ORIGINAL ARTICLE

Utility of VCS Parameters as a Cost-effective and Early Marker of Sepsis: A Hospital-based Study

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Abstract

Introduction: Sepsis is a life-threatening condition. Nowadays, hospitals rely on laboratory parameters like CRP and procalcitonin to detect sepsis. There is a need to evaluate and validate more accurate and early predictors of sepsis in critically ill patients. We analyzed volume, conductivity, and scatter (VCS) parameters of leukocytes in sepsis patients and compared them with the control group with no illness.

Materials and methods: It was a prospective case-control study. A total of 80 patients were studied with 40 sepsis cases and 40 controls. Peripheral smear examination was done in all the cases. Other parameters, such as WBC count, neutrophil%, absolute neutrophil count (ANC), – High-sensitive C-reactive protein (hs-CRP), procalcitonin, and blood cultures were analyzed. We took the data of the patients from medical records and correlated it with other tests. Complete blood picture reports were generated by the Beckman Coulter LH series (LH 750 and 780). VCS parameters for neutrophils, lymphocytes and monocytes were compared between both groups. The results were analyzed using SPSS software (16.0 version)

Results: The age group was 20–85 years with male predominance. The mean neutrophil volume (MNV) and mean monocyte volume (MMV) were higher in the sepsis group when compared with the control group. The mean neutrophil conductivity and scatter was lower in the sepsis group and comparatively higher in the control group but it was insignificant. The mean neutrophil volume values were higher in the sepsis group even with low total leukocyte count (TLC) when the patient had sepsis. There is no change in the mean lymphocyte VCS parameter and mean monocyte conductivity, scatter in both the groups.

Conclusion: The mean neutrophil volume and MMV are found to be good sensitive markers in the prediction of sepsis. Even when TLC is on the lower side in patients with sepsis, these parameters predict sepsis accurately. This helps clinicians to assess sepsis in patients at an early stage and has an important practical implication.

Keywords: Mean neutrophil volume, Mean monocyte volume sepsis, Volume, conductivity, scatter.

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Introduction

Sepsis is a life-threatening condition.[1] It is difficult to predict sepsis at an early stage due to the non-specificity of symptoms such as fever.[2,3] Therefore, now hospitals rely on laboratory parameters such as CRP and procalcitonin (PCT) to detect sepsis. Due to escalating burden of complications and mortality associated with sepsis, there arises a necessity to assess and authenticate more precise indicators of sepsis in critically ill patients. The gold standard for diagnosing sepsis is blood culture but it has time constraints. Till now, pathologists rely on morphological examination of neutrophils (toxic granulations, vacuolization, left shift, Dohle bodies) in peripheral smears for the prediction of sepsis, but this process has person-to-person variability and is time-consuming.[4–6] Typically, the data are acquired by analyzing approximately 8000 leukocytes within seconds, employing impedance to gauge cell volume, radiofrequency opacity to assess internal cellular composition, and a laser beam to measure light scatter for cytoplasmic granulations and nuclear characteristics.[5] Leukocyte VCS parameters in sepsis patients were compared with those of a control group unaffected by any illness. Extensive studies have been conducted on VCS parameters of neutrophils within the Western population and have been proven to be a sensitive parameter.[7] We evaluated the clinical utility of these parameters.

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Materials and Methods

The study design was a prospective case-control study conducted in the Department of Lab Medicine at a tertiary care hospital located in New Delhi over a 2-month period. We divided the patients into two groups, one with blood culture positive "SEPSIS group" and the other age-matched "CONTROL group" with no illness. A total of 80 patients were included in the analysis, evenly divided into two groups with 40 cases each. The "SEPSIS group" includes all cases with positive blood cultures. We analyzed the data of the

Table 1: Comparison of various parameters between sepsis and control group

Parameters	*Sepsis*	*Control (No sepsis)*
Number of cases	40	40
Mean age (years)	55.3 ± 20.8	43 ± 21.5
Age range (years)	20–85	20–80
Sex M:F ratio	3.4:1	4:1
Fever	30/40	Not present
TLC (cells/cumm)		
<4000	3	0
4000–11000	9	40
>11000	28	0
Neutrophil%	78.1 ± 13.1	64.2 ± 9.2
Mean ANC (Absolute neutrophil count)	12.9 ± 9.7	4.9 ± 1.04
Blood culture	Positive	Negative
HSCRP In 14/40	15.9 ± 14.3	Not done
Procalcitonin 20/40	8.14 ± 10.5	Not done
Peripheral smear examination	Left shift, Toxic change	Nil diagnostic
Mean neutrophil volume (MNV)	159.8 ± 13.1	146.7 ± 6.56
Mean neutrophil conductivity (MNC)	139.2 ± 6.5	143 ± 4.3
Mean neutrophil scatter(MNS)	135.4 ± 8.3	145.3 ± 6.3
Mean lymphocyte		
Volume (MLV)	87.4 ± 7.3	83.5 ± 3.4
Conductivity (MLC)	112.2 ± 5.8	111.5 ± 3.7
Scatter (MLS)	69.1 ± 7.9	63.7 ± 6
Mean monocyte		
Volume (MMV)	176.6 ± 13.7	164.7 ± 5.7
Conductivity (MMC)	119.5 ± 6	120 ± 3.5
Scatter (MMS)	86.5 ± 6.05	88.6 ± 5.7

patients from medical records and correlated them with other tests. Peripheral smear examination was done in all the cases. Other parameters, such as fever, WBC count, neutrophil%, ANC, – High-sensitive C-reactive protein (hs-CRP), procalcitonin, and blood cultures were analyzed. About 40 control group samples were taken who came for normal health check-ups with no associated illness. Complete blood picture reports were generated for all the cases by LH 750 and LH 780 hematology analyzer (Beckman Coulter). volume, conductivity, and scatter (VCS) parameters for neutrophils, lymphocytes, and monocytes were compared between the two groups.

Statistical analysis: The data were analyzed using SPSS software.

Results

A total of 80 cases (Forty cases in each group) were evaluated prospectively. The data are presented in Table 1. In the sepsis group, the mean age was 55 years ranging from 20 to 85 years, while in the control group, the mean age was 42 years, also ranging from 20–85years. Male: Female (M: F) ratio in the sepsis group was 3.4:1 and in the control group was 4:1. In the sepsis group, fever was present in 30 cases out of 40, varying from mild-to-severe degree. The mean WBC count was 15.4 ± 9.6 cells/cumm with a range of 2,200–43,900 cells/cumm in the sepsis group and 7.6 ± 1.2/cumm (range 4.9–9.6) in the control group. In the sepsis group, the mean hemoglobin was 10.3 ± 2.6 g/dL while in the control group, it was 12.7 ± 1.2 g/dL. The mean platelet count was 245 ± 152.3/cumm in the sepsis group and 236 ± 64/cumm in the control group. The mean neutrophil% in the sepsis group was 78.1 ± 13.1%, whereas in the control group, it was 64.2 ± 9.2%. The mean lymphocyte% in the sepsis group was13.8 ± 9.4%, and in the control group, it was 26.4 ± 7.7%. The mean monocyte% was 5.8 ± 4.03% in the sepsis group and in the control group 6.7 ± 2.2%. The mean absolute neutrophil count (ANC) in the sepsis group was 12.9 ± 9.7 cells/cumm and in the control group, it was 4.9 ± 1.04 cells/cumm.

Table 2: The AUC of VCS parameters

Test	*Area under curve (AUC)*
TLC	0.775
ANC	0.77
MNV	**0.80**
MNC	0.33
MNS	0.17
MMV	**0.82**
MMC	0.46
MMS	0.38

The bold values indicates the highest value of area under the curve (AUC) i.e more than 0.8 in our study.

The mean neutrophil volume (MNV) in the sepsis group was 159.8 ± 13.1 (128.4–192.8), whereas in the control group, it was 146.1 ± 6.5. The mean neutrophil conductivity (MNC) and mean neutrophil scatter (MNS) in the sepsis group were 139.2 ± 6.5 and 135.4 ± 8.3, whereas in the control group, they were 143 ± 4.3 and 145.3 ± 6.3. The mean lymphocyte VCS in the sepsis group were 87.4 ± 7.3, 112.2 ± 5.8, and 69.1 ± 7.9, whereas in the control group, they were 83.5 ± 3.4, 111.5 ± 3.7, and 63.7 ± 6, respectively. The mean monocyte volume (MMV), mean monocyte conductivity (MMC), and mean monocyte scatter (MMS) in the sepsis group were 176.6 ± 13.7, 119.2 ± 6.0, and 86.5 ± 6.0, whereas in the control group were 164.7 ± 5.7, 120 ± 3.5, and 88.6 ± 5.7 respectively. Table 1 Comparison of parameters between the sepsis group and the control group.

ROC curves were plotted for parameters { total leukocyte count (TLC), ANC, neutrophils, VCS (MNV, MNC, MNS), monocyte VCS (MMV, MMC, MMS)} in the sepsis group and the control group. The area under the curve (AUC) was highest for MNV and MMV at 0.8 and 0.82. The AUC for TLC and ANC were 0.77 and 0.77, respectively (Table 2 and Fig. 1).

The most sensitive test for the prediction of sepsis was MNV and MMV when compared with other parameters. MNC, MNS, MMC and MMS were found to be insensitive markers for the prediction of sepsis.

At a cutoff of 150, MNV demonstrated a sensitivity of 72.5% and a specificity of 70%, whereas with a cutoff of 155, a sensitivity of 60%, and specificity of 90% was achieved. When setting the cutoff of 170 for MMV, the sensitivity was 83.3% and the specificity was 77.3, whereas when a cutoff of 175 was set, the sensitivity of 90% and specificity of 63.3% was achieved (Table 3).

Discussion

Fully automated hematology analyzers have revolutionized the way we practice laboratory medicine.[5] Automated hematology analyzers are based on the principle of VCS technology.[8] They are used in all clinical laboratories for accurate and precise differential

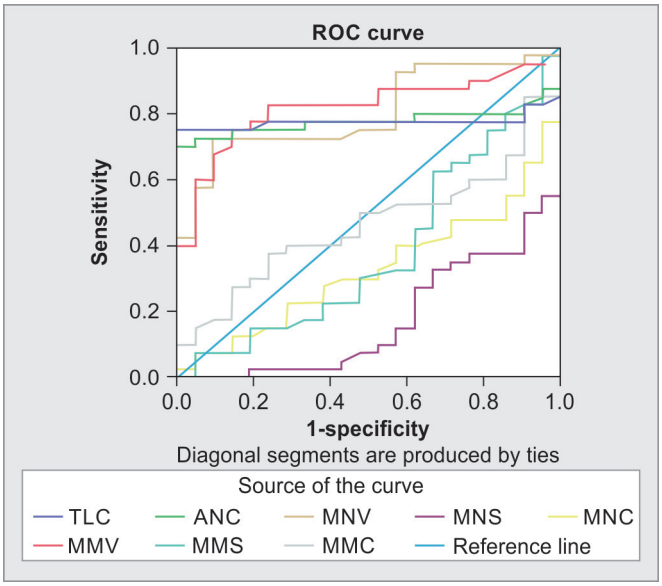

Fig. 1: ROC curve of VCS parameters

K Pooja et al.,[11] Purohit,[10] Chaves[6] and other studies found a statistically significant difference between both groups with lower values in sepsis patients.[12,13] The decrease in the MNS was attributed to a left shift in neutrophils. Only Kannan et al. found that MNS was higher in cases than control,[7] they stated that elevation in MNS might be attributed to an increase in the presence of toxic granulations in certain cases. We did not find any significance in both groups.

Celik et al. also found a significant increase in MNV and a decrease in MNC and MNS in septic newborns.[14]

There was no significant difference in MNC in both groups. Kannan et al., Purohit, Chaves 2005, and Suresh et al. [6,7,10] also stated the same, but Lee AJ et al. described a lowering of MNC values in sepsis patients when compared with the control group. [4]

Both groups showed no variance in lymphocyte VCS parameters, monocyte conductivity (MMC), and monocyte scatter (MMS). Our study revealed a significant increase in MMV within the sepsis group, while it was found to be lower in the control group. With a cutoff of 170, sensitivity was 83.3% and specificity was 77.3%. Lee AJ stated that MMV is more sensitive to sepsis than MNV.[4] We also found a similar finding with the area under the curve for MMV being 0.82

Table 3: Comparison of sensitivity and specificity of MNV and MMV in various national and international studies

No.	*Study*	*Year*	*MNV cutoff*	*Sensitivity*	*Specificity*	*MMV cutoff*	*Sensitivity*	*Specificity*
1	Chaves et al.[6]	2005	150	70%	91%	–	–	–
2	Mardi et al.[17]	2010	150	76%	63%	170	86%	40%
3	Celik et al.[14]	2012	157	79%	82%	–	–	–
4	Lee AJ et al.[4]	2013	150.5	88.9%	52.5%	175.5	83.3%	59.3%
5	Abiramalatha et al.[18]	2016	151	71.3%	71.9%	–	–	–
6	SK Pooja et al.[11]	2016	150	72%	70%	170	80.6%	77.5%
7	Kannan A et al. [7]	2017	129.3	92.7%	40%	157.4	42.27%	–
8	Arora P et al.[19]	2019	150.2	79.1%	95%	168.3	80.6%	77.5%
9	Nesagri P et al.[16]	2020	157	97%	96%	156	95%	86%
10	Our study	2019	**150**	72.5%	70%	**170**	83.3%	77.3%
	″	″	**155**	60%	90%	**175**	90%	63.3%

The bold values signifies the values present in our study.

counts. Volume conductivity, scatter parameters are not routinely reported in daily practice. VCS technology made it possible to analyze a large number of white blood cells (approx. 8,000) in a fraction of seconds and classify them with high efficacy.

Most of the patients in our study are elderly with a male predominance. Kannan A et al. also had more males than females in their study with a mean age of 49.4 ± 19.6 years.[7]

The total leukocyte count was high in most of the sepsis cases but in a few, leukopenia was also present. The mean neutrophil volume was higher in the sepsis group with a mean of 159.8 ± 13.1 fl when compared with the control group.

We found significant differences in the values of TLC, ANC, and neutrophil% between the sepsis group and the control group, as similar findings were noted in other studies also.[6,9–11]

There was a significant difference between MNV and MMV in sepsis and the control group with higher values in the sepsis group. The mean neutrophil volume was found high even in cases with TLC <11000 cells/cumm. Similar findings were observed in other studies.[6,10]

MNS was lower in the sepsis group when compared with the control group, but no statistical significance was found. Suresh and the AUC for MNV being 0.8. The AUC values between 0.7 and 0.8 suggest moderate and high test accuracy. The accuracy of the use of MNV may vary depending on age group, the nationality of patients as well as the model of analyzer used.[15] Table 3 displays the sensitivity and specificity in various studies nationally and internationally.

The mean neutrophil volume and MMV have proved to be very potential, cost-effective, and sensitive markers in predicting sepsis. A-Lin Jee et al. conducted a comparison between the sensitivity and specificity of procalcitonin and MNV. At a cutoff of 0.32, PCT exhibited a sensitivity of 94.4% and a specificity of 72%. If we compared our data with A-Lin Jee, using a cutoff of 150 for MNV and 175 for MMV, the sensitivity of 72.5% and 90% and specificity of 70% and 63.3%, respectively were achieved. So, in terms of cost, MNV and MMV have comparable sensitivity and specificity to procalcitonin.

Nesargi P et al. conclusion indicated that an MNV greater than 157 demonstrated a sensitivity of 97% and specificity of 96% with an AUC (area under the curve) of 0.99 in cases of proven sepsis. Furthermore, an MNV greater than 156 showed 95% sensitivity and 86% specificity with an AUC OF 0.97 in cases of proven and probable sepsis.[16]

The current study was prospective with a smaller sample size. VCS parameters can offer several advantages in different clinical scenarios associated with neutrophilic leucocytosis, such as tissue hypoxia or ischemia, chronic inflammation, use of glucocorticoids, and various myeloproliferative disorders.[9]

Limitation

The limited sample size might have introduced incorporation bias, potentially overestimating the diagnostic efficacy of the investigated markers. Consequently, large-scale prospective studies are required to address this matter comprehensively.

Conclusion

In our study, a significant difference was found in MNV and MMV values in both groups. No significant difference was found in MNC, MNS, Lymphocyte VCS, MMC and MMS. MNV and MMV were the sensitive and cost-effective tests in predicting sepsis in hospitalized patients. It is a very cost-effective indicator of early sepsis in hospitals and made it possible to predict sepsis in critically ill patients to initiate antibiotic therapy at the right time.

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