Critical Rounds Newsletter
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Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you **"Critical Rounds Newsletter"** which contain latest and interesting news in the field of Critical Care.

This issue contains:

1. Predictive indicators for poor outcomes in patients receiving emergency hemodialysis in the emergency department

2. Relationship between mortality and lactate levels in septic shock patients

3. Investigation of the status of RBC transfusions in critically ill patients

4. Case report on Multiorgan failure and stroke as the first signs of lupus

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Best Regards,
Medical Team, Micro Labs Limited

1. Predictive indicators for poor outcomes in patients receiving emergency hemodialysis in the emergency department

Introduction

Emergency hemodialysis (HD) refers to initiating dialysis within 24 hours of a patient presenting with a life-threatening disease.[1] It is attributed to patient-related factors (e.g., non-compliance, refusal of dialysis, drug toxicity), systemic illness (e.g., sepsis, cardiovascular, peripheral vascular disease, autoimmunity, secondary renal involvement), and accelerated renal function due to volume overload, symptoms of uremia or hyperkalemia, and significantly elevated serum creatinine on routine blood testing.[2] Acute on chronic kidney disease (CKD) is a common reason for emergency department (ED) visits, necessitating emergency HD. Patients with CKD are more likely to present to the emergency department than the general population. Patients receiving emergency hemodialysis (HD) in the ED are frequently experiencing poor outcomes such as 60-day mortality, ICU admission and need for mechanical ventilation.[1] This study aimed to identify predictors of poor clinical outcomes for emergency HD patients who visited the ED within 24 hours.

Among patients with acute renal failure who needed emergency hemodialysis (HD), severe metabolic acidosis, hyperkalemia, and mechanical ventilation were substantially linked to poor outcomes.

Methods:

This retrospective observational study included all patients referred to a tertiary teaching hospital's emergency department who underwent emergency HD for medical reasons other than trauma within 24 hours of admission. This study included all medical patients admitted to the ED who underwent emergency HD within 24 hours of admission, whether in the ED or a non-ED setting. Exclusion criteria were individuals who had received HD treatment prior to going to the ED and trauma conditions. The primary and secondary outcomes were 60-day mortality, requirement for mechanical ventilation, and ICU admission. Binary logistic regression analysis was performed to identify risk factors for poor clinical outcomes.

Results:

A total of 177 patients were included in the study. Most of the participants (56.50%) were between 40 and 65 years old, with 36.72% being over 65. The study sample is predominantly male (55.37%). Categorical analysis revealed that most emergency HD patients had no prior history of HD, experienced fluid overload, needed mechanical breathing, and died within 60 days (P<0.05). Severe metabolic acidosis (adjusted odds ratio (OR) 3.01; 95% confidence interval (CI): 1.29, 7.00; P=0.10), severe hyperkalemia (adjusted OR 2.98; 95% CI: 1.16, 7.60); P=0.002), and mechanical ventilation in the ED (adjusted OR 3.53; 95% CI: 1.59, 7.82); P=0.002] were also associated with a higher risk. The AUC for 60-day mortality was 0.74 (95% CI: 0.64, 0.84), with a P-value of <0.001. Severe metabolic acidosis (adjusted OR 2.78 (95% CI: 1.10, 7.01); P=0.03), performing HD in the ED (adjusted OR 0.33 (95% CI: 0.14, 0.79); P=0.01), and having a history of regular HD (adjusted OR 0.21 (95% CI: 0.06, 0.70); P=0.01) were all significant predictors of ICU admission (AUC 0.77 (95% CI: 0.68, 0.87); P<0.001). Shortness of breath [adjusted OR 4.95 (95% CI: 2.25, 10.920); P<0.05] and significant hyperkalemia at presentation [adjusted OR 2.95 (95% CI: 1.16, 7.52); P=0.02] were predictive of mechanical ventilation, with an AUC of 0.72 (95% CI: 0.64, 0.79); P<0.05 (Table 1).

Variables	Univariable logistic regression			Multiple logistic regression[a]		
	b	Crude OR (95% CI)	P	b	Adjusted OR (95% CI)	P
60-mortality						
Severe metabolic acidosis (pH <7.1)	1.36	3.9 (1.76, 8.53)	0.001	1.10	3.0 (1.29, 7.01)	0.01
Severe hyperkalemia (K >6.5 mmol/L)	1.39	4.0 (1.67, 9.57)	0.002	1.09	2.9 (1.16, 7.60)	0.02
Mechanical ventilation	1.41	4.0 (1.92, 8.70)	<0.001	1.26	3.5 (1.60, 7.82)	0.02
Emergency HD in ED	0.85	2.3 (1.01, 5.02)	0.03	0.98	2.7 (1.12, 6.40)	0.03
ICU admission						
Emergency HD in ED	−0.69	0.5 (0.23, 1.10)	0.85	−1.08	0.3 (0.14, 0.8)	0.01
Known HD case	−1.77	0.2 (0.06, 0.51)	0.02	−1.59	0.2 (0.06, 0.66)	0.08
Severe metabolic acidosis (pH ≤7.1)	1.49	4.4 (1.96, 10.1)	<0.001	1.13	3.1 (1.25, 7.62)	0.01
Mechanical ventilation						
SOB at presentation	1.26	3.5 (1.73, 7.23)	0.01	1.6	4.9 (2.25, 10.9)	<0.001
Severe hyperkalemia (K >6.5 mmol/L)	0.74	2.1 (0.92, 4.82)	0.08	1.08	2.9 (1.16, 7.52)	0.02
Known HD case	−0.59	0.6 (0.28, 1.08)	0.084	−0.75	0.5 (0.23, 0.97)	0.04

[a], forward LR multiple logistic regression model was applied. Multicollinearity and interaction term were checked and not found. Hosmer-Lemeshow test (P>0.05), classification table and area under the ROC (both more than 70%) were applied to check the model fitness. OR, odds ratio; CI, confidence interval; HD, hemodialysis; ED, emergency department; ICU, intensive care unit; LR, logistic regression; ROC, receiver-operating characteristic.

Table 1. Factors associated with adverse clinical outcomes for emergency hemodialysis patients using univariable and multiple logistic regression models

Discussion:

This study compared clinical and non-clinical characteristics of patients undergoing emergency HD at ED versus non-ED locations. This study showed that there were no significant differences in clinical or non-clinical characteristics between the two groups. However, individuals getting HD in ED had a higher proportion of a history of fluid overload, including refractory fluid overload. This study found that patients with fluid overload and no prior history of HD are more likely to receive emergency HD at the ED location.[1] This is consistent with a previous study indicating that undiagnosed CKD patients who presented to the emergency department had worse conditions. Patients experiencing fluid overload may require quick admission to a resuscitation unit due to their unstable condition.[3]

Conclusion:

Severe metabolic acidosis, hyperkalemia, and mechanical ventilation were linked to poor outcomes in ED patients with acute renal failure requiring emergency HD. Therefore, caution should be used when addressing cases with these clinical characteristics in the emergency department.

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2. Relationship between mortality and lactate levels in septic shock patients

Introduction

Sepsis is a life-threatening organ malfunction induced by an abnormal host response to infection. Although the exact prevalence of sepsis is unclear, estimations show that it is a leading cause of mortality and serious illness globally. It was anticipated that sepsis would become more common, with increased public health and cost implications.[1] The diagnostic criteria and diagnosis of sepsis and septic shock underwent a significant modification in 2016 with the introduction of the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). Recent guidelines suggest using lactate decrement to guide resuscitation in sepsis patients, and the consensus added a serum lactate concentration more than 2 mmol/L as a criterion to identify septic shock. The guidelines placed a strong emphasis on screening and initial resuscitation, with discussions of sepsis treatment heavily depending on lactate levels. Static lactate indices, particularly the level at admission, have been widely studied and accepted as a poor prognostic indicator for sepsis and mortality. However, kinetic changes in lactate levels have not been adequately clarified or compared to static levels.[2] This study determined the correlation between mortality and lactate levels in septic shock patients, as well as to compare the effectiveness of static lactate levels vs lactate kinetics at specific time points.

Lactate levels at 48 hours after admission can be used as a prognostic predictor for septic shock patients.

Methods

This retrospective cohort study used archived records from patients admitted to the intensive care unit (ICU) and included patients over 18 years old who satisfied septic shock criteria and had new-onset infection. Serum lactate levels were assessed upon ICU admission and after 2, 6, 12, 24, and 48 hours. Patients who died within 48 hours of admission were also excluded from the study because data on lactate levels at 48 hours (L48) would be insufficient. Patients' clinical and demographic information including age, gender, Acute Physiology and Chronic Health Evaluation II (APACHE II) score at admission, vital signs at shock recognition, previous medical history, and baseline laboratory values were collected. The study evaluated 28-day

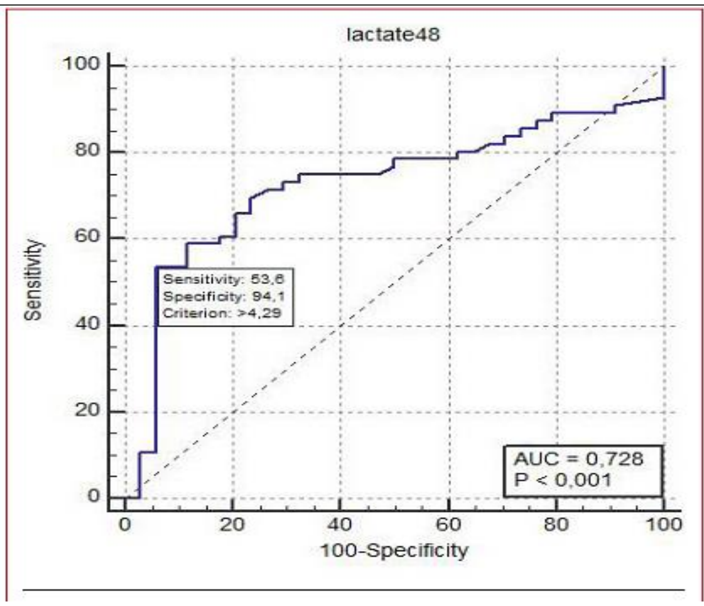

Figure 1. Lactate value from the receiver operating characteristic curve 48 hours after ICU admission for septic shock mortality prediction

mortality, the requirement for mechanical ventilation, length of stay in the hospital and ICU, and septic shock patient care regimens. The Spearman Rho correlation coefficient and Mann-Whitney U test were used to assess the relationship between variables and mortality.

Results

During the study, 90 patients in the intensive care unit with septic shock satisfied eligibility criteria. Lactate levels at admission and six hours later did not differ between non-survivors and survivors (2.8 mmol/L vs. 2.42 mmol/L and 3.38 mmol/L vs. 2.61 mmol/L, respectively). The non-survivor group had higher lactate levels at 2, 12, 24, and 48 hours after admission, with statistically significant differences. There were no statistically significant differences in delta lactate levels across groups at any time point. Lactate levels at 48 hours provided the strongest predictive value, according to the analysis of the Receiver Operating Characteristic (ROC) curve for 28-day mortality, with an Area Under the Curve (AUC) of 0.728 (Figure 1).

Discussion

The Surviving Sepsis Campaign advised measuring lactate at admission if it was more than 2 mmol/L and then testing again six hours later. The study indicated that lactate levels at 48 hours were superior to static and kinetic lactate levels.[2] A previous study by Bruno et al. found that lactate clearance six hours after admission was an independent predictor of outcome, regardless of SOFA score or the need for organ support.[3] In another study by Lee et al. found that Lactate6 was more accurate in predicting 30-day mortality than lactate clearance at six hours or initial lactate level at admission.[4]

Conclusion

This study found that lactate levels at 48 hours after admission can be used as a prognostic predictor for septic shock patients. Recent advancements in septic shock management have turned the focus from resuscitation endpoints to microcirculation parameters. In the future, the lactate kinetics of critically ill patients may be examined based on disease classification.

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3. Investigation of the status of RBC transfusions in critically ill patients

Introduction:

Red blood cell (RBC) transfusions are prevalent in ICU patients. RBC transfusion is a potentially lifesaving treatment, but it may be limited due to the shortage of blood products and has potential risks for patients such as transfusion-associated circulatory overload and transfusion-related acute lung injury. Several randomized controlled trials (RCTs) in various critically ill populations have indicated that a more restrictive transfusion regimen (i.e., a lower hemoglobin [Hb] level of 7 to 8 g/dL as the threshold for RBC transfusion) is safe.[1] These guidelines recommend considering Hb thresholds, clinical judgement, and other physiological indicators. However, the physiological parameters for RBC transfusion are unclear, thus doctors rely on their subjective opinion.[2] The purpose of this study was to assess the current status of RBC transfusions in critically ill patients.

Despite using a high number of RBC transfusions against the restrictive strategy, the prognosis for severely ill patients remained unchanged.

Methods

This cohort study was undertaken at five hospitals and included 307 non-traumatic, anemic patients admitted to intensive care units via emergency departments. The inclusion criteria consist of patients aged ≥18 years, without trauma, and with Hb levels ≤10 g/dL. Transfusion triggers, clinical outcomes, and whether patients got RBC transfusions were all determined. The major outcome variable for the patients' clinical course was the 28-day mortality rate. The study also examined the length of ICU and hospital stays, as well as the percentage of patients who survived and were discharged.

Results

Of 307 patients, 154 (50.2%) had RBC transfusions during the first 24 hours. The median age in the transfusion group was 68 years (IQR 57-80 years), while in the non-transfusion group it was 76 years (IQR 68-83 years). Among 154 patients who underwent RBC transfusions, 71 (46.1%) had a hemoglobin level of 7 or above. Triggers other than hemoglobin levels included elevated lactate levels in 75 patients (48.7%), tachycardia in 47 (30.5%), and hypotension in 46 (29.9%). There was no significant difference in 28-day death rates between the transfusion and non-transfusion groups (21.4% vs. 26.8%, P=0.288) (Table 1). The length of stay in intensive care units and hospitals, as well as the percentage of survival to discharge, did not differ between the two groups. The prognosis followed the same pattern across subgroups.

Variable	Non-transfusion (n=153)	Transfusion (n=154)	P-value
28-Day mortality	41 (26.8)	33 (21.4)	0.288
Duration of ICU admission (day)	6.0 (4.0–12.0)	5.0 (3.0–11.0)	0.404
Duration of hospital admission (day)	13.0 (8.0–20.0)	11.0 (7.0–21.0)	0.367
Survival discharge	114 (74.5)	119 (77.3)	0.596

Values are presented as number (%) or median (interquartile range).
ICU: intensive care unit.

Table 1: Outcomes for Transfusion and Non-Transfusion groups

Discussion

For decades, RBCs have been transfused to keep hemoglobin levels over 10 g/dl. RBC transfusions are used to provide oxygen to tissues. Hb levels are simple to monitor and have a defined cut-off value. Even with the same Hb level, a patient's RBC demand may vary based on their condition and tissue oxygen consumption.[2] New guidelines suggest taking into consideration multiple measures, including Hb level, blood pressure, heart rate, electrocardiogram, oxygen partial pressure, central venous oxygen saturation, arteriovenous oxygen difference, lactate, and more.[3]

Conclusion

The prognosis of critically ill patients did not significantly change, even when a significant number of RBC transfusions were administered against the restrictive strategy. To reduce unnecessary RBC transfusions, it's important to promote transfusion guidelines and do research on criteria based on individual patient situations.

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4. Case report on Multiorgan failure and stroke as the first signs of lupus

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease characterized by immunological dysregulation in multiple organs. It is associated with comorbidities such as cardiovascular disease (CVD), cancer, metabolic syndrome, and thyroid disease, all of which have an impact on disease manifestations and progression and raise the chance of death. Patients with SLE commonly experience fatigue and joint pain, which, coupled with psychological manifestations such as anxiety and depression that have an impact on quality of life and necessitate the need for patient care and more effective treatment choices.[1] SLE-related strokes typically occur within a year of diagnosis and are often associated with disease in other organs. Lupus nephritis (LN) is a severe form of glomerulonephritis that affects multiple organs. Approximately 50% of SLE patients acquire LN over their lifespan. SLE is a chronic autoimmune condition that can cause mild to severe symptoms, necessitating hospitalization and critical care. More studies are needed to optimize care and enhance patient outcomes in these difficult cases.[2] In this case, a patient was admitted to the ICU after being diagnosed with SLE while also experiencing stroke and LN.

> A multidisciplinary approach, including rheumatologists, neurologists, nephrologists, and intensivists, is required for timely diagnosis and management of SLE-related complications, especially in intensive care.

Case Presentation:

This case involves a 30-year-old female Caucasian nonsmoker who presented to the emergency department (ED) with right-side hemiplegia, aphasia, and an abrupt onset of altered mental status. A relative found her collapsed on the floor at home, around two and a half hours after she was last seen. Her medical history includes the recent onset of lower limb edema and arterial hypertension managed with nebivolol/hydrochlorothiazide 5/12.5 mg once a day. Additional medical history, particularly about the musculoskeletal, mucocutaneous, and reproductive systems, as well as a known history of autoimmune disease, was not previously documented. A neurological examination performed upon admission to the emergency department (ED) showed a Glasgow Coma Scale (GCS) score of 10 (E3, V1, M6) and a National Institutes of Health Stroke Scale (NIHSS) score of 30 due to aphasia, right-side hemiplegia, conjugate ocular deviation to the left, and right facial paralysis. Her heart rate was 101 beats per minute, her blood pressure was 146/115 mmHg, and she was afebrile. Auscultation of the heart and lungs revealed nothing unusual. She had noticeable, symmetrical edema in both lower extremities that reached her thighs. In addition to a normal mean corpuscular volume (86.5 fL) and mean corpuscular hemoglobin (29.3 pg), the laboratory findings showed a decreased hemoglobin level (11.1 g/dL). Urea levels were 146 mg/dL and serum creatinine was 2.85 mg/dL (baseline creatinine was 0.6 mg/dL). Hematuria and proteinuria (200 mg/dL) were confirmed by urinalysis. The grey-white matter junction in the left frontal lobe and insular areas showed mildly reduced attenuation and swelling, according to head computed tomography (CT) (Figures 1A, 1B). CT angiography revealed a blockage of the left middle cerebral artery at its proximal M1 segment (Figure 1C). These findings indicated an acute ischemia infarction in the left middle central artery (MCA) area. She underwent a primary thrombectomy five hours after last seen well. The ultimate thrombolysis score for cerebral infarction was 2b, indicating successful reperfusion (Figure 1D). She was subsequently admitted to the stroke unit. On admission, laboratory tests showed a high erythrocyte sedimentation rate of 93 mm/h, a C-reactive protein level of 2.89 mg/dL (N <0.5 mg/dL), proteinuria in the nephrotic range (albumin/creatinine ratio of 10365 mg/g), and hypoalbuminemia (1.8 g/dL). The autoimmune panel showed positive antinuclear antibodies (ANAs) with a titer of 1:1280, a speckled pattern, hypocomplementemia (C3 and C4), positive anti-SSA, and a significantly positive anti-ds DNA titer of 182 IU/mL. Transthoracic echocardiography indicated a mild pericardial effusion with no additional significant findings.

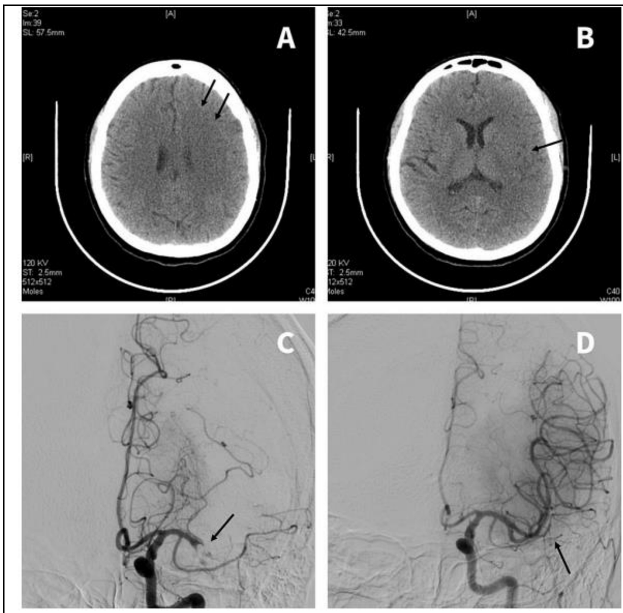

Figure 1. Intracranial imaging. A plain head computed tomography scan shows decreased attenuation of the grey-white matter junction in the left frontal lobe (black arrows) (A), the left insular area (black arrow) (B); CT angiography shows blockage of the left middle cerebral artery in the proximal M1 segment (black arrow) (C) and effective reperfusion (black arrow) and a TICI score of 2b (D).

Within 48 hours of admission to the stroke unit, the patient's health deteriorated, resulting in a GCS score of 9 (E3, V1, M5). She had acute pulmonary edema and hypoxemic respiratory failure, necessitating invasive mechanical ventilation. She also sustained stage III acute renal damage, oliguria, and anasarca. A thoracic CT scan identified bilateral large-volume pleural effusion, ground-glass opacities, and mild pericardial effusion. She was admitted to the ICU with an APACHE II score of 23, indicating a 46% risk of mortality. Within 24 hours of ICU admission, a neuro-imaging reassessment revealed additional infarct regions in the anterior cerebral artery territory and left MCA, accompanied with parenchymal edema. There was no hemorrhagic transformation, thus 100 mg of Aspirin was administered daily. The patient was diagnosed with SLE based on their medical history, clinical presentation, and examination findings, meeting the criteria established by the Systemic Lupus International Collaborating Clinics (SLICC) 2012 and the European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) 2019. The patient's clinical instability led to a postponement of the kidney biopsy. To begin treatment, methylprednisolone pulses (1 g for 3 days) were given immediately, followed by a maintenance dose of 1 mg/kg/day and 400 mg/day of hydroxychloroquine. As the patient's condition worsened, she began receiving cyclophosphamide (CYC) in a low-dose Euro-Lupus regimen of 500 mg IV every two weeks for six doses, while tapering corticosteroid treatment. Gradual clinical and laboratory improvements resulted in serum creatinine normalization (from 2.85 mg/dL to 0.63 mg/dL), significant reduction in proteinuria (albumin/creatinine ratio from 10365 mg/g to 1609 mg/g), and normalization of complement levels. Sequential head CT revealed considerable reduction in cerebral edema and development of ischemic regions to encephalomalacia. On day 53, she was transferred to the internal medicine ward with global aphasia, ICU-acquired muscle weakness, and a GCS score of 11 (E4, V1, M6). The patient in this case had a remarkably good recovery despite having a significant neurological deficit upon admission and a lengthy ICU stay. After three months in the hospital, she was transferred to a rehabilitation facility for a 10-week stay. At the six-month follow-up, the patient was able to walk alone and conduct everyday tasks independently. Currently, she was on mycophenolate mofetil 2 g/day, prednisolone 5 mg/day, and hydroxychloroquine 400 mg/day. She still had Broca's aphasia and a Glasgow Outcome Scale Extended score of 6, indicating upper-moderate impairment.

Discussion

This case report presents a patient with systemic involvement at the outset of SLE, who experienced fast deterioration and was admitted to the ICU. Stroke as the initial indication of SLE is unusual.[2] A 2018 literature analysis found 10 such cases, mostly among young women with undiagnosed SLE. The stroke mechanism was unclear, thus immunosuppression and anticoagulation were used to prevent secondary strokes.[3] In the present case, due to the absence of aPL, the treatment was limited to immunosuppression, antiplatelet therapy, and cardiovascular risk factors control resulting in a favorable outcome.[2]

Conclusion

This case marked the difficulty in diagnosing and managing SLE, especially when significant multiorgan involvement is present as an initial presentation. Lupus should be considered as an underlying cause of acute stroke and multiorgan failure in young adults with unexplained clinical symptoms, as evidenced by the patient's fast deterioration and admission to critical care. This case highlights the importance of a multidisciplinary approach, including rheumatologists, neurologists, nephrologists, and intensivists, for timely diagnosis and management of SLE-related complications, especially in intensive care.

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