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Evaluating Monocyte Distribution Width (MDW) as an Early Indicator of Sepsis in Comparison to C-Reactive Protein and Procalcitonin

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Abstract

Objectives: To evaluate and compare the diagnostic accuracy of Monocyte Distribution Width (MDW) in Beckman coulter DxH900 with sepsis biomarkers Procalcitonin and C-Reactive protein(CRP).

Background: Early detection of sepsis is crucial for improving patient outcomes. Conventional biomarkers, such as Procalcitonin (PCT) and C Reactive protein(CRP), are frequently employed but have drawbacks, especially when it comes to early sepsis identification. Through the detection of morphological alterations in monocytes during inflammation, Monocyte Distribution Width(MDW), a novel haematological parameter, has become a promising early sepsis indicator compared with CRP and PCT. With this background, we aimed to evaluate the efficacy of MDW as an early indicator of sepsis and to compare its diagnostic accuracy with established biomarkers such as CRP and PCT.

Methodology: We conducted a prospective observational study on patients suspected of sepsis with the age ranged from 1 to 90 years. MDW, CRP, and PCT levels were measured. Continuous variables are expressed in Mean & Standard deviation (SD) and the area under the curves (AUCs) obtained from receiver operating characteristic curves were used to evaluate and compare MDW with CRP and PCT.

Results: Our study revealed that MDW is increased among sepsis patients along with biomarkers like CRP and PCT. The AUC for MDW comparable with PCT and CRP are 0.917 and 0.864 respectively. We found statistical significance for MDW with both PCT (0.001) and CRP (0.001).

Conclusion: MDW outperforms conventional biomarkers like CRP and PCT as an early and accurate indication of sepsis, especially in the early stages of the illness. By adding MDW to routine blood tests, a quick, easy, and affordable way to increase early detection, which is essential for prompt intervention and better patient outcomes is provided.

Keywords: MDW, Biomarker and Sepsis.

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INTRODUCTION

Sepsis is a systemic and life-threatening response to infection that can rapidly progress to severe organ dysfunction and death if not promptly treated. Sepsis continues to be a leading cause of morbidity and death globally, especially in critical care settings, despite advances in medical care.[1] According to data released in 2020, there were 11 million sepsis-related fatalities and 48.9 million cases globally, accounting for 20% of all deaths. Sepsis is thought to occur in 15 hospitalised patients out of every 1000 as a side effect of medical treatment.[2]

Since the signs of sepsis are ambiguous and sometimes coexist with other illnesses, it is still difficult to diagnose the disease quickly and accurately, despite the fact that prompt treatment is necessary. The most recent guidelines for sepsis care (SEPSIS-3) recommend using the Sequential Organ Failure Assessment (SOFA) score to diagnose impending sepsis.[3,4]

At the moment, a number of biomarkers have been used to help diagnose sepsis; the most extensively researched and utilized ones are Procalcitonin (PCT) and C-reactive protein (CRP). Acute-phase proteins like CRP rise in response to inflammation, and bacterial infections cause a large increase in PCT, a precursor to calcitonin. Although PCT and CRP have both been shown to be useful in the diagnosis of sepsis, their specificity and sensitivity may be restricted, especially in the early phases of the illness. Patient outcomes may deteriorate if these biomarkers grow slowly since it may take longer to diagnose and treat patients.[5,6]

Monocyte distribution width (MDW) is a new haematological metric that has shown promise as a marker of early sepsis. MDW is a type of white blood cell that is involved in the immunological response to infection. It represents variations in the size and variability of monocytes. Monocytes shift morphologically during sepsis as a result of their activation in response to systemic inflammation. Compared to more conventional indicators, the assessment of MDW using normal complete blood count (CBC) testing provides a rapid and easily accessible way to identify these alterations, possibly giving an earlier indication of sepsis.[7,8] With this background we aimed to evaluate the efficacy of Monocyte Distribution Width (MDW) as an early indicator of sepsis and to compare its diagnostic accuracy with established biomarkers such as C-reactive protein (CRP) and Procalcitonin (PCT).

METHODOLOGY

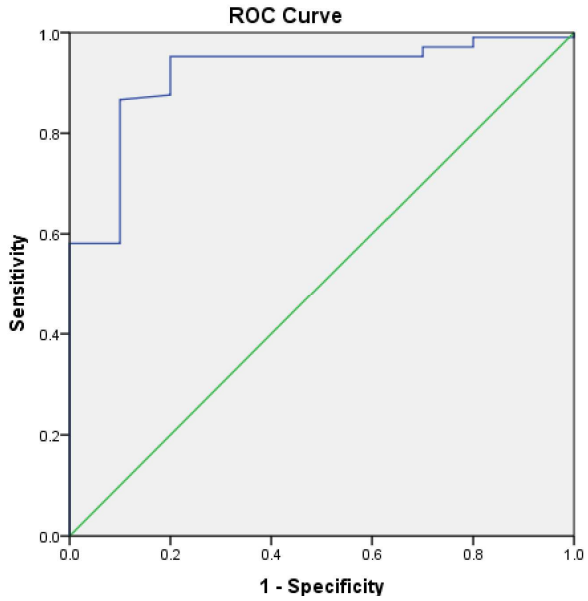
This prospective observational study was conducted among 115 patients between May 2024 to July 2024 who were admitted at Tertiary Care Centre with the suspicion of sepsis. The patient's ages ranged from 1 to 90 years and who were hospitalised for more than 24 hours with the suspected sepsis were included. The patients on immunosuppressive therapy, known haematological malignancies, pregnant women and patients with known chronic inflammatory conditions were excluded. Blood samples were collected in EDTA tubes, and MDW was measured using the UniCel DxH 900 haematology analyzer. MDW values ≥ 20 was considered indicative of sepsis based on prior studies. Serum CRP levels was measured using QDx Instacheck TM hsCRP, this uses fluorescence immunoassay for the quantitative determination of CRP in human whole blood/serum/plasma. The cutoff value for positive CRP is greater than 05 mg/L. Serum PCT levels was measured using QDx Instacheck TM PCT Plus which uses fluorescence immunoassay for the determination of PCT in human whole blood/serum/plasma. Our PCT reference ranges followed the previously published article (i.e., <0.05 healthy adult, 0.05 to <0.5 systemic infection is unlikely but localized infection is possible, 0.5 to <2 systemic infections are possible but other conditions [e.g., major trauma, recent surgery, severe cardiogenic shock] may also induce significant PCT rises, 2 to <10 systemic infections is likely, and ≥ 10 high likelihood of severe bacterial sepsis or septic shock.[9] Data were collected and analysed using SPSS v.21. Continuous variables are expressed in Mean & SD and the area under the curves (AUCs) obtained from receiver operating characteristic curves were used to evaluate and compare MDW with CRP and PCT.

RESULTS

The mean & SD of age among our patients are 49.93 ± 18.23 years and the majority of the patients are males. The mean values are shown in the figure 1.

In our study, we found that MDW is increased among sepsis patients along with biomarkers like CRP and PCT. A receiver operating characteristic (ROC) curve shows the relationship between MDW with PCT and CRP. On the construction of AUC, MDW comparable with PCT, the AUC was 0.917

which shows test quality is excellent. The AUC for MDW comparable with CRP was found to be 0.864 which shows test quality is very good. We found statistical significance for MDW with both PCT (0.001) and CRP (0.001).



Diagonal segments are produced by ties.

Fig. 1: Mean values of MDW, CRP and Procalcitonin

On comparing MDW with PCT, the MDW had a sensitivity of 95.2% and specificity of 20% at a cut-off value of 21.00 (figure. 2). With the same cut-off value of 21.00 had a sensitivity of 97.1% and specificity of 23.1% with CRP (fig. 3).

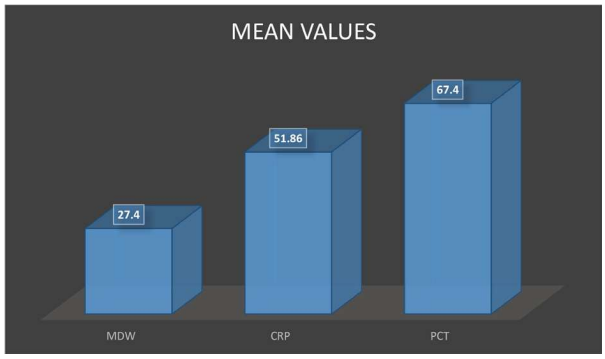
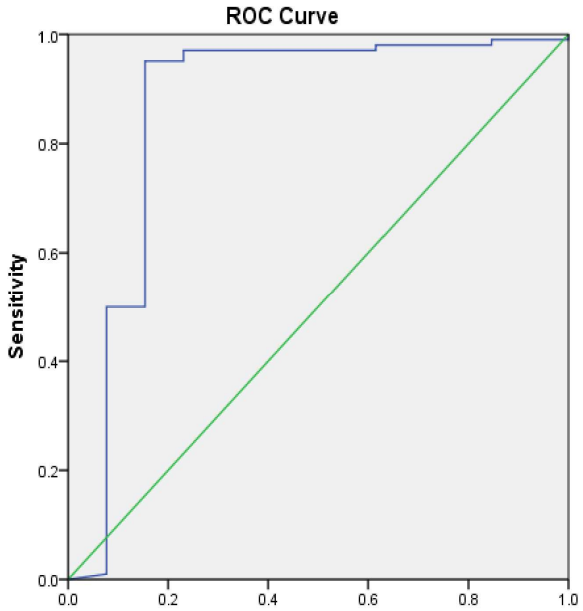


Fig. 2: AUC on MDW with PCT



Diagonal segments are produced by ties.

Fig. 3: UC on MDW with CRP

Table 1: Demographic characteristics of patients

Variables		No of patients (n = 115)
Age		49.93 ± 18.23
Gender	Male	66 (57.4)
	Female	49 (42.6)

Table 2: Biomarkers of Sepsis among patient

Parameter	Mean & SD (n = 115)
MDW	27.4 ± 6.43
CRP	51.86 ± 48.82
PCT	67.4 ± 54.05

Values		MDW	ROC curve	p-value
PCT	67.4 ± 54.05	27.4 ± 6.43	0.917	0.001
CRP	51.86 ± 48.82		0.864	0.001

DISCUSSION

Our study's findings revealed that MDW could be a useful tool for sepsis early identification. The morphological heterogeneity of monocytes, which rises in response to inflammation and systemic infection, is reflected in MDW. Increase in

conventional inflammatory markers like PCT and CRP may be preceded by an early immune system reaction, which shows up as alterations in monocyte size and morphology. As a result, MDW may be able to identify sepsis early on, allowing for timely treatment and lowering the chance of consequences like multi-organ failure or septic shock.

Ciaccio AM et al conducted a study and found, at a cut-off of 20.1, MDW's Area Under the Curve (AUC) of 0.849, sensitivity of 87.3%, and specificity of 71.7% allowed it to distinguish the sepsis group from all other groups. When combined with white blood cells (WBC), MDW enhances sepsis detection performance. In both the previous study and in our study MDW in significantly increased in sepsis.[10] A similar study by Meraj F et al found that septic patients had significantly higher levels of MDW, PCT, and CRP ($p < 0.001$) which is the same as our study findings. MDW's AUC (0.794) was similar to PCT's. The MDW has a significant cutoff value of above 20.24 U, with 73% specificity and 86% sensitivity. In our study, MDW comparable with MDW had a sensitivity of 95.2% and specificity of 20% at a cut-off value of 21.00.[11]

In another contrary study by Hausfater P et al For MDW and MDW with WBC, the AUCs for the diagnosis of sepsis were 0.81 and 0.86, respectively. When MDW and WBC were analysed together, the AUC for sepsis detection was higher than PCT and comparable to CRP alone. This previous study indicates When evaluated in patients with a decreased pretest sepsis likelihood, MDW and WBC together have the diagnostic accuracy to identify sepsis.[12] Woo AL et al conducted a study at the emergency department and found in the sepsis group, MDW had the highest median value (24.0) whereas in our study the mean & SD of 27.40 ± 6.43 which is close to their study findings. White blood cells, PCT, MDW, and CRP all had AUC values of 0.71, 0.75, 0.76, and 0.61 for sepsis prediction, respectively which indicates MDW was similar to that of standard diagnostic markers.[13] A Systematic Review and Meta-Analysis by Huang YH et al showed MDW's combined sensitivity and specificity were 68% and 84%, respectively. The area under the summary receiver operating characteristic curve (SROC) was 0.85 and the predicted diagnostic odds ratio was 11.11. Similar to procalcitonin and CRP, MDW is a valid diagnostic biomarker for sepsis, according to the meta-analysis's findings which is also consistent with our study findings.[14] Another meta-analysis by Motawea KR et al revealed When compared to controls, there is a statistically significant association between sepsis and greater levels of MDW and PCT. Additionally, the overall ROC Area for MDW is higher than the entire ROC Area for PCT, suggesting that MDW has a higher diagnostic accuracy than PCT. In emergency conditions, MDW can be utilised as a diagnostic marker for individuals with sepsis.[15]

CONCLUSION

Comparing monocyte distribution width (MDW) to Procalcitonin (PCT) and C-reactive protein (CRP), MDW showed considerable promise as a biomarker for sepsis identification. Regular CBC can measure MDW automatically in a few minutes and at no additional costs. This could avert life-threatening septic shock by quickly identifying patients at high risk of sepsis, whose diagnosis can be verified by additional clinical and other laboratory markers based on the test's availability. Larger-scale research is necessary to validate these results and investigate MDW's function in sepsis care procedures.

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Conflict of Interest: Nil

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