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(RESEARCH ARTICLE)

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Prediction quality of patients' composited outcomes of interest and how much variations on the outcomes explained by the patients' sodium levels

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Abstract

Background: Hypernatremia can be caused by medications, glucose/urea-related hyperosmolarity, overdiuresis, compartmental fluid distribution imbalances, iatrogenic hypertonic saline excess, renal concentrating performance defects, overdiuresis, and hypermetabolic states. Patients who are in critical condition, encompassing ailments of the heart, liver, lungs, brain, and kidneys, frequently manifest hyponatremia (sodium < 135 mEq/L). Similar to hypernatremia, hyponatremia signifies the severity of the illness and a bleak prognosis. Hyponatremia is less lethal than central pontine myelinolysis, which overcorrects sodium concentrations urgently.

Aim: The objective of this research endeavour was to investigate the strength of correlations, the extent to which the independent variables account for the overall variability in the dependent variable, and the accuracy of the dependent variable's predictions. In addition, the purpose of this test was to extract the coefficients required to present the Binary Logistic Regression models that were investigated.

Methods: Between May 2018 and May 2021, this study examined two Na-based prognosticators for overall mortality in critically ill patients admitted to the King Hussein Medical Centre. An investigation was conducted on 2155 cases utilising Receiver Operating Characteristic (ROC) and Sensitivity Indices Test analyses to ascertain the most effective cut-off points, specificities, sensitivity, predictive values, likelihood ratios, Youden and accuracy indices, and mortality rates. The research discovered that serial termination points with lower values suggested more robust evidence for a positive actual state, whereas higher values suggested less robust evidence for a negative actual state. A Binary Logistic Regression (BLgR) test was performed to examine correlations, the extent of total variations in the dependent variable, and the accuracy of the prediction for each Na-related mortality prognosticator in relation to overall mortality. The analysis was conducted utilising version 25 of SPSS for Windows.

Results: The research revealed that the AUROC for cNa was considerably greater in magnitude compared to its prognosticator that is genealogically related to Na. 129.35 mEq/l and 131.05 mEq/l were the optimal cut-off points, TPRs, TNRs, PPVs, NLRs, YIs, and AIs for the two comparative Na investigated statutes. The BLgR models were developed in order to simulate the relationship between the corrected and measured Na levels of patients and their overall mortality rate. For critically ill patients, the probabilities of overall mortality at the optimal cutoff operating Na levels were 79.59 and 81.62 percent, respectively.

Keywords: Hospitalized patients' overall risk; Natraemia statuses; Prediction Quality; Variations on the Outcomes

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1. Introduction

Major clinical impacts can be attributed to dysnatremia conditions or dysnatremias in hospitalised patients who are critically unwell or even patients who are not critically ill. Particularly among these effects are mortality rates and duration of stay days (LOS). Dysnatremias, characterised by a sodium level that deviates significantly from the established normal range, are frequently observed in critically ill patients who have been admitted to the ward. This may transpire during the course of treatment or at the moment of admission. It is not unusual for hospitalised patients to exhibit or develop dysnatremias either prior to their admission or during their hospitalisation. [1-2]

Hyponatremia often manifests in conjunction with hypersecretions and osmotic and non-osmotic arginine vasopressin (AVP), also known as antidiuretic hormone (ADH). The induction of non-osmotic AVP hypersecretions is often attributed to the contraction of intravascular volume, the stimulation of tension, pain, and narcotics. When performing hypotonic-isotonic intravenous fluid administration, vigilant monitoring of urine diluting capacity is of the utmost importance. Cystic patients may exhibit hyponatremia as a means of communicating the severity of their liver cirrhosis stages. In addition, throughout this process, hyponatremia can serve as an indicator of the severity of hepatic encephalopathy. While it is true that hyponatremia can occur asymptomatically, neurological complications may become apparent, especially among critically ill patients. Elevated concentrations of gastric residuals have been associated with compromised consciousness, convulsive or non-convulsive convulsions, and cardiovascular collapse among patients who are in critical condition. Dysnatremias are correlated with these outcomes. Changes in sodium levels are significant because they can function as an independent variable in determining the prognosis of critically ill patients and as an indicator of the severity of the disease. [3-5]

2. Material and Methods

Approved by the Royal Medical Services, Jordan local Institutional Review Board committee (IRB), this study was retrospectively conducted on the Intensive Care Unit (ICU) to investigate the two proposed Na-based prognosticators against the overall mortality for critically ill patients admitted to the ICU at King Hussein Medical Centre between January 2018 and May 2021. All admitted critically ill patients, including those who were mechanically or non-mechanically ventilated, were included in this study. The variables under investigation were obtained from the Electronic Medical Record System (Hakeem) of our institution. Patients who had predominantly failed to provide data for the parameters that were primarily investigated or the variables that were compared will be excluded from our study.

To begin, the area under the receiver operating characteristic (ROC) curve (AUROC) for each of the two comparative Na investigated statutes [Measured vs. Corrected Na serum levels] concerning the overall mortality of critically ill patients [Survivors' cohort (0) vs. non-Survivors' cohort (1)] was calculated using the ROC analysis. Additionally, after establishing the AUROC for each mortality-related prognosticator under investigation, the Sensitivity Indices Test was applied to a total of 2155 processed cases [of which 1715 cases were classified as positive actual states, 440 cases were classified as negative actual states, and 5 cases were considered missing data]. The purpose of this analysis was to determine the most effective cut-off points, specificities and specificities (TPRs and TNRs), as well as positive and negative predictive values (PPVs and NPVs). It is worth mentioning that serial termination points with lower values suggested a stronger case for a positive actual state [Overall Mortality], while those with higher values suggested a weakened case for a negative actual state [Overall Survival].

Furthermore, for each of the assessed prognosticators of mortality related to Na and overall mortality, a Binary Logistic Regression (BLgR) test was performed on an individual basis. This was done to investigate the extent of correlations, the percentage of cases that the independent variables can explain for the range of total variations in the dependent variable (VR), and the quality of predictions for the dependent variable. Furthermore, the purpose of this test was to extract the essential coefficients required for presenting the investigated BLgR models and to demonstrate the BLgR-related models.

The analyses were conducted utilising version 25 of SPSS for Windows (SPSS Inc., Chicago, IL, USA). The threshold for statistical significance was set at $p < 0.05$.

3. Results

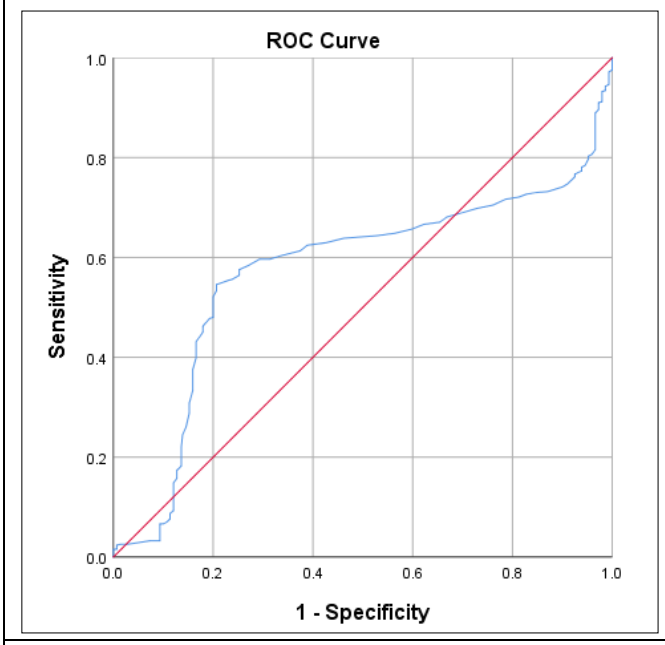
While both comparative prognosticators yielded AUROCs that fell within the unsatisfactory ranges (0.5-0.6), the AUROC±SEM for cNa was considerably greater than that of its prognosticator that is genealogically related to Na

[0.595±0.013 (95% CI; 0.570-0.621) versus 0.571±0.014 (95% CI; 0.544-0.599)]. [129.35 mEq/l, 54.6%, 79.32%, 91.14%, 30.94%, 57.27%, 263.89%, 33.90%, 59.63%, and 79.59% versus 131.050 mEq/l, 30.79%, 83.41%, 92.42%, YIs and AIs, and %MOR] were the optimal cut-off points, TPRs, TNRs, PPVs and NPVs, NLRs and PLRs, YIs and AIs, and the%MOR for the two comparative Na investigated statutes. The analyses of the ROC and Sensitivity Indices tests were comprehensively summarised and visually represented in Figure 2 and Table 2, respectively.

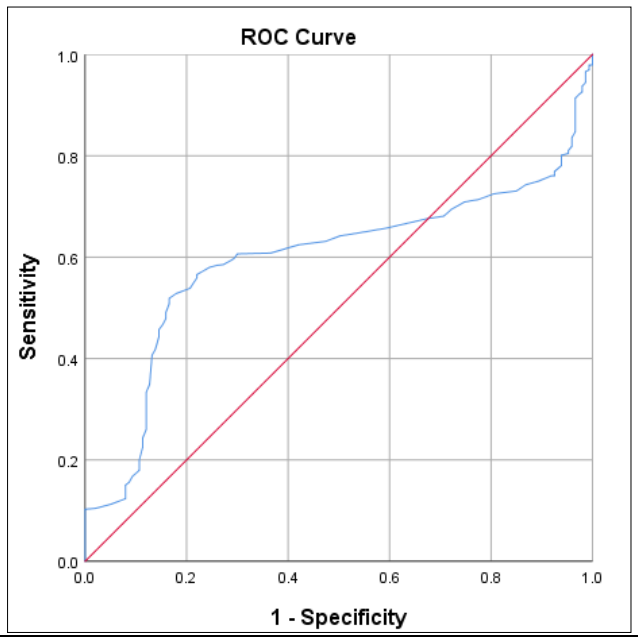
Table 1 The sensitivity test results

Prognostic Indicator	Optimal Cutoff	TPR	FPR	YI	TNR	PPV	NPV	NLR	PLR	AI	%MOR
Na (mEq/l)	129.35	54.6 %	20.7 %	33.90 %	79.32 %	91.14 %	30.94 %	57.27 %	263.89 %	59.63 %	79.59 %
cNa mEq/l	131.05	51.9 %	16.6 %	35.30 %	83.41 %	92.42 %	30.79 %	57.67 %	312.79 %	58.33 %	81.62 %

TPR: True positive rate (sensitivity); FPR: False positive rate; YI: Youden index.; TNR: True negative ratio (specificity); PPV: Positive predictive value; Na+: The measured sodium level in mEq/l; MOR: Overall mortality; AI: Accuracy index; PLR: Positive likelihood ratio; NLR: Negative likelihood ratio; NPV: Negative predictive value; cNa+: The corrected sodium level in mEq/l.



Na



cNa

Na+: The measured sodium level in mEq/lcNa+: The corrected sodium level in mEq/l.

Figure 1. The area under the receiver operating characteristic (ROC) curve for each of the two compared Na investigated statutes [Measured vs. Corrected Na serum levels] regarding the overall mortality of critically ill patients (Survivors' cohort (0) vs. non-Survivors' cohort (1)) was calculated using the ROC analysis (Figure 1). While both comparative prognosticators yielded AUROCs that fell within the unsatisfactory ranges (0.5-0.6), the AUROC±SEM for cNa was considerably greater than that of its prognosticator that is genealogically related to Na [0.595±0.013 (95% CI; 0.570-0.621) versus 0.571±0.014 (95% CI; 0.544-0.599)]

The logistic regression models (BLgRs) were developed to simulate the relationship between the corrected and measured Na levels of patients and their overall mortality rate. The BLgR models were defined as follows: (e (14.465-0.099HcNa)/1+ e(5.888-0.035×Na)) and (e (14.465-0.099×cNa)/1+ e. Based on the previously constructed 2 BLgR models, the probabilities of overall mortality for critically ill patients at the two investigated optimal cutoff operating Na levels were 79.59% and 81.62% at 129.35 mEq/l and 131.05 mEq/l, respectively, with estimated sensitivities and specificities of 54.6% and 79.32% versus 51.9% and 83.41%. The two BLgR models that were constructed exhibited statistical significance [$\chi2(8) = 420.462$, $p < 0.0005$ and $\chi2(8) = 434.751$, $p < 0.0005$, respectively]. The proportions of explained variations in the dependent variable varied between 1.2% and 1.9% and 0.2% and 0.3%, respectively, and

were dependent on whether the Cox & Snell R2 or Nagelkerke R2 methods were utilised. The models accurately classified around 79.6% of the cases. Table 3 and Figure 3 provide comprehensive representations of the BLgR test analysis and illustrations pertaining to the two comparative Na investigated statutes [Measured vs. Corrected Na serum levels] concerning the overall mortality of critically ill patients.

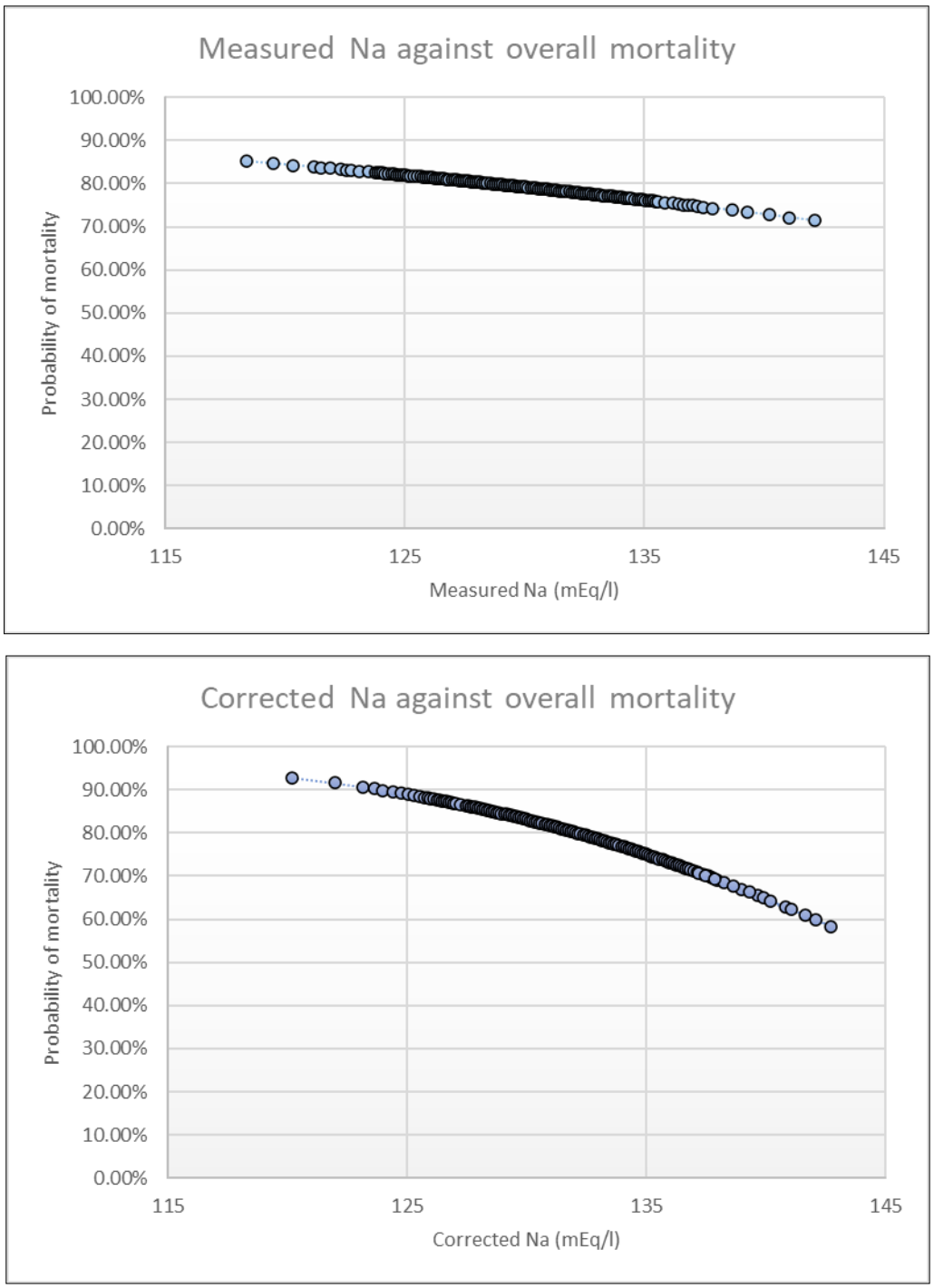


Figure 2 The analysis of two comparative Na investigated statutes [Measured vs. Corrected Na serum levels] concerning the overall mortality of critically ill patients at the King Hussein Medical Centre, Royal Medical Services, Jordan from January 2018 to May 2021, as depicted by the Binary Logistic Regression model

Table 2 The outcomes of binary logistic regression analyses

Tested predictors	B±SEM	Wald	Sig.	Exp(B)	95% C.I.for EXP(B)		χ^2(df)	VR	%Cases
					Lower	Upper			
Mortality	$e^{(5.888-0.035\times Na)}/1+e^{(5.888-0.035\times Na)}$								
Constant	5.888±2.214	7.076	0.008	360.752			(8) 420.462	0.2%-0.3%	79.6%
Na (mEq/l)	-0.035±0.017	4.193	0.041	0.966	0.934	0.999			
Mortality	$e^{(14.465-0.099\times cNa)}/1+e^{(14.465-0.099\times cNa)}$								
Constant	14.465±2.621	30.445	0.000	1.9×10^6			(8) 434.751	1.2%-1.9%	79.6%
cNa (mEq/l)	-0.099±0.020	25.078	0.000	0.905	0.871	0.941			

4. Discussion

Irrespective of the co-morbidity burden assessed at baseline, hospitalised medically ill patients with hyponatremia had substantially higher 30-day mortality rates (adjusted HR ratio: 1.3-1.7), according to a Danish cohort study. Irrespective of any prior medical interventions undertaken by the patients, this outcome persisted. However, the Danish cohort study did not make any adjustments to the measured Na levels of the patients whose blood glucose levels were also measured, in contrast to our research. In addition, the analysed HR did not account for the blood glucose levels of the patients, a substantial potential confounding variable. Table [] Hyperosmolality results from hyperglycemia; consequently, this induces the withdrawal of water molecules from intracellular compartments. A dilutional hyponatremia status is brought about by extracellular water redistribution. [6-7]

Furthermore, several prior investigations reached the consensus that patients with chronic kidney disease (CKD), hemorrhagic or ischaemic stroke, liver cirrhosis, hyponatremia-related congestive heart failure (CHF), and chronic kidney disease (CHF) were autonomously correlated with a clinically and statistically significant unfavourable prognosis. This resulted in increased days of admission and mortality rates. The prevailing theory posits that hyponatremia is predominantly caused by storms of sympathetic, vasopressin, and renin hypersecretion in the co-morbidities mentioned above. [8-9]

5. Conclusion

Dysnatremias are associated with the effects experienced by patients who are hospitalised. The fluctuations in sodium levels are substantial among hospitalised patients, particularly those who are critically ill. Sodium levels can serve as an autonomous factor in assessing the prognosis of critically ill patients and as an indicator of the disease's severity.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest in this manuscript.

Statement of ethical approval

There is no animal/human subject involvement in this manuscript.

Statement of informed consent

Owing to the retrospective design of this study, the informed consent form was waived.

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