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Monocyte distribution width in the detection of sepsis and prediction of mortality in critically ill patients

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Abstract

Introduction: Sepsis is the leading cause of intensive care unit (ICU) admission. Delayed recognition of sepsis is associated with increased morbidity and mortality. Monocyte distribution width (MDW) represents the width of a set of monocyte volume values, which increases as infections progress in severity. This study evaluated the diagnostic and prognostic accuracy of MDW and white cell count (WCC) for sepsis and mortality.

Methods: This was a prospective cohort study of 100 patients who were grouped into sepsis and non-sepsis according to the Sepsis-3 definition. MDW and WCC were collected on admission to ICU and for the subsequent 3 days.

Results: On admission, MDW was diagnostic of sepsis with an AUC of 0.86 (95% CI, 0.7–0.94) with a cut-off threshold of 20.97. Serial MDW on days 1 and 2 were also shown to be predictive of sepsis. MDW has a high sensitivity of 92.1% (95% CI, 82.4–97.4%) but a specificity of only 68.8% (95% CI, 50.0– 83.9%). The positive predictive value and negative predictive value of MDW using the new cut-off threshold in this study

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were found to be 83.6% (95% CI, 73–91.2 %) and 81.5% (95% CI, 61.9–93.7%), respectively.

Conclusions: MDW is an effective screening tool in the detection of sepsis upon admission to the ICU. As part of the differential in some complete blood count analysis machines, MDW provides a cost-effective and widely available test at present. Early detection of sepsis allows initiation of sepsis care bundle and better clinical outcomes.

Keywords: biomarker, blood cell count, critical illness, death, sepsis

Introduction

Sepsis is one of the leading causes of mortality in hospitals and hence a major financial burden on the Malaysian health care system. The intensive care unit (ICU) mortality rate was 18.6% with the all-cause mortality in severe sepsis at 42.3%.[1] Delay in initiating sepsis protocol as per surviving sepsis guidelines is associated with worse sepsis-related clinical outcomes, such as hospital and ICU lengths of stay, morbidity (*e.g.*, organ failure), and mortality.[2-5] The medical field is in dire need of a widely available and cost-effective test that is able to effectively differentiate septic from non-septic patients. This prevents the delay in initiating the sepsis care bundle and antimicrobial therapy in order to reduce or prevent sepsis-related clinical outcomes. White cell count (WCC) has an 88% sensitivity for sepsis detection but unfortunately with a downfall of low specificity.[6]

To date, available biomarkers of sepsis, such as procalcitonin (PCT) and C-reactive protein (CRP) are typically used to confirm the presence of sepsis after the initial encounter in the emergency department (ED), but with limitations of cost and availability.[7] As infections progress to sepsis, the size of the white blood cells increases. Circulating immune cells, particularly monocytes and neutrophils, are rapidly activated. This is reflected by the change in their size and shape,[8,9] and the release of chemokines and cytokines for the recruitment and activation of other immune cells in the body.[10,11] Another postulation is that sepsis causes the release of larger, immature monocytes into the circulation, leading to an increase in immune cell size.[12]

Early studies on the utility of monocyte distribution width (MDW) for sepsis detection have shown promising results in emergency departments[6,13] and ICU populations.[14,15] However, to the best of our knowledge, there have been limited studies investigating the prognostic value of MDW. Since MDW measurement is one

of the haematologic parameters of complete blood count (CBC), it does not incur an added cost and is available widely as part of the CBC measurement. Hence, we investigated its utility as a diagnostic marker for sepsis in our local ICU settings. The primary objective of the study was to compare the serial level of MDW and WCC in sepsis and non-sepsis patients in ICU in the first 3 days of admission. The study also compared the diagnostic ability of MDW in sepsis and the prognostic ability of MDW in 30-day mortality.

Methods

This study was a prospective cohort conducted between December 2020 and March 2021, on patients admitted to ICU of Sultan Ahmad Shah Medical Centre (SASMEC) in Kuantan, Pahang, Malaysia. Inclusion required patients having CBC in their initial evaluation within 24 hours of admission to IIUM Medical Centre. Subsequently, patients were reviewed over 3 days for evidence of sepsis. This study was registered with the Kulliyyah of Medicine Research Committee (KRC) and obtained approval from the IIUM Research Ethics Committee (IREC) on June 20, 2020, IREC number 2020-079. All patients admitted during the study period were screened for eligibility to be included in the study and written consent was taken from the patients or their relatives. This study enrolled adults, aged 18 years and above, whose evaluation included a CBC with differential upon admission to ICU. Exclusion criteria included patient refusal to join the study, readmission to ICU within 12 hours, and prior study enrolment.

CBC and MDW were evaluated in all patients as part of the routine investigations collected daily in the ICU. Blood samples were collected in K_2-EDTA anticoagulated tubes and analysed within 4 hours using UniCel DxH 900 (Beckman Coulter, Inc., Brea, CA, USA) with volume, conductivity, and scatter technology. In short, signals obtained by bioelectrical impedance analysis of cell volume, conductivity, and light scatter can evaluate the morphological changes in monocytes. MDW represents one standard deviation from the mean of the monocyte distribution. Maintenance and calibration of the equipment were performed according to the manufacturer's instructions. Quality of the assay was constantly monitored through the internal and external quality assurance programme.

Demographical data of the patients were recorded. Routine blood investigations, which included CBC with differential, were taken for all patients on admission. MDW and WCC were recorded as day 0. Patients were subsequently grouped into sepsis and non-sepsis groups based on Sepsis-3 Criteria. Patients were categorized as sepsis when there was a clinical suspicion of infection (with or without positive

culture) and a Sequential Organ Failure Assessment (SOFA) score of 2 and above; otherwise, they were grouped into non-sepsis. For patients with pre-existing medical illness, for example, chronic kidney disease, an increase in SOFA score of at least 2 above the baseline score was taken if the baseline parameter was available. If baseline value was not known, a non-renal SOFA score was taken into consideration. Infection was defined according to related clinical signs and symptoms supported by suitable imaging findings and relevant biomarkers for infection and positive cultures. Patients were reviewed for evidence of sepsis subsequently on day 1, day 2, and day 3, where MDW was recorded.

Statistical analysis

The sample size required in this study was calculated based on estimation in the diagnostic test method by Obuchowski[16] and the data from a study by Piva *et al.*[14] with an area under the curve (AUC) of 0.7 for MDW in critically ill patients with sepsis upon admission to ICU. In order to estimate an AUC of 0.7 with 95% confidence, degree of precision of estimate 0.1, and power of study of 90%, the required sample size was a minimum of 79 subjects with at least 19 septic patients.[16] Analysis was conducted using STATA/SE 12.0 (StataCorp, College Station, TX, USA). Continuous variables were presented in mean (standard deviation, SD) or median (interquartile range, IQR) depending on the normality of data distribution. Categorical data were presented as frequency and percentage. Independent Student t-test or Mann-Whitney U-test were used to compare mean differences between groups for numerical variables. To investigate the association between categorical variables, we employed Pearson's chi-square statistical test or Fisher's exact test.

Analysis using receiver operating curve (ROC) was utilised to measure the inherent validity of MDW as a diagnostic test. From the ROC, complete information on the accuracy of the diagnostic capability was obtained, which included sensitivity, specificity, threshold value, positive predictive value (PPV), and negative predictive value (NPV). For better visualisation, a ROC plot was generated to display the complete information of the trade-off between the sensitivity (true positive rate) and 1-specificity (false positive rate) across a series of threshold values. The global performance of MDW as a diagnostic test was summarized by the area under the ROC curve (AUC). As for identifying the optimal threshold cut-off point, we utilised the Youden index, which maximizes the vertical distance from the line of equality to a point on the ROC curve. The Youden index provided a maximum correct classification of sepsis or non-sepsis patients in our study.

Results

A total of 104 patients admitted to the ICU were screened for eligibility. Four patients were excluded from the study because they did not meet the inclusion criterion of the age 18 years and above. Eventually, a total of 100 patients were enrolled into the study and grouped into sepsis and non-sepsis according to Sepsis-3 definitions. There were no deviations from the study protocol and data from all 100 participants were analysed. Figure 1 shows the flow of recruitment in our study. Out of a total of 100 admissions, the prevalence of sepsis in this ICU population was 66%.

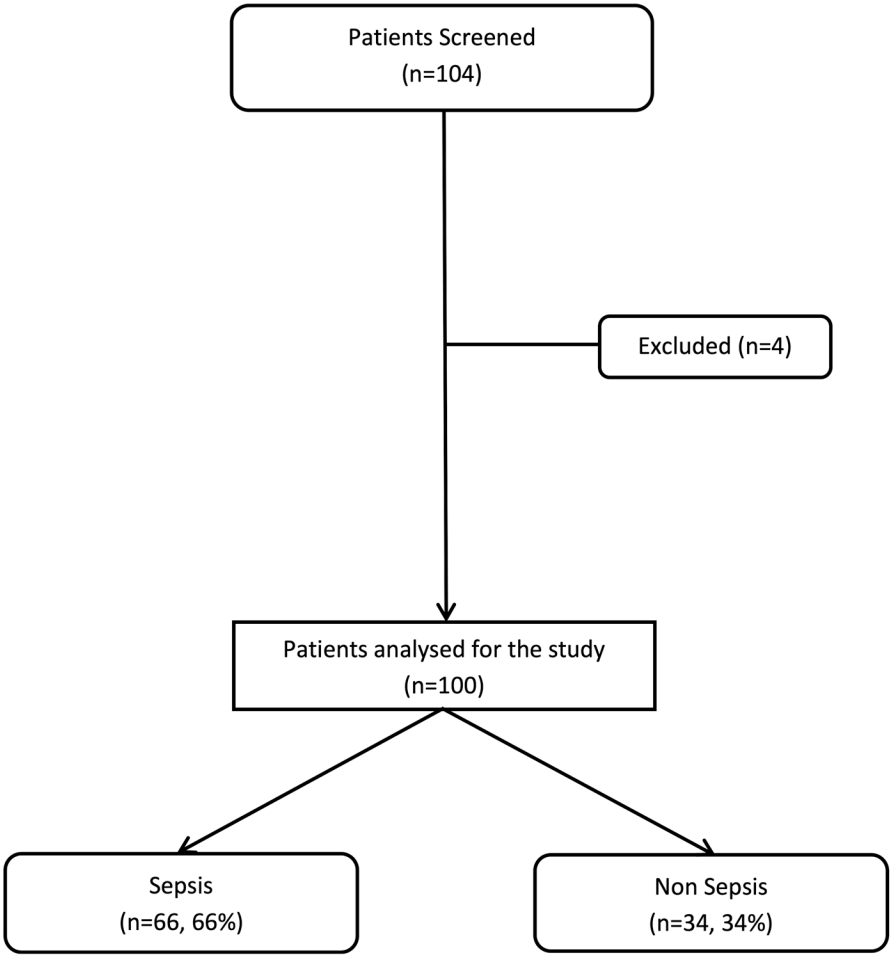

Fig. 1. STROBE flow diagram for patient recruitment into sepsis and non-sepsis groups.

Demographic, clinical characteristics, and outcome

Table 1 illustrates the background characteristics of the patients in this study. Hypertension was the leading pre-existing medical illnesses among the patients (72%), followed by diabetes mellitus (56%) and renal disease (40%). Of these three comorbidities, diabetes mellitus was found to be significantly higher in the sepsis group with a *p*-value of 0.0032. The sources of sepsis in 66 patients (63.4%) were primarily of respiratory origin (*n* = 33, 50.0%), followed by gastrointestinal (*n* = 14, 21.2%), with the rest from blood, soft tissue, and urinary tract.

Table 1. Patients' demographic, clinical features, and outcomes

Variable	**All (*n* = 100)**	**Group**		***p*-value**
		Non-sepsis (*n* = 34)	**Sepsis (*n* = 66)**	
Age	64 (56.5–70)	64 (55–70)	64 (57–70)	0.43
Gender				
Male	60 (60)	18 (30)	42 (70)	0.30
Female	40 (40)	16 (40)	24 (60)	
Ethnicity				
Malay	91 (91)	31 (34.1)	60 (65.9)	1.00
Chinese	9 (8)	3 (37.5)	5 (62.5)	
Indian	1 (1)	0 (0)	1 (100)	
Comorbidity				
Chronic obstructive pulmonary disease	2 (2)	0 (0)	2 (100)	0.55
Bronchial asthma	2 (2)	1 (50)	1 (50)	1.00
Chronic lung disease	3 (3)	0 (0)	3 (100)	0.55
Renal disease	40 (40)	11 (27.5)	29 (72.5)	0.26
Liver disease	1 (1)	1 (100)	0 (0)	0.34
Hypertension	72 (72)	23 (31.9)	49 (68.1)	0.49
Diabetes mellitus	56 (56)	14 (25)	42 (75)	0.03
Others	40 (40)	15 (37.5)	25 (62.5)	0.55

Variable	All (*n* = 100)	Group		*p*-value
		Non-sepsis (*n* = 34)	Sepsis (*n* = 66)	
Source of admission				
Operating theatre	19 (19)	13 (68.4)	6 (31.6)	0.001
Emergency department	40 (40)	13 (32.5)	27 (67.5)	
Ward	41 (41)	8 (19.5)	33 (80.5)	
APACHE II score	16.6 ± 6.9	13.1 ± 6.4	18.4 ± 6.6	< 0.0001
SOFA score	3 (2–5)	2 (0–3)	4 (3–6)	< 0.0001
Death within 30-days	23 (23.0)	3 (8.8)	20 (30.3)	0.02
In survivor (*n* = 77)				
Length of ICU stay (days)	7.03 ± 9.32	3.76 ± 4.26	9.23 ± 11.1	0.003
Duration of hospital stay (days)	24.9 ± 28.6	19.9 ± 28.7	28.3 ± 28.4	0.21

Data expressed as mean ± SD, n (%), or median (lower quartile–upper quartile). APACHE II: Acute Physiological and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment

The mean Acute Physiological and Chronic Health Evaluation (APACHE) II score in the sepsis group, 18.4 ± 6.6, was statistically higher than the non-sepsis group, 13.1 ± 6.4 ($p < 0.0001$). The SOFA score in septic patients was also higher than in non-septic patients, 4 (3–6) *versus* 2 (0–3), $p < 0.0001$. Twenty-three of the 100 patients died within 30 days of ICU admission, higher among the sepsis group (20, 30.3%) compared to the non-sepsis group (3, 8.8%), ($p = 0.002$). Patients with sepsis stayed longer in the ICU compared to non-sepsis; however, there was no difference in the duration of hospital stay.

Serial profile of MDW and WCC between sepsis and non-sepsis

Figure 2 shows the serial profile of MDW and WCC between sepsis and non-sepsis from admission up to 3 days. MDW was higher during the first 3 days in patients with sepsis compared to non-sepsis (repeated measures ANOVA, $p = 0.001$). MDW decreased from day 1 to day 3 by 1.73 in the sepsis group (95% CI, -3.29 to -0.18) with a *p*-value of 0.028, compared to the non-sepsis group, which increased by 2.35 (95% CI, -0.55 to 5.27) with a *p*-value of 0.113 (Fig. 2). On the other hand, WCC was not different in patients with sepsis compared to non-sepsis ($p = 0.630$ with repeated measures ANOVA).

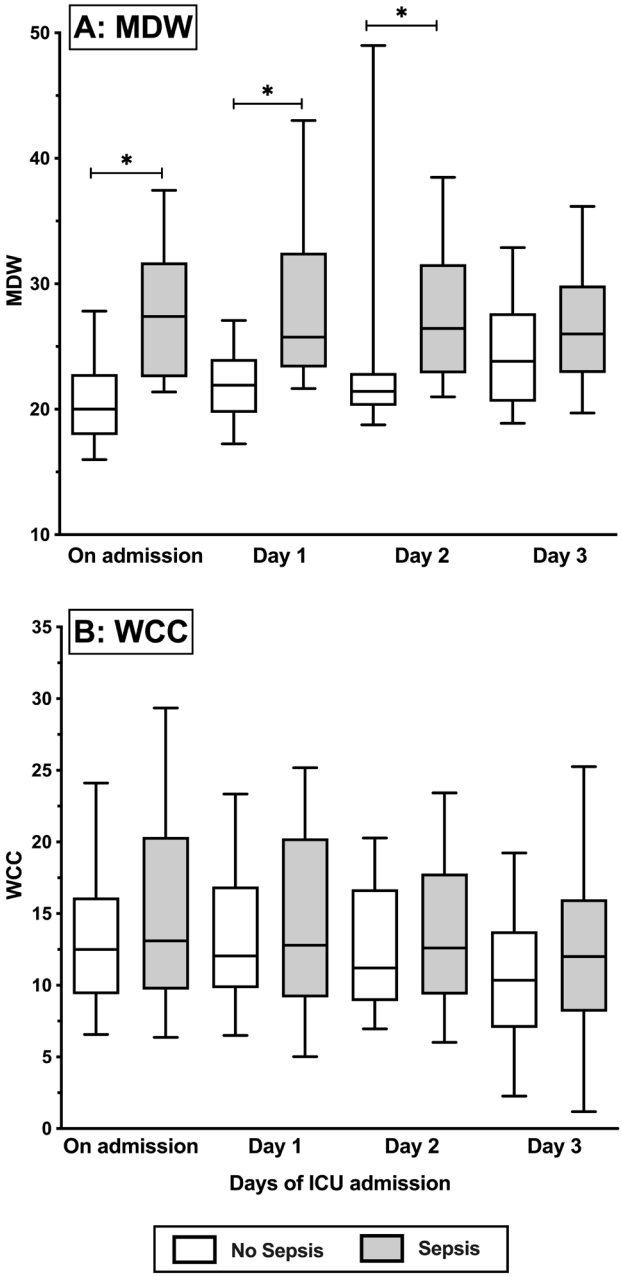

Fig. 2. Serial profile of monocyte distribution width (MDW) and white cell count (WCC) from admission up to 3 days.

Diagnostic performance of MDW for sepsis

MDW measured on ICU admission and during the first 2 days (on 0 hour, 24 hours, and 48 hours) were diagnostic for sepsis, whereas MDW on day 3 (on 72 hours) was not diagnostic (Fig. 3 and Table 2). The estimated AUC, optimal cut-off point, sensitivity and specificity are shown in Table 2. On ICU admission, the AUC of MDW for diagnosis of sepsis was 0.86 (95% CI, 0.77–0.94) with a cut-off threshold of 20.97 based on the Youden index. MDW had a high sensitivity of 92.1% (95% CI, 82.4–97.4%) but a specificity of only 68.8% (95% CI, 50.0–83.9%). Using the new cut-off threshold, the PPV and NPV of MDW were found to be 83.6% (95% CI, 73–91.2 %) and 81.5% (95% CI, 61.9–93.7%), respectively.

On the other hand, WCC measured on admission and throughout the first 3 days was not diagnostic of sepsis (Fig. 3). The AUC of WCC on admission for sepsis was 0.58 (0.47–0.70). The combination of WCC and MDW did not increase the AUC for MDW alone (AUC of 0.82 [0.74–0.91], χ^2 statistic = 0.74, p = 0.39).

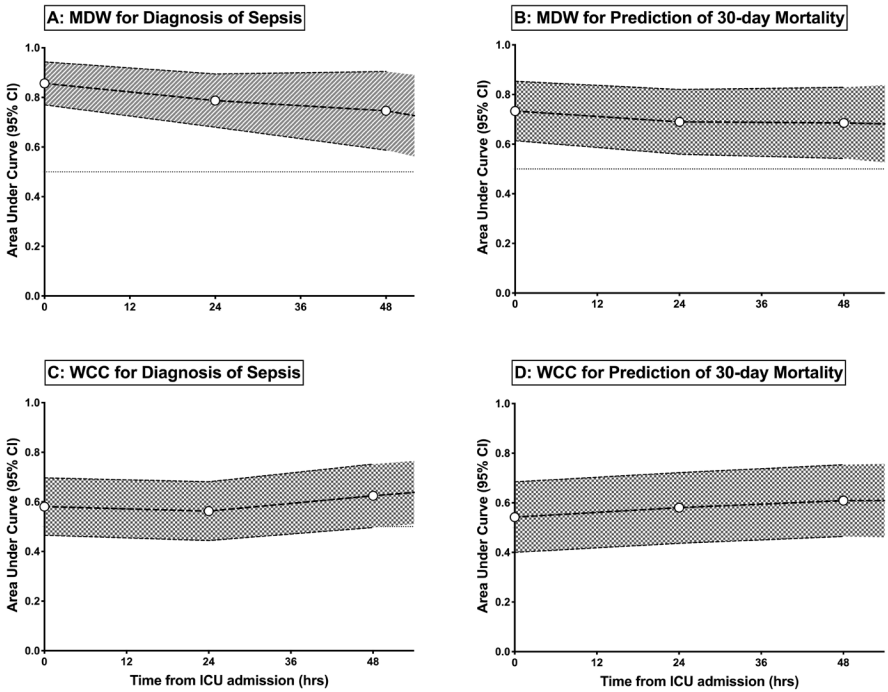

Fig. 3. Area under curve of the receiver operating characteristic curve of MDW for diagnosis of sepsis (A), prediction of 30-day mortality (B), and WCC for diagnosis of sepsis (C), prediction of 30-day mortality (D) from admission up to 3 days.

Table 2. AUC and optimal cut-off point for diagnosis of sepsis

BM	Day	AUC (95% CI)	Optimal cut-off point	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)
Diagnosis of sepsis					
MDW	0	0.86 (0.77 to 0.94)	20.97	92.1 (82.4–97.4)	68.8 (50.0–83.9)
	1	0.79 (0.68 to 0.89)	24.01	69.7 (55.9–81.2)	77.8 (57.7–91.4)
	2	0.75 (0.59 to 0.90)	22.90	76.0 (61.8– 86.9)	81.3 (54.4–96.0)
	3	0.63 (0.44 to 0.82)	20.69	88.9 (75.9–96.3)	40.0 (12.2–73.8)
Prediction of mortality					
MDW	0	0.74 (0.61 to 0.85)	25.97	73.9 (51.6 – 89.8)	68.1 (56.0–8.6)
	1	0.69 (0.56 to 0.82)	23.86	84.2 (60.4–96.6)	53.1 (40.2–65.7)
	2	0.69 (0.54 to 0.83)	22.31	93.8 (69.8–99.8)	38.0 (24.7 – 52.8)
	3	0.67 (0.48 to 0.86)	30.01	50.0 (21.1–78.9)	88.4 (74.9 – 96.1)

BM: biomarker; AUC: area under the curve

Prognostic performance of MDW for 30-day mortality and survival analysis

Twenty-three patients (23%) died within 30 days of ICU admission. Due to the limited number of deaths in the study, a greater number of patients would be needed to predict mortality significantly. Nevertheless, the analyses were performed to simulate the expected findings and MDW measured on admission up to 3 days were indeed predictive of death within 30 days, whilst WCC was not (Fig. 3). The optimal cut-off points of MDW, based on the limited data, for prediction of 30-day mortality are shown in Table 2. Kaplan-Meier survival analysis of MDW measured on admission for 30-day mortality showed lower survival for patients with MDW above the cut-off point of 25.97 compared to those with below the cut-off point (log-rank test, $p < 0.0001$, Fig. 4). After correction for age and SOFA score, Cox regression analysis showed a hazard ratio of 4.08 (1.55 to 10.75), $p = 0.004$. While the above data may not represent the population due to the limitation, a similar finding is expected to be reproduced in future studies with an appropriate sample size.

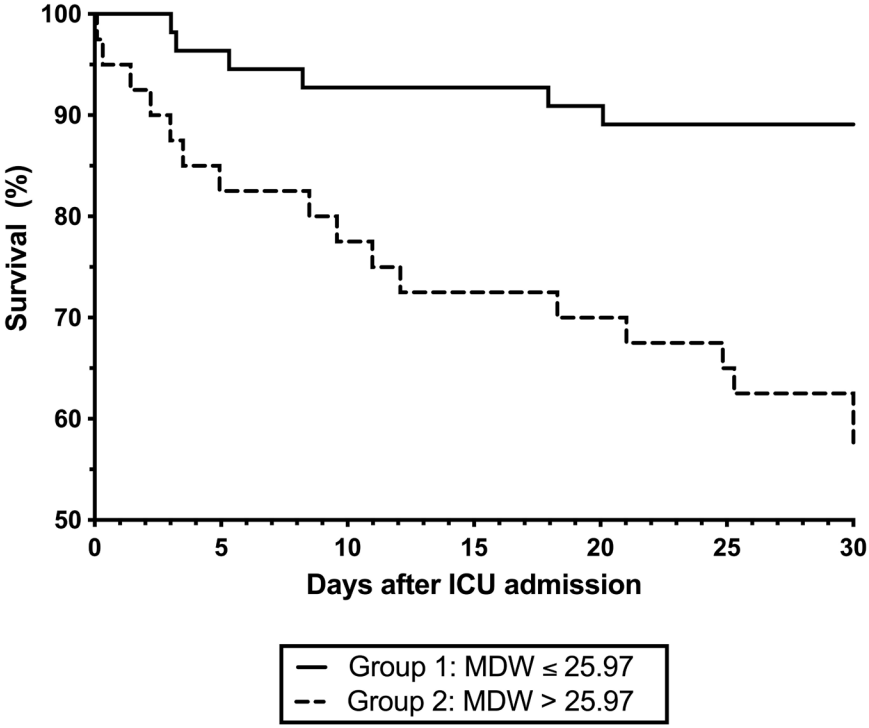

Fig. 4. Survival analysis curve for monocyte distribution width (MDW) on admission (log-rank test, $p < 0.0001$)

Discussion

This study showed that 66% of patients recruited had sepsis, with higher severity scores compared to those with no sepsis. MDW measured on ICU admission was diagnostic of sepsis with an AUC of 0.86 (95% CI, 0.7–0.94) with a cut-off threshold of 20.97. In addition, MDW on days 2 and 3 was also diagnostic. With the limited number of deaths among the sepsis patients to significantly predict 30-day mortality in this study, MDW above the cut-off value of 25.97 was associated with increased mortality. Patients with MDW greater than 25.97 were 4 times more likely to die within 30 days of ICU admission compared to those with a lower than the cut-off point. These results are highly hoped to be simulated in future studies with a larger sample size. On the other hand, the same data showed WCC on admission and throughout 3 days were not diagnostic of sepsis nor associated with increased mortality.

Early studies investigating the utility of MDW for sepsis detected were conducted by Crouser and team back in 2017 and 2019.[6,13] They showed that MDW alone and in combination with WCC were effective in the early detection of sepsis in the ED. Early detection of sepsis allows initiation of sepsis care bundles, wherein delay in treatment is associated with higher morbidity and mortality. However, more studies emerged in the past 2 years that compared MDW with other sepsis biomarkers such as CRP and PCT in ED populations,[17-19] infectious disease units,[20] and ICU settings.[14,15]

The prevalence of sepsis in our ICU population was high, comparable to our local data[21,22] but higher than other studies.[6,13,14] Given that most septic patients especially benefit from ICU admission for standardized care, we concur that the ICU population is the most appropriate for sepsis biomarker evaluation. Of all the comorbidities, diabetes mellitus showed a positive correlation with sepsis, $p = 0.03$. Diabetes may alter the immune system and is associated with a higher risk of community-acquired pneumonia, biliary disease, cutaneous infections, and aspiration pneumonia during hospitalisations, leading to an elevated risk of developing sepsis.

Volumetric increases are an early manifestation of immune cell response to infections and hence have shown potential as a sepsis biomarker. Of all the volumetric metrics in CBC, MDW was found to best discriminate sepsis in the ED population based on AUC with a 97% NPV of a normal MDW.[6] It was postulated that MDW outperformed other parameters because circulating monocytes are the first to respond to infections, leading to an acute increase in the monocyte size. MDW was predicted to provide added value to sepsis predictability on initial presentation. Moreover, CBC with differential is routinely taken in all patients admitted to ICU to screen for acute disease and help guide in the differential diagnosis. Traditionally, WCC is the first laboratory parameter to point to severe infections with a high sensitivity of 88% but poor specificity.[13]

In this study, we showed that the diagnostic performance of MDW in sepsis detection according to Sepsis-3 definitions was found to be excellent (AUC of 0.86), which is comparable to other studies.[6,14,20] Of interest, two studies investigated the utility of MDW for sepsis detection in critically ill patients. In a pilot study involving 96 ICU patients in Italy, MDW was shown to be higher in those with sepsis, and on-the-day sepsis was diagnosed in those without sepsis on admission.[15] In another larger study involving 506 critically ill patients, MDW value increased with increasing severity of sepsis to septic shock compared to those without sepsis. It was diagnostic of sepsis, with an AUC of 0.785 and a cut-off point of 24.63.[14]

The study also showed a positive correlation between MDW and PCT ($r = 0.543$) and CRP (5 = 0.509).[14] When compared with other biomarkers, the AUC of MDW was comparable to PCT but better than CRP in the detection of sepsis in the ICU.[14]

Similarly, two other studies showed comparable AUC of MDW and PCT between 0.82 to 0.87 in 260 patients in the infectious disease unit,[20] and in 1,517 ED patients.[18] The advantage of MDW is that it is available at no extra cost on some particular models of the routine CBC analyser machine, hence making it a convenient and cost-effective alternative for early sepsis predictability when PCT is not available, especially in primary centres. WCC performed poorly in our study as a biomarker of sepsis and hence should not be used as a sole diagnostic tool, similar to the findings of a previous study.[14] We also showed that the combination of WCC and MDW added no benefit in Sepsis-3 diagnosis, consistent with other studies.[17,18]

In addition, we showed that the MDW cut-off threshold for sepsis was 20.97. With that, MDW had a sensitivity of 92.7% and NPV of 81.5% in the screening of sepsis. The discrepancy between the cut-off point identified in our study and other studies could be explained by several reasons, including the different clinical settings (ED *versus* infectious disease unit *versus* ICU), the different calculation methods, and the type of anticoagulant used for blood sample collection (K_2-EDTA *versus* K_3-EDTA). The effect of the anticoagulant on MDW values has been described in the instrument's manual. In short, blood samples collected with K_2-EDTA are associated with lower MDW levels than those collected with K_3-EDTA. Hence, the manufacturer strongly recommends not to use the same cut-off points for different anticoagulants to avoid the risk of false-positive or false-negative results. In this context, the cut-off points of our study and those of Piva *et al.*[14] showed a discrepancy (20.97 *versus* 24.63) despite the same ICU setting, the same calculation method by Youden index, and the same K_2-EDTA anticoagulant in blood sampling. The cut-off threshold from studies using K_3-EDTA ranged from 21.5 to 23.5[18,20,23] compared to 19.8 to 24.6 for K_2-EDTA.[13,14,17] Another study on MDW in healthy blood donors has suggested a reference interval of approximately 16 to 23,[23] which is different from the manufacturer's recommendation. In a nutshell, these suggested that MDW was highly affected by the underlying medical conditions and characteristics of the study population.

Previously, Crouser *et al.*6[6] suggested in their limitations that the nature of the infectious agents could have important implications on MDW. However, Piva *et al.*14[14] showed that MDW was not affected by the aetiology of sepsis, be it Gram-positive or negative bacteria, fungal or viral infections, or even COVID-19 infection. On the contrary, PCT showed the highest value in Gram-negative bacteria but low values in fungal and viral sepsis, particularly severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We were unable to evaluate this due to the lack of microbiological evidence in our study, as most cultures may have been negative due to the delay in testing.

Our study also compared the trend of MDW in both sepsis and non-sepsis groups after admission to ICU. We found that MDW in septic patients dropped by 6% from 28.38 to 26.64 within 48 hours, with $p = 0.028$. We posit that this fall may reflect on the response to the sepsis care bundle and may be used as a prognosticating tool. This is supported by the findings from Piva *et al.*[14] wherein MDW in sepsis survivors decreased from a median of 29.14 (IQR: 26.22–32.52) on the first day to 25.67 (IQR: 22.93–30.28) on the end of the stay. In contrast, MDW in patients who developed ICU-acquired sepsis increased from a median of 21.33 (IQR: 19.47–21.72) to 29.19 (IQR: 27.46–31.47).

Another interesting point to highlight from Woo *et al.*[17] is that MDW should be interpreted with caution according to the patient's immune status. The AUC of MDW in immune-competent patients was higher than that in immune-compromised patients (0.73 *versus* 0.66). Their overall MDW performance was rather disappointing compared to other studies due to the relatively high proportion of immune-compromised patients (more than 50% of the overall population). Therefore, future studies should consider excluding immune-compromised patients to improve the diagnostic accuracy of MDW in sepsis.

Even with the limited number of mortality cases in this study, our study was able to demonstrate that MDW within the first 3 days was consistently predictive of 30-day mortality. Of interest is the early measurement of MDW in the prediction of mortality, as this can be used for risk stratification. Piva *et al.*[14] showed that, in non-survivors with sepsis, MDW was significantly different from the first to last value, whereas there was no difference in those who survived. Even after adjusting for age and severity score, patients with MDW above the cut-off point were 4 times more likely to die compared to those with those below the cut-off point. To the best of our knowledge, we are the first to report on the utility of MDW to predict mortality in the Malaysian ICU population.

Limitations

We acknowledge several limitations in this study. First, there is no gold standard for the diagnosis of sepsis to date; thus, the possibility of misclassification cannot be excluded, and this inevitably limits the biomarker's accuracy. Second, investigators were not blinded to the PCT and CRP values ordered as the standard of care, which may have led to bias and overestimation of the prevalence of sepsis, and again, the accuracy of the biomarker. Third, missing data from some patients may have also skewed the biomarker's accuracy. The use of a single biomarker (MDW) in this study is also a limitation.

Recommendations
This study was conducted with the aim of paving the way for further research on MDW in guiding sepsis management in Malaysia. More research is necessary to compare MDW in sepsis in multiple centres locally or internationally, with larger sample sizes to produce a more reliable and accurate representation of the Malaysian population, and even the global population. Future studies should also be conducted to compare MDW with other biomarkers, such as PCT and CRP. Ultimately, it would be important to determine how the availability of MDW could guide sepsis management in the ICU and its implication on sepsis-related clinical outcomes, such as ICU length of stay, morbidity, and mortality.

Conclusion

In summary, MDW is an effective screening tool to detect sepsis and predict mortality upon admission to ICU. As part of the differential in CBC, MDW provides a cost-effective and widely available test at present. Therefore, MDW may be use as a biomarker for early detection of sepsis, allowing early initiation of sepsis care bundle and improved clinical outcomes.

Declarations

Ethics approval and informed consent
Informed consent was obtained from all individuals included in this study prior to enrolment. The local Institutional Review Board deemed the study exempt from review. This study had been registered with the Kulliyyah of Medicine Research Committee (KRC), and had obtained approval from the IIUM Research Ethics Committee (IREC) on June 20, 2020, IREC number 2020-079.

Competing interests
Dr. Azrina Md Ralib serves as Deputy Chief Editor and Dr. Mohd Basri Mat Nor serves in the Advisory Board of Malaysian Journal of Anaesthesiology. Neither has been involved in any part of the publication process prior to manuscript acceptance; peer review for this journal is double blind. The remaining authors state no conflict of interest.

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None to declare.

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