P, Bhakta N. Estimated national and state level incidence of childhood and adolescent cancer in India. Indian Pediatr 2021;58:417–423.
3. Kebudi R, Kurucu N, Tuğcu D, Ayan I, Bayhan T, Darendeliler E, *et al*. Febrile neutropenia in children with cancer in the era of newer broad-spectrum antibiotics: Lessons from 2,494 episodes from a single center in Turkey. Pediatr Hematol Oncol 2021;38:440–451.
4. Scheler M, Lehrnbecher T, Groll AH, von Lilienfeld-Toal M, Simon A, Castagnola E, *et al*. Management of children with fever and neutropenia: Results of a survey in 51 pediatric cancer centers in Germany, Austria, and Switzerland. Infection 2020;48:607–618.
5. Erbaş IC, Çakıl Güzin A, Özdem Alataş Ş, Ceylan A, Yılmaz S, Güneş A, *et al.* Etiology and factors affecting severe complications and mortality of febrile neutropenia in children with acute leukemia. Turk J Haematol 2023;40:143–153.
6. Düzenli Kar Y, Özdemir ZC, Bör Ö. Evaluation of febrile neutropenic attacks of pediatric hematology-oncology patients. Turk Pediatri Ars 2017;52:213–220.
7. Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, *et al*. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis 2011;52:e56–e93.
8. Castagnola E, Fontana V, Caviglia I, Faraci M, Fioredda F, Haupt R, *et al*. A prospective study on the epidemiology of febrile episodes during chemotherapy-induced neutropenia in children with cancer or after hemopoietic stem cell transplantation. Clin Infect Dis 2007;45:1296–1304.
9. Barton CD, Waugh LK, Nielsen MJ, Paulus S. Febrile neutropenia in children treated for malignancy. J Infect 2015;71:S27–S35.
10. Castagnola E, Garrè ML, Bertoluzzo L, Faraci M, Fioredda F, Losurdo, *et al*. Epidemiology of febrile neutropenia in children with central nervous system tumor: Results from a single center prospective study. J Pediatr Hematol Oncol 2011;33:e310–e315.
11. Siddiqui B, Azmat R, Tikmani SS, Rafi S, Syed B, Khan MT, *et al*. Frequency of bloodstream infection in febrile neutropenic patients, experience from a developing country. Ann Med Surg (Lond) 2018;34:71–74.
12. Chaves F, Tierno B, Xu D. Quantitative determination of neutrophil VCS parameters by the Coulter automated hematology analyzer. Am J Clin Pathol 2005;14:440–444.
13. Beckman Coulter Inc. Coulter LH 750 system reference manual. Miami, FL: Beckman Coulter Inc.; 2004. Publication No. 4277248DD.

14. Zini G, Garzia M, Di Mario A, Ricerca BM, Piccioni P, Tarnani M, *et al*. Fully automated identification of dysplastic neutrophil in peripheral blood using the positional parameters provided by the coulter LH750 analyzer. Blood 2005; 106:4904
15. Bharti A, Palta A, Bedi RK, D'Cruz S. An analytical observational study for diagnostic accuracy of volume, conductivity and scatter (VCS) indices of neutrophils for diagnosis of sepsis in an emergency hospital setting. Indian J Med Res 2024;160:179–185.
16. Sudhakar R, Yuva Vishalini R, Kathiresan J. Clinicopathological relevance of volume, conductivity and scatter parameters in critically ill patients. Natl J Basic Med Sci 2018;9:27–34.
17. Zhou N, Liu L, Li D, Zeng Q, Song X. VCS parameters of neutrophils, monocytes and lymphocytes may indicate local bacterial infection in cancer patients who accepted cytotoxic chemotherapeutics. Eur J Clin Microbiol Infect Dis 2016;35:41–48.
18. Iskander I, Mekkawy AH, El-Fattah AE–A. Role of automated volume, conductivity and scatter (VCS) parameters of neutrophils as indicators of sepsis. Hematol Transfus Cell Ther 2022;44:209–215.
19. Goyal H, Singhal A, Joseph M. Utility of VCS parameters as a cost-effective and early marker of sepsis: A hospital-based study. Indian J Crit Care Med 2023;27:647–650.
20. Mardi D, Fwity B, Lobmann R, Ambrosch A. Mean cell volume of neutrophils and monocytes compared with C-reactive protein, interleukin-6 and white blood cell count for prediction of sepsis and nonsystemic bacterial infections. Int J Lab Hem 2010;32:410–418.
21. Kannan A, Selvam P. Potential of using VCS parameters of neutrophils and monocytes as an early diagnostic tool in acute bacterial infections. Natl J Lab Med 2017;6:38–43.
22. Nesargi P, Niranjan HS, Bandiya P, Benakappa N. Neutrophil volume, conductivity and scatter (VCS) as a screening tool in neonatal sepsis. Sci Rep 2020;10:4457.

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