Research Article

Monocyte Distribution Width (MDW): A Promising Early Marker for Sepsis Detection

Hemikha A[1], Eliz Thomas[2*]

[1]Department of Pathology, Madha Medical College and Hospital, Chennai, Tamil Nadu, India
[2] Department of Pathology, PSG Institute of Medical Sciences and Research, Coimbatore – 04, Tamil Nadu, India

(Received: 27-05-2025 Revised: 28-06-2025 Accepted: 01-07-2025)

Corresponding Author: ***Eliz Thomas*** Email: elshaddai4eliz@gmail.com

ABSTRACT

Introduction & Aim: Sepsis is a global public health issue with high morbidity and mortality. Early detection is a key healthcare objective, with biomarkers playing a vital role in improving patient outcomes. Monocyte distribution width (MDW), a quantitative morphological parameter in the Unicel DxH900 (Beckman Coulter) is easily and quickly available as part of the complete blood count (CBC). This study aimed to validate the utility of MDW for diagnosis and management of sepsis.

Materials and Methods: This study included all patients >18 years of age, presenting to the Emergency Department and those admitted to the Intensive Care Units for a period of 3 months. Patient diagnosis, CBC with MDW, CRP, PCT, serum lactate values, and blood culture reports were retrieved from the hospital information software.

Results: 1633 patients were enrolled in this study. They were categorized as non-infection (61%), infection without sepsis (31%), sepsis (4%) and septic shock (4%) using Sepsis-3 criteria. MDW had a sensitivity of 77.6% and specificity of 77.7% at a cut-off of 22.75 (established using ROC curve at a significant p-value of <0.05) in detecting sepsis in both ED and ICU patients. It outperformed all other sepsis parameters such as CRP (sensitivity-63.2% and specificity-63.6%).), PCT (sensitivity-70.6% and specificity-71%).), NLR (sensitivity-62.4% and specificity-62.5%).) and serum lactate(sensitivity-60.6% and specificity-60.1%). The combined sensitivity of MDW and NLR was 97.6% with a negative predictive value of 99.5%.

Conclusion: Integrating MDW with existing diagnostic practices could enhance early sepsis detection and improve patient management strategies. Sepsis can be excluded with high reliability when the MDW value is below the cut-off and more so when used in conjunction with NLR.

Keywords: MDW, Sepsis, biomarkers for sepsis

1. INTRODUCTION

Sepsis is a life-threatening organ dysfunction and a global public health issue, causing over 3 million hospitalizations annually. Despite advancements in modern medicine, it leads to more than 5.3 million deaths each year. Sepsis remains the leading cause of death in critically ill patients in non-coronary ICUs, with a mortality rate of around 30%. Its incidence continues to rise globally, particularly among comorbid and hospitalized patients, contributing to high morbidity and mortality [1, 2]. Early diagnosis and treatment of sepsis and related organ dysfunction are crucial for reducing healthcare costs and improving patient survival.

The primary healthcare objective of numerous societies is the early detection of sepsis in order to enhance survival. Sepsis biomarkers vary with the pathogenesis of sepsis and our current state of understanding. The early hyperinflammatory phase was primarily characterised by pro-inflammatory cytokines that produced Systemic inflammatory response syndrome (SIRS)- TNF,

IL-1β, and IL-6 and C-reactive protein (CRP). Later procalcitonin (PCT) was added [3].

Monocytes play a key role in inflammation and infection by secreting cytokines and acting as immune effector cells to protect against pathogens. In 1993, changes in monocytes during sepsis were observed. Monocytes in sepsis contribute to antigen presentation, pathogen phagocytosis, and cytokine production. Monocyte Distribution Width (MDW), a quantitative measure of monocyte activation, can now be used as an early indicator of inflammation [4].

The complete blood count (CBC) and leukocyte differential (DIFF), along with other biomarkers, are commonly used to detect sepsis. The UniCel DxH800/900 (Beckman Coulter) analyzer measures Monocyte Distribution Width (MDW), reflecting monocyte size variability in peripheral blood. MDW has shown promise in the early detection of sepsis, especially in emergency departments and intensive care units. In resource-limited settings, MDW offers a cost-effective and feasible solution for sepsis detection, as it can be performed with routine CBC, unlike more expensive and time-consuming tests like CRP, PCT, and serum lactate. MDW could improve early sepsis care and treatment efficiency.

2. MATERIALS AND METHODS

This prospective observational study, approved by the Institutional Human Ethics Committee (IHEC 22/290), included routine blood samples from patients over 18 years, sent for complete blood count (CBC) and peripheral smear examination. Conducted over 3 months, all samples were analyzed using the Beckman Coulter DXH900 within 2 hours, without the confirmed clinical diagnoses. CBC, DIFF count, and MDW values were obtained from reports, while missing clinical details, CRP, procalcitonin, serum lactate, and blood culture results were retrieved from hospital software. Patients were grouped into four categories: Non-infection, infection without sepsis, sepsis, and septic shock, based on clinical diagnosis using Sepsis-3 criteria. Blood culture was not used as gold standard in categorizing the cases due to limited availability of culture reports. Also there were cases of culture-negative septic shocks and cases of viral/fungal sepsis with sterile blood cultures.

3. RESULTS

1633 patients were enrolled in this study. Most of the patients were in the 6th and 7th decades of life followed by other age groups. Female patients were the majority study population.

Out of the 1633 study population, 1004 (61%) did not have any evidence of infection while the remaining 629 (39%) had an evidence of infection. Cases with infection were further sub-divided as infection without sepsis (31%, n=504), sepsis (4%, n=62) and septic shock (4%, n=63).

Comparison of age with diagnoses

Age and diagnoses were compared using Pearson's Chi-Square test and the results were 2=58.438, p=0.0005, signifying that there was a statistically significant correlation between patient's age and diagnoses. This means that infection, sepsis and septic shock were more common in elderly population.

WBC count and diagnoses

The total WBC count was available for all patients, and it was compared with the diagnoses.

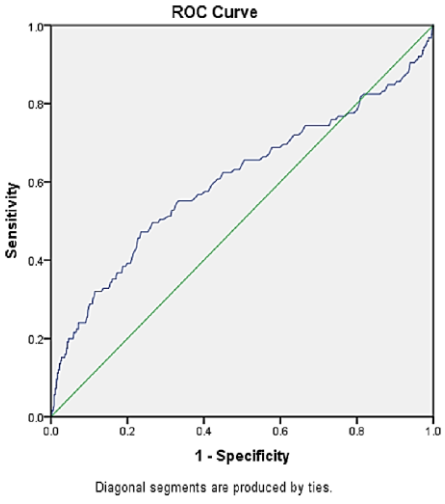

Figure 1: WBC count compared with diagnoses

Results showed that elevated WBC count (>11.5x10^3/mm^3) correlated with sepsis and septic shock cases, with a p value that was highly statistically significant (p=0.0005). This signifies

that elevated WBC count should raise a suspicion of sepsis in patients.

WBC compared with diagnoses when plotted in Receiver operating characteristics (ROC) curve gives sensitivity 59.2% and specificity of 58.0% when the cut -off was maintained at $11.5x10^3/mm^3$. This was highly statistically significant at a p-value of <0.05. This is depicted in Figure 1.

Neutrophil-lymphocyte ratio (NLR) between diagnoses

The neutrophil-lymphocyte ratio was calculated from differential count of neutrophils and lymphocytes, and this ratio was compared with the diagnoses. The results showed that raised NLR correlated with severity of infection in patients with a p value that showed high statistical significance (p=0.0005).

NLR compared with diagnoses when plotted in receiver operating characteristics (ROC) curve gave sensitivity 62.4% and specificity of 62.5% when the cut -off was maintained at 7.9. This was highly statistically significant at a p-value of <0.05. This is depicted in Figure 2.

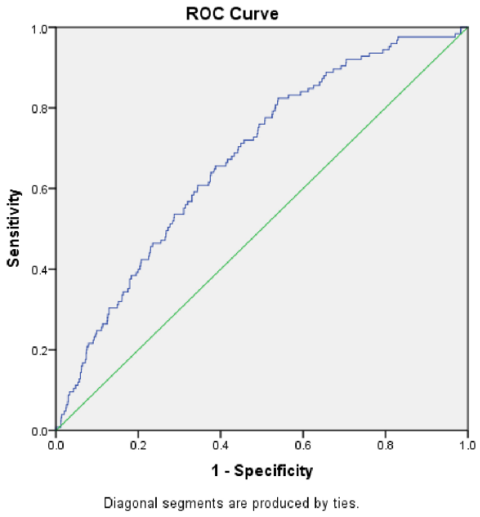

Figure 2: NLR compared with diagnoses

C-reactive protein (CRP) and *diagnoses*

CRP was performed in 244 cases and the values were compared with the diagnostic categories. The results showed that elevated CRP levels positively correlated with severity of infection indicating that maximum average CRP was seen in septic shock cases.

CRP compared with diagnoses when plotted in receiver operating characteristics (ROC) curve gave sensitivity and specificity of 63.2% and 63.6% respectively, when the cut–off was maintained at 7.44 mg/dl. This was highly statistically significant at a p-value of <0.05.

Procalcitonin and diagnoses

Procalcitonin was performed in 496 cases and the results were compared with case diagnoses. There was a positive correlation between raising procalcitonin levels and severity of infection at a p value < 0.05 which was highly statistically significant.

Procalcitonin compared with diagnoses when plotted in Receiver operating characteristics (ROC) curve gave sensitivity and specificity of 70.6% and 71.0% respectively, when the cut -off was maintained at 1.96 ng/ml. This was highly statistically significant at a p-value of <0.05.

Serum lactate and diagnoses

Serum lactate values were available in 469 cases and these were compared with the diagnostic sub-divisions. The results pointed that raised serum lactate values correlated positively with severity of infection at a p-value of <0.05 signifying those patients with septic shock had the highest serum lactate level.

Blood culture

Blood culture reports were available for 745 cases. Of these, 641 were sterile. The remaining 104 cases were culture positive. The commonest organisms in each category are given in Table 1.

Table 1: Organisms detected in the study population

GRAM NEGATIVE BACTERIA	GRAM POSITIVE BACTERIA	FUNGI
Neisseria gonorrhea	*Streptococcus pneumoniae*	*Candida albicans*
Bergeyella	*Methycillin resistant Staphylococcus aureus*	*Candida glabrata*
Burkholderia	*Staphylococcus epidermidis*	
Escherichia coli	*Streptococcus constellatus*	
Klebsiella		
Pseudomonas aeruginosa		
Ralstoniamannitolilytica		
Salmonella typhi		
Stenotrophomonas		
Sphingobacterium		

Blood culture compared with diagnoses when plotted in Receiver operating characteristics (ROC) curve gave a low sensitivity (21.2%) and high specificity (95.1%).This was statistically significant at a p-value of <0.01. Thus, positive blood culture definitively correlates with presence of infection.

Monocyte distribution width (MDW) and diagnoses: MDW values were available in all cases and these were compared with the diagnostic sub-divisions. The results pointed that raised MDW values correlated positively with severity of infection with a p-value of <0.05. This signifies that elevated MDW signifies the presence of infection and the levels were proportional to the severity of infection.

MDW cut off establishment, sensitivity and specificity

MDW compared with diagnoses when plotted in Receiver operating characteristics (ROC) curve gave sensitivity and specificity of 77.6% and 77.7% respectively, when the cut -off was maintained at 22.75. This was highly statistically significant at a p-value of <0.05.

Comparison of sensitivity, specificity between MDW and other parameters

ROC curves of MDW and other parameters were plotted in the same curve [Figure 3].

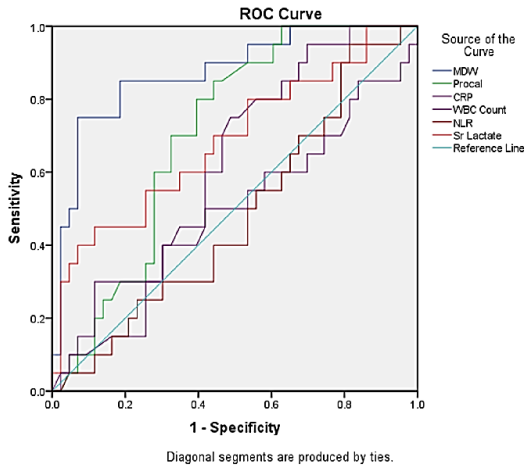

Figure 3: Specificity and sensitivity of MDW compared with all other parameters

Area under the curve of MDW was greatest among all signifying that MDW outperforms other parameters indiagnosing infection/sepsis in a patient.

Combined sensitivity and specificity of MDW and NLR

MDW and NLR values were plotted in the same curve against all diagnostic categories. The combined sensitivity and specificity were 97.6% and 42.1% with a positive predictive value of 12.3% and negative predictive value of 99.5%. Since the sensitivity and negative predictive value are very high, this signifies that MDW when combined with NLR is an excellent screening tool for sepsis.

4. DISCUSSION

Infections, including sepsis and septic shock, cause an estimated 5 million deaths annually, representing one-fifth of global mortality. The complete blood count (CBC) is often one of the first tests performed in patients suspected of sepsis. While white blood cell count may fluctuate in sepsis, it is nonspecific. Biomarkers like C-reactive protein (CRP) and procalcitonin (PCT) are used to diagnose sepsis but require more time than CBC and may not be ordered during a patient's initial hospital visit.

Monocytes activate and divide into subsets during infection, increasing Monocyte Distribution Width (MDW), which can serve as an early sepsis indicator (ESId). The UniCelDxH 900 Coulter analyzer, using Automated Intelligent Morphology (AIM) technology, combines CBC and VCSn analyses to measure MDW and other parameters, aiding early sepsis detection.

Our sample size of 1633 patients correlated with previous studies [5-7]. Some other studies had sample size more than 2000 [8, 9]. However, their studies were conducted for 6 months and 10 months respectively compared to our study period of 3 months.

With regard to age of the patients, most were in the 6^{th} and 7^{th} decades of life. This was in concordance with other studies [5-8]. This may be due to the fact that disease prevalence and severity of disease increases as age advances and the average life expectancy in the country.

Patients in the 5th and 8th decades of life fell next in line, further substantiating the point.

In our study, male patients (60.1%) outnumbered female patients (39.9%) and this trend continued in all diagnostic categories as well. A similar gender distribution was observed in other studies [5, 10]. However, other studies had female predominant overall study population and in all diagnostic categories [6-9]. This could be purely coincidental. Whatsoever, no correlation between sepsis/infection with gender was identified in any of the studies as in our study.

White blood cell (WBC) count is a commonly used marker for infection but has limited utility in diagnosing sepsis. While leukocytosis or leukopenia may occur during septic shock, its sensitivity (59.2%) and specificity (58%) for distinguishing sepsis from non-sepsis are low. In this study, WBC levels were higher in sepsis patients than in septic shock cases. Notably, patients with infections but no sepsis showed WBC counts at the upper limit of the normal range, rather than elevated levels. This was also observed in the study by Seigel *et al.,* [11], where half of patients presenting to the hospital with bacteremia had a normal WBC.

The neutrophil-lymphocyte ratio (NLR) is useful for detecting infection/sepsis when only CBC reports are available. At a cut-off of 7.9, sensitivity and specificity were 62.4% and 62.5%, respectively. This contrasts with Ljungström et al.'s study, where NLR showed higher sensitivity (96%) but lower specificity (10%) at a cut-off >3. Specificity improved to 56% with a higher cut-off (>10), though sensitivity dropped to 80%.[12] In an ICU study, NLR >10 had 66% sensitivity and 53% specificity for sepsis [13].

At a CRP cut-off of 7.4 mg/dL for diagnosing sepsis, sensitivity was 63.2% and specificity 63.6%, consistent with studies by Anush et al and Woo *et al.,* [14, 15]. While procalcitonin (PCT) is more specific in bacterial infections, CRP is more cost-effective and reliable for serial monitoring of sepsis resolution or worsening. In this study, PCT had a sensitivity of 70.6% and specificity of 71% at a cut-off of 1.96 ng/ml. This aligns with a meta-analysis showing an ROC curve of 0.85, indicating PCT's ability to differentiate sepsis from non-infectious SIRS. However, PCT results should be interpreted alongside clinical findings [16].

Other studies comparing CRP and Procalcitonin with MDWshowed overall higher sensitivity and specificity compared to our study [5, 10, 16]. This could be due to the variation in ethnicity of study population and less availability of data i.e. not all patients had CRP and PCT testing in our population.

In this study, the sensitivity and specificity for serum lactate levels were 60.6% and 60.1% respectively when the cut-off was established at 1.79 mmol/L. The cut off point of serum lactate level used in most studies was 2.0 mmol/L [17]. The findings of study by Nichol et al. pointed that a sustained lactate levels as low as 0.75-1.0 mmol/L were associated with increasing the adverse outcomes (OR = 2.0, $p < 0.0001$) [18].]Kliegel *et al.,* examined patients resuscitated for cardiac arrest and those with sustained hyperlactatemia (> 2.0 mM after 48 hours) were associated with higher mortality [19].

Blood culture reports were available in over half of the patients. Compared with infection status, blood culture showed high specificity (91.4%) and negative predictive value (89.2%), but low sensitivity (42%) and positive predictive value (48.1%). Blood culture is considered the gold standard for confirming sepsis, and a negative result reliably rules out sepsis, as noted in Opota et al.'s review [20].

The study aimed to validate the hypothesis that variations in monocyte size could independently predict sepsis in clinical practice. Monocytes play a key role in the early immune response to bacterial infection, with documented morphological changes during sepsis. Measuring monocyte size alongside routine blood counts offers a promising method for monitoring monocyte activation, particularly valuable in low-resource settings and in challenging cases such as neonatal patients, where other sepsis biomarkers may be cost-prohibitive.

Preliminary studies have linked monocyte width variability to immune activation during sepsis. In

our study, an MDW cut-off of 22.75 demonstrated sensitivity and specificity of 77.6% and 77.7%, respectively, for distinguishing sepsis from non-sepsis cases. Beckman Coulter's collective research concluded that a cut-off of 20 is optimal for sepsis diagnosis in emergency departments (ED) using K2EDTA as the anticoagulant, while a slightly higher cut-off of 21.5 is recommended for samples collected with K3EDTA. In this study, samples collected in K2EDTA were used to assess MDW and the slight difference in cut-off than what prescribed by the manufacturer might be due to ethnic difference as most studies were based in U.S [21]. Table 2 gives the MDW cut-off, sensitivity and specificity found in various studies [5, 9, 10, 22, -24] which are comparable to our study.

MDW showed the highest sensitivity and specificity compared to WBC count, NLR, CRP, procalcitonin, and serum lactate in diagnosing sepsis, with the maximum area under the curve. This contrasts with a meta-analysis by Huang et al., which found MDW's area under the ROC curve (0.88) comparable to procalcitonin (0.82) and CRP (0.86). While MDW had higher pooled sensitivity than procalcitonin, its specificity was lower, likely due to the lower pretest probability of sepsis in patients when MDW is used, as it is available for all patients, whereas procalcitonin is typically ordered for those with high sepsis suspicion [25].

The higher sensitivity and specificity of MDW compared to CRP and Procalcitonin could also be partly due to non-availability of CRP and Procalcitonin results in all cases. Even when the patient was suspected to have sepsis, clinicians preferred doing either CRP or Procalcitonin for personal and financial reasons, and both parameters were available in few patients only.

Not many studies are available comparing MDW with serum lactate. However, MDW was used for discriminating false positive blood cultures in a study by Jo *et al.* ,[7]. Measured values of MDW were higher for the blood culture positive group than that of the blood culture contamination group or blood culture negative group establishing its role as a screening tool in sepsis.

CBC is routinely ordered for all patients upon arrival in the ED, whether or not sepsis is suspected. It is cost-efficient with a turnaround time of less than 1 hour, and parameters like NLR and MDW can be assessed immediately as these are parameters driven from hematology analyzers. The combined sensitivity and specificity for MDW and NLR in diagnosing sepsis were 97.6% and 42.1%, respectively, with a positive predictive value of 12.3% and negative predictive value of 99.5%. Therefore, MDW, when combined with NLR, serves as an excellent screening tool for sepsis. If both are below the prescribed cut-off values, sepsis can be confidently ruled out, consistent with other studies. This significantly eliminates the time-lag between patient admission and detection of sepsis as it is is a parameter which comes with CBC, a commonly ordered test in all patients presenting to EMD, unlike other sepsis parameters which are ordered only when there is a clinical suspicion of sepsis. The only drawback is the availability of DxH-900 analyzer in peripheral settings where the amount of sample in-flow might be less and affordability of the analyzer is doubtful.

5. CONCLUSION

In summary, our study underscores the significant role of Monocyte Distribution Width (MDW) as an early sepsis indicator (ESId) and highlights its potential advantages over traditional diagnostic markers. Given the global impact of sepsis, accounting for approximately 5 million deaths annually, early and accurate detection is crucial for improving patient outcomes. While conventional tests like white blood cell (WBC) count, C - reactive protein (CRP), and procalcitonin (PCT) have established roles in diagnosing sepsis, MDW offers a promising complementary approach, especially in settings with limited resources.

MDW's integration into clinical practice is highly appealing due to its status as a parameter within the CBC. Therefore, its assessment is uncomplicated, rapid, and inexpensive, and it does not necessitate an additional blood sample, as is the case with the measurement of other

biomarkers. It could be accessible to all clinicians at any point in the patient's path of care, even when there is no suspicion of sepsis.

Our findings indicate that MDW, with a sensitivity of 77.6% and specificity of 77.7% at a cut-off of 22.75, demonstrates a strong capacity to distinguish between sepsis and non-sepsis cases. This performance aligns well with previous studies, supporting MDW's reliability as a diagnostic tool. Furthermore, MDW's potential utility in various clinical settings, ranging from high-resource hospitals to low-resource environments, emphasizes its versatility and cost-effectiveness.

The clinicians should monitor the patient and conduct additional investigations to corroborate the suspicion of sepsis, as an altered MDW value should be interpreted as a "red flag." Therefore, sepsis can be excluded with high reliability when the MDW value is below the cut-off.

Overall, integrating MDW with existing diagnostic practices could enhance early sepsis detection and improve patient management strategies. Future studies with larger and more diverse cohorts, including varied ethnic populations, are needed to confirm these findings and refine the MDW cut-off values for broader application.

Acknowledgement

We would like to thank the service team of Beckman Coulter for their technical assistance and supply of reagents.

Conflict of Interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Funding Information

No funding was received for this research work.

Ethical Information

Ethical clearance was obtained from the Institutional Human Ethics Committee.

REFERENCES

1. Hotchkiss RS, Moldawer LL, Opal SM, Reinhart K, Turnbull IR, Vincent JL. Sepsis and septic shock. *Nat Rev Dis.* 2016;2(1):16046. doi:10.1038/ nrdp.2016.462.
2. Rudd KE, Johnson SC, Agesa KM, *et al.*, Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the global burden of disease study. *Lancet.* 2020;395(10219):200–211. doi:10.1016/S0140-6736(19)32989-7.
3. Wu J, Li L, Luo J. Diagnostic and prognostic value of monocyte distribution width in sepsis. *Journal of Inflammation Research*. 2022 Jan 1:4107-17.
4. Haveman JW, Kobold AM, Tervaert JC, Van den Berg AP, Tulleken JE, Kallenberg CG, The TH. The central role of monocytes in the pathogenesis of sepsis: consequences for immunomonitoring and treatment. *The Netherlands journal of medicine.* 1999 Sep 1;55(3):132-41.
5. Hausfater P, Robert Boter N, Morales Indiano C, Cancella de Abreu M, Marin AM, Pernet J, Quesada D, Castro I, Careaga D, Arock M, Tejidor L. Monocyte distribution width (MDW) performance as an early sepsis indicator in the emergency department: comparison with CRP and procalcitonin in a multicenter international European prospective study. *Critical Care*. 2021 Dec;25:1-2.
6. Yu S, Am Song S, Jun KR, Park HY, Lee JN. Clinical performance of monocyte distribution width for early detection of sepsis in emergency department patients: A prospective study. *Annals of Laboratory Medicine*. 2022 Mar 1;42(2):286-9.
7. Jo SJ, Kim SW, Choi JH, Choi SP, Lee J, Lim J. Monocyte distribution width (MDW) as a useful indicator for early screening of sepsis and discriminating false positive blood cultures. *Plos one.* 2022 Dec 20;17(12):e0279374.
8. Piva E, Zuin J, Pelloso M, Tosato F, Fogar P, Plebani M. Monocyte distribution width (MDW) parameter as a sepsis indicator in

intensive care units. *Clinical Chemistry and Laboratory Medicine (CCLM).* 2021 Jun 25;59(7):1307-14.

9. Crouser ED, Parrillo JE, Seymour CW, Angus DC, Bicking K, Esguerra VG, Peck-Palmer OM, Magari RT, Julian MW, Kleven JM, Raj PJ, Procopio G, Careaga D, Tejidor L. Monocyte Distribution Width: A Novel Indicator of Sepsis-2 and Sepsis-3 in High-Risk Emergency Department Patients. *Crit Care Med*. 2019 Aug;47(8):1018-1025.
10. Polilli E, Sozio F, Frattari A, Persichitti L, Sensi M, Posata R, Di Gregorio M, Sciacca A, Flacco ME, Manzoli L, Di Iorio G. Comparison of Monocyte Distribution Width (MDW) and Procalcitonin for early recognition of sepsis. *Plos one.* 2020 Jan 10;15(1):e0227300.
11. Seigel TA, Cocchi MN, Salciccioli J, *et al.*, Inadequacy of temperature and white blood cell count in predicting bacteremia in patients with suspected infection. *J Emerg Med* 2012;42:254-9.
12. Ljungström L, Pernestig AK, Jacobsson G, *et al.*, Diagnostic accuracy of procalcitonin, neutrophillymphocyte count ratio, C-reactive protein, and lactate in patients with suspected bacterial sepsis. *PLoS One* 2017;12:e0181704.
13. Westerdijk K, Simons KS, Zegers M, *et al.*, The value of the neutrophil-lymphocyte count ratio in the diagnosis of sepsis in patients admitted to the Intensive Care Unit: a retrospective cohort study. *PLoS One* 2019;14:e0212861.
14. Anush MM, Ashok VK, Sarma RI, Pillai SK. Role of C-reactive protein as an indicator for determining the outcome of sepsis. Indian Journal of Critical Care Medicine: Peer-reviewed, *Official Publication of Indian Society of Critical Care Medicine.* 2019 Jan;23(1):11.
15. Woo AL, Oh DK, Park CJ, Hong SB. Monocyte distribution width compared with C-reactive protein and procalcitonin for early sepsis detection in the emergency department. *PLoS One.* 2021 Apr 15;16(4):e0250101.
16. Wacker C, Prkno A, Brunkhorst FM, *et al.*, Procalcitonin as a diagnostic marker for sepsis: a systematic review and meta-analysis. *Lancet Infect Dis* 2013;13:426-35.
17. Malmir, J., Bolvardi, E., Afzal Aghaee, M. Serum lactate is a useful predictor of death in severe sepsis and septic shock. Reviews in Clinical Medicine, 2014; 1(3): 97-104.
18. Nichol A, Bailey M, Egi M, Pettila V, French C, Stachowski E, Reade MC, Cooper DJ, Bellomo R. Dynamic lactate indices as predictors of outcome in critically ill patients. *Critical Care.* 2011 Oct;15:1-0.
19. Kliegel A, Losert H, Sterz F, *et al.*, Serial lactate determinations for prediction of outcome after cardiac arrest. *Medicine (Baltimore).* 2004;83:274-279.
20. Opota O, Croxatto A, Prod'Hom G, Greub G. Blood culture-based diagnosis of bacteraemia: state of the art. *Clinical Microbiology and Infection*. 2015 Apr 1;21(4):313-22.
21. Malinovska A, Hinson JS, Badaki-Makun O, Hernried B, Smith A, Debraine A, Toerper M, Rothman RE, Kickler T, Levin S. Monocyte distribution width as part of a broad pragmatic sepsis screen in the emergency department. *Journal of the American College of Emergency Physicians Open.* 2022 Apr;3(2):e12679.
22. Riva G, Castellano S, Nasillo V, Ottomano AM, Bergonzini G, Paolini A, Lusenti B, Milić J, De Biasi S, Gibellini L, Cossarizza A. Monocyte Distribution Width (MDW) as novel inflammatory marker with prognostic significance in COVID-19 patients. *Scientific reports.* 2021 Jun 16;11(1):12716.
23. Hou SK, Lin HA, Chen SC, Lin CF, Lin SF. Monocyte distribution width, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio improves early prediction for sepsis at the emergency. *Journal of personalized medicine.* 2021 Jul 28;11(8):732.
24. Agnello L, Bivona G, Vidali M, Scazzone C, Giglio RV, Iacolino G, Iacona A, Mancuso S, Ciaccio AM, Lo Sasso B, Ciaccio M. Monocyte distribution width (MDW) as a

screening tool for sepsis in the Emergency Department. *Clinical Chemistry and Laboratory Medicine (CCLM).* 2020 Oct 25;58(11):1951-7.

25. Huang YH, Chen CJ, Shao SC, Li CH, Hsiao CH, Niu KY, Yen CC. Comparison of the diagnostic accuracies of monocyte distribution width, procalcitonin, and C-reactive protein for sepsis: a systematic review and meta-analysis. *Critical Care Medicine.* 2023 May 1;51(5):e106-14.