

Prognostic Analysis of Hyponatremia for Diseased Patients Using Multilayer Perceptron Classification Technique

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Abstract

INTRODUCTION: The sodium electrolyte deficiency in the human serum is known as Hyponatremia. The deficiency of sodium in the blood indulges many problems for the patients. If the sodium range in human serum not managed and treated it creates difficulties such as longer hospital stays and mortality.

OBJECTIVES: This paper focuses on forecasting the sodium ranges of patient using the machine learning algorithm supported by the past health records of the patients.

METHODS: The vital patient information including the disease history, age, gender, and serum sodium level before and after hospital admission are analysed using the logistic regression, k-nearest neighbour, multilayer perceptron, and extra-trees ensemble classification algorithm. The results of the classification algorithm show that the proposed MLP algorithm produces higher prediction results as compared to other machine learning algorithms. Also, the confusion matrix, Kappa score, R square value and error metrics.

CONCLUSION: The results show that the MLP classification is more suitable prognostic analysis of the hyponatremia for diseased patients.

Keywords: Sodium electrolyte, Hyponatremia, MLP, Prediction, Arginine vasopressin

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1. Introduction

Once human beings are affected by life-threatening diseases such as stroke, central nervous system diseases, chronic diseases, and imbalance of kidney electrolytes, they are more likely to have the same or related side effects later. Poor diagnosis, treatments, or other health problems of patients may increase the chances of a second occurrence. These types of deadly diseases need to be actively served and managed with intensive treatment.

Typically, the human body should maintain the homeostatic levels within the normal range [1]. A healthy adult human body should have the following limit; Deserum sodium (Na +) 136-145 mmol / L; Serum

potassium (K +) as 3.3-4.5 mmol / L; Serum chloride (Cl-) 96-108 mmol / L; Urinary sodium 40-220 mg / day; Urinary potassium 25-125 mg / day; Urine serum chloride 110-250 mg / day [2,3]. Any abnormalities in these recommended limits may have adverse effects on the human body, and its severity depends on the degree of homeostatic concentration or dilution.

Improper antidiuretic hormone secretion can lead to rapid loss of sodium in human serum. Loss of serum sodium concentration in human blood is called hyponatremia. The amount of sodium in the blood is diluted by excessive water intake and frequent urination. In general, hyponatremia is a common disorder and is seen in many hospitalized patients [4]. If the necessary essential treatments are not provided, it can lead to the death of the patient. The mortality rate for patients with hyponatremia

is high despite adequate intensive care [5]. Hyponatremia is also seen in patients with high levels of the arginine vasopressin (AVP) hormone in the blood plasma.

Hyponatremia can be classified as acute and chronic based on the concentration of serum sodium. Deficient serum sodium concentrations can be very harmful and affect other organs' normal functioning in the human body [6]. In general, frequent hyponatremia can lead to severe complications in the central nervous system. Patients with severe hyponatremia should be given intensive and immediate treatment; Otherwise, it can be life-threatening. Chronic hyponatremia causes non-renal disease in other human body organs, often leading to morbidity and mortality.

Patients with hyponatremia are given poor prognosis and treatment, especially heart patients [7]. Hyponatremia patients can be optimally managed with immediate treatment, increasing serum sodium concentration, and reducing severity and hospital death. The primary diagnosis and optimally approved treatments for hyponatremia in patients can improve their physical condition and allow them to be admitted to a standard hospital, reducing hospitalization time and hospitalization costs [8].

A very rapid increase in serum sodium concentration can lead to life-threatening diseases and persistent side effects. The recommended dose should only increase serum sodium; otherwise, it increases the risk of dangerous heart or neurological disorders [9]. One of the mainstays of treatment for hyponatremia is associated with inhibition of arginine vasopressin receptors' action. It tries to resist electrolytes' removal during urination; it may increase serum sodium concentration [10].

Serum sodium concentration should be administered within the recommended range, based on homeostatic means, AVP, renal excretion, and thirst. Any abnormal changes in blood electrolytes, renal chemistry levels, and water levels can lead to hyponatremia. Even a small imbalance in renal function, if not carefully treated, can lead to chronic illness or even death in severe cases [11, 12]. Encourages research into the adverse effects of hyponatremia on the human population. The prognosis of future sodium limitations and patients are likely to study due to hyponatremia. This research work uses regression and neural networks for the analysis of sodium limits.

The rest of the section is organized as follows. Section 2 refers to existing literary works on hyponatremia. Symptoms, causes, existing diagnosis, treatments, and consequences of hyponatremia. Section 3 describes the proposed method and its step-by-step description of predicting future sodium limits in patients under hyponatremia treatment. The forecast results, analysis, and evaluation of the proposed method are given in Section 4. Finally, Section 5 concludes with future improvements.

2. Literature survey

This summarizes the current scholarly work on the importance of hyponatremia and its appropriate treatment. Numerically, hyponatremia is defined as a decrease in serum sodium concentration (Na^+) below 136 (normal range 133-145) mEq / l . The disorder type is familiar to many hospitalized patients. As mentioned earlier, excessive water retention or persistent urination can lead to dehydrated hyponatremia [13]. Water intake should not exceed the capacity of the kidneys. If too much, it causes dilution of sodium in the serum, leading to hyponatremia, hypo-tonicity, and hypo-osmolality [14].

In general, patients with inappropriate antidiuretic hormone (SIADH) syndrome drink more water; Because SIADH patients always feel thirsty. Treatments and medications are given to hyponatremia patients based on their age, severity, hormonal conditions, renal failure, chronic disease, adrenal status, and endocrine system [15, 16]. A variety of medications associated with hyponatremia treatment include diuretics containing are sulfur, vasopressin receptor antagonists, tolvaptan, and desmopressin; these medications can reduce the risks associated with hyponatremia. The false prediction of low serum sodium concentration is called pseudo-hyponatremia. This can occur when patients have extreme hyperlipidemia or hyperproteinemia and can be identified by flame photometry or direct potentiometry [17].

In most cases, excessive AVP secretion is the main problem causing hyponatremia due to lack of elevated plasma osmolality. As AVP secretion is elevated, the kidneys may retain water. Thus, decreased water discharge and increased AVP concentration are directly related [18]. Patients have high AVP secretion, and their water intake exceeds 800 ml/day, which can cause water retention and dehydration of the fluid vessels, which causes hyponatremia.

According to age, the incidence of hyponatremia increases. Documented studies show that the elderly have a higher percentage, which means that 60-year-olds make up 53% of the disorder in a year. Furthermore, SIADH disorder is more common in hospitalized patients with hyponatremia [19]. Valproic acid plays a significant role in regulating Na^+ channels. It is an 8-carbon 2-chain fatty acid, which is metabolized by the human liver [20]. Valproic acid mediates the management and recovery of serum sodium concentrations by depolarizing spinal and cortical neurons in patients.

Generally, its treatment range should not exceed 50-100 mcg/ml [21]. In contrast, its content produces positive responses with minimal side effects experienced by patients. Furthermore, the level of valproic acid in the blood should be monitored and changed at short intervals but within the recommended range at regular intervals based on patients' responses. The time it takes for valproic acid to infect the human body varies from patient to patient [22].

The sub-therapeutic/supra-therapeutic levels of valproic acid to patients might make them to the risk conditions or indulges in toxic side effects. If required, additional testing/treatments should be given to the patients based on

Table.1 Sample record of cleaned dataset

Gender	Age	Diabetes	Pneumonia	Liver Disease	Malignancy	Pulmonary	Sepsis	Sodium Range
1	1	1	0	0	1	0	0	1
1	1	0	0	0	0	1	0	3
1	2	0	0	0	0	0	0	3
1	0	1	0	0	0	0	0	3
0	1	0	0	0	0	0	0	6
1	2	0	0	0	0	0	0	3
1	1	0	0	0	1	0	0	4
0	0	0	0	0	0	0	0	3
1	3	0	0	0	0	0	0	3
1	2	0	0	0	0	0	0	3

medication's effectiveness/ineffectiveness, patient's side effects, effects on the central nervous system, and other patients' complications [23]. Further, the patients with multiple medications should be taken additional care with continuous evaluation of valproic acid level because of other medications' interaction. The blood's protein level is virtually monitored because the supra-therapeutic valproic acid level has more influence on it [24].

The research gap in predicting the patients' future sodium range motivates this research work and analysis of the possibility of readmission due to hyponatremia. The Interferon-gamma (IFNG), Oxytocin (OXT), Arginine Vasopressin (AVP), TRPV4 (Transient Receptor Potential Cation Channel Subfamily V Member 4) are the most evident genes and hormones with the hyponatremia.

3. Methodology

This section describes the methodologies for predicting the future sodium ranges of the patients affected by hyponatremia. The multilayer perceptron (MLP) and other classification techniques such as Logistic Regression (LR), K-Nearest Neighbour (KNN), and Extra Trees (ET) are adopted in this work for the prediction of future values of sodium.

The proposed method analyses and predicts the futuristic sodium levels based on the history of patients' health conditions. This research work also facilitates the use of artificial intelligence-based methods to predict the likelihood of recurrence of hyponatremia. Furthermore, the proposed research work has developed the MLP based future health prognosis algorithm to follow patients' future health based on their future disease/illness history.

3.1. Dataset

The database of this research is derived from the Cerner Health Facts database. The database covered hospitalized patients in January 2000 and November 2014 and was collected from various clinics and hospitals in the United States [9]. The database contains 1048576 numbers of patient information. The dataset includes features of

patients such as hypertension, patient's length of stay, heart_failure, coronary_artery_disease, end_stage_renal_disease, chronic_kidney_disease, chronic_liver_disease, cirrhosis, lung_cancer, COPD, hypothyroidism, depression, dementia, peripheral_vascular_disease, adrenal_insufficiency, cerebrovascular_disease, myocardial_infarction, hemiplegia, rheumatologic_disease, peptic_ulcer_disease, diabetes_complication, metastatic_cancer_diabetes, pulmonary, glucose_level_24_hr_before_admission, SIADH, sodium_levels, pneumonia, gender, age, race, serum_sodium_categories, malignancy, sepsis, and outcomes [9].

Patients gender (G), age (A), pneumonia (B), diabetes (D), malignancy (M), liver disease (L), sepsis (SA), lung (P), SIADH (S), and sodium levels (Na) are taken for this research analysis. Patients were grouped into four categories based on their age. Age groups were (i) 18 to <45, (ii) 45 to <65, (iii) 65 to <75, (iv) ≥75 years [9]; The sodium range is classified as <120 to 1; 2 ≥ 120 to <125; ≥ 125 to <130 3; 4 ≥ 130 to <135; 5 to 5 135 to <138; And 6 ≥ 138 to <140. Similarly, based on gender, patients were grouped as male and female for MLP mechanisms training and learning.

The data preprocessing and cleaning process removes the missing and outliers data values from the dataset. After preprocessing, the resulted dataset is reduced to one million patient records with the above listed 10 required relevant features of patient details. In this dataset, approximately about 49658 records are missing the essential required patient details. The numerical features from the dataset are taken as the input attributes and one feature (Sodium range) is considered as the output attribute. A sample of the patient's information is presented in Table.1.

3.2 Multilayer Perceptron (MLP)

This work proposes and develops the MLP based future sodium prediction algorithm. The MLP algorithm works using the artificial neural network. Typically, in a simple three-layer network, there will be an input layer in the first, a hidden layer in the middle, and the output layer in the last. In the input layers, the input dataset will be fed. The output layer contains the output generated based on the dataset

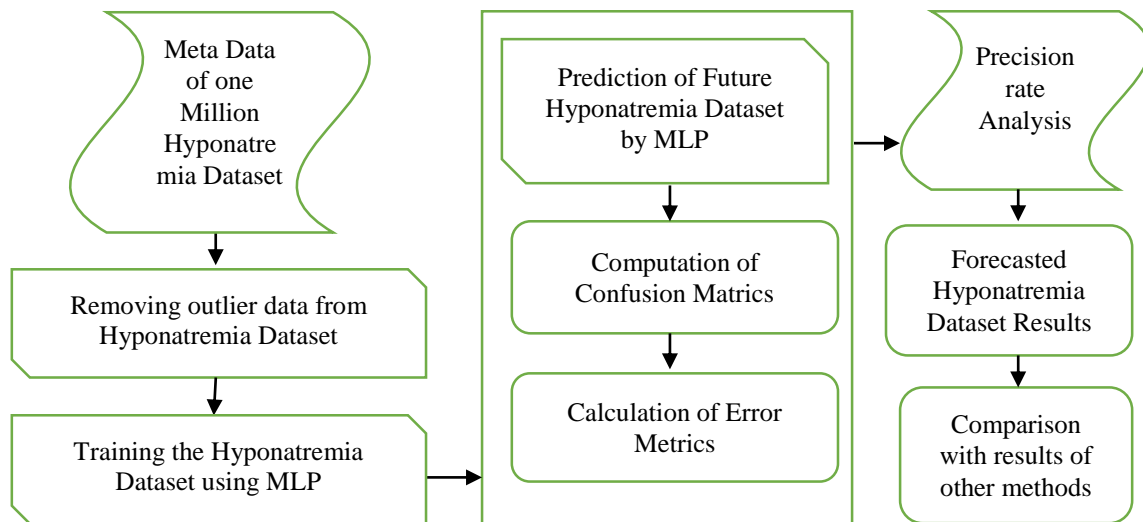


Fig. 1. Block diagram of the proposed model

given to the input layer and computations from the hidden layer. The hidden layer number can be varied (increased/decreased) based on the complexity of the given problem [37]. In general, any neural network model's main objective is to optimize or approximate the given function $f(x)$. Similarly, the multilayer perceptron neural network model will find the best optimized or approximate solution to the given complex problem by using techniques such as classification, regression, or mapping functions [31].

In the proposed MLP based supervised learning technique, each neuron uses a nonlinear activation function and back-propagation for training. The proposed MLP network consists of several chained functions. Let consider a classifier problem $y = f(x)$; here, the output y is driven by the input x and its corresponding mapping solution given by MLP based on the best approximation of the given classifier function. The MLP computes the best-optimized solution as $y = f(x; \theta)$, where θ is the learning parameter of the given problem. For example, the three-layer MLP network can be formulated as $f(x) = f(x_3) (f(x_2) (f(x_1) (x)))$. The MLP performs several defined transformation and/or linear summation functions with the inputs in each layer. In MLP, each of these layers is symbolized as $y = f(W \cdot x + T + b)$; where the activation functions are denoted as f , the weights or set of the parameter of the problem are indicated as w , the variable x is the input, and b represents the bias vector [32].

In the proposed MLP algorithm, the output of the previous layer is the input to the next layer. Such that the layers of the MLP of fully connected layers in the network. Thus, each unit functions of the layer are always connected to all other layers' unit function in the neural network. Each layer's unit functions (i.e., weights and other sets of parameters) are independent of the other layer's unit functions. It means the weights of each layer's unit functions are unique. Further, the MLP network defines the loss function, which can measure the performance (sodium prediction) of the proposed MLP classification technique. When the loss function has a high value, the MLP doesn't

make an accurate classification or prediction solution to the given problem, and otherwise, it is vice versa [31, 32].

Fig.1 depicts the flow of the proposed MLP based future sodium prediction algorithm. Firstly, one million patients hyponatremia dataset was collected from the hospitals. The outlier and missing data are removed from the hyponatremia dataset using the imputation process. Then the 0.5 million hyponatremia dataset is given to the input layer as the input, and it is trained using the multilayer perceptron algorithm. To obtain a better optimal prediction model, the number of hidden layers is varied from two to twenty by the unit of two. This MLP learning and training process gives the prediction results in the output layer.

The prediction results are evaluated with the error performance metrics such as Mean Squared Error (MSE), Root Mean Squared Error (RMSE), Mean Absolute Error (MAE), Mean Absolute Relative Error (MARE), and Root Mean Squared Relative Error RMSRE (RMSRE) are computed for the prediction results [33, 38]. The performance results of the future sodium prediction dataset are analyzed with the precision rate and compared with other existing results.

4. Results Evaluation and Discussion

This section gives detailed results analysis, evaluation of performance metrics, and comparative result analysis. The Anaconda Jupiter notebook and various libraries of scikit-learn have been used to implement the proposed work with an i3 processor, 3 GB RAM system. The taken dataset has been split into 70 %, 15%, and 15% for the training, validation, and testing. To evaluate and validate the performance of the machine learning model, resampling methods are adopted. This method estimates the prediction ability of the machine learning algorithm on new unseen input data. In this work, the 'k' value is chosen as 10; therefore, it can be called a 10-fold cross-validation

Table.2 Performance Error Metrics resulted by MLP

Metrics/Neurons	MSE	RMSE	MAE	MARE	RMSRE
2	0.052	0.2281	0.1521	0.0418	0.073
4	0.1012	0.3181	0.2791	0.071	0.0919
6	0.0227	0.1505	0.0691	0.0196	0.0441
8	0.0942	0.3069	0.273	0.07	0.0898
10	0.0563	0.2372	0.1693	0.0492	0.1017
12	0.1092	0.3304	0.2975	0.0752	0.0956
14	0.1014	0.3184	0.2832	0.0728	0.0967
16	0.1018	0.3191	0.2862	0.0727	0.0914
18	0.0806	0.2839	0.248	0.0636	0.0773
20	0.1005	0.317	0.2848	0.0722	0.0894

resampling method. The 10-fold cross-validation method intends to reduce the bias of the prediction model.

4.1 Results of MLP Algorithm

The multilayer perceptron algorithm trains the dataset containing the 0.5 million patients' information such as age (A), gender (G), information about diabetes (D), pneumonia (P), liver-disease (L), malignancy (M), pulmonary (Pu), sepsis (Se), SIADH (S), and sodium level (Na) of the patients during admission to the hospital. To determine the quality dataset for the prediction of the future sodium values, the number of hidden neurons is varied from two to twenty [34, 36]. Table. 2 summarizes the resultant performance error metrics values such as MSE, RMSE, MAE, MARE, and MSRE for the MLP algorithm with several different neurons.

The prediction accuracy, confusion matrix, Mean Square Error (MSE), Kappa, R2 scores of MLP in comparison with logistic regression, K-nearest neighbour, and extra trees algorithms are depicted in in the figures 2, 3, 4, 5, and 6 respectively. The results of the confusion matrix suggest that the MLP has higher true positive rate and true negative rate.

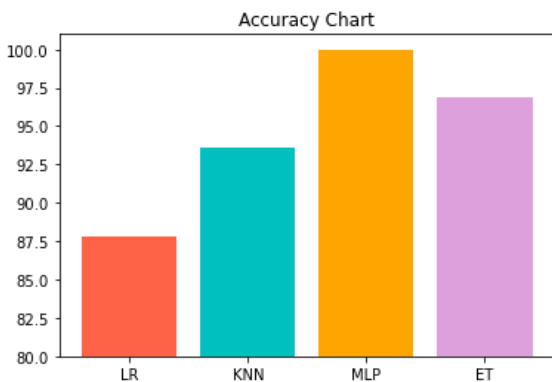


Fig. 2. Comparison of Na+ prediction results by MLP and other classifiers

In Table. 2, the lowest MSE value is highlighted as neuron 6. The error performance metric values for the MSE, RMSE, MAE, MARE, and MSRE for the neuron 6 by MLP algorithm are 0.0227, 0.1505, 0.0691, 0.0196, and 0.0441 respectively; it is the lowest among other neurons. Therefore, the corresponding dataset of neuron 6 is considered the appropriate and optimistic solution for the given hyponatremia patient dataset.

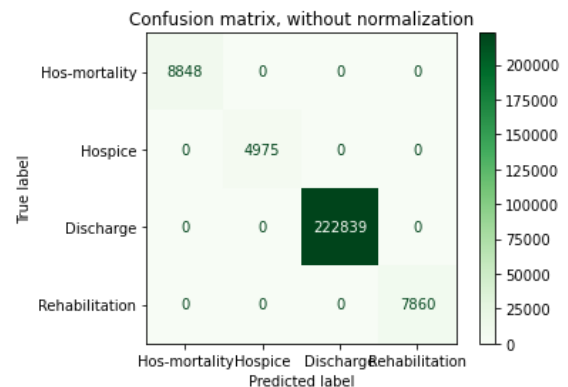


Fig. 3. Confusion matrix of Na+ prediction results by MLP

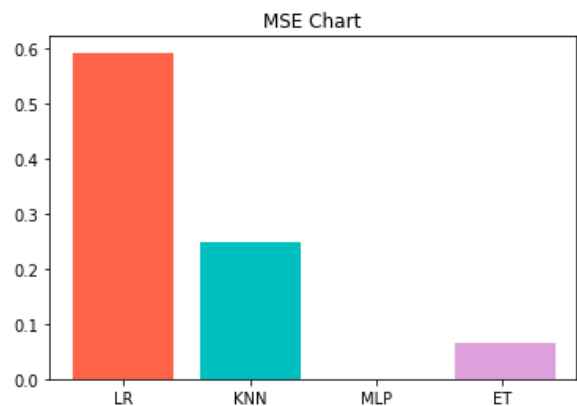


Fig. 4. Comparison of MSE for Na+ prediction results

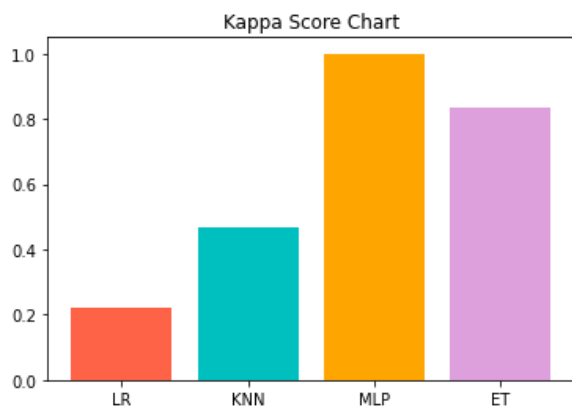


Fig. 5. Comparison of Kappa score for Na⁺ prediction results

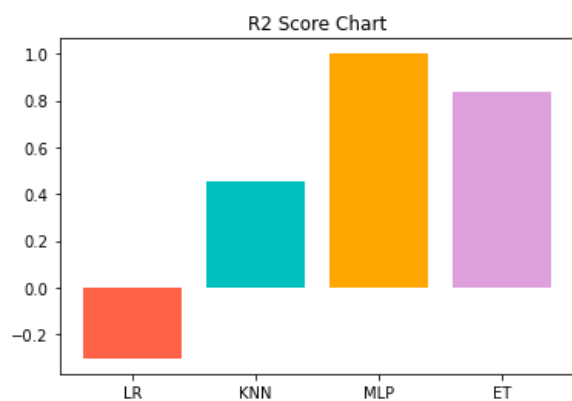


Fig. 6. Comparison of R2 score for Na⁺ prediction results

5. Conclusion

This work was concentrated on predicting the future sodium range for the patients based on various health history factors such as age, gender, health problems, etc., to predict the hypo/hyponatremia. The proposed MLP algorithm has produced an accurate future serum sodium prediction range than the LR, KNN, and ET algorithms. The LR algorithm has a 41-72 % prediction accuracy rate, whereas the MLP neural network algorithm has an accurate prediction of 91-99 %. The MLP algorithm-based prediction results have 27-50 % improved prediction accuracy than the KNN algorithm-based prediction results. Moreover, the proposed MLP algorithm-based prediction results in 57.1 % of the reduced MSE error rate than the LR, KNN, and ET results in predicting future sodium ranges of patients. The outcome of the proposed MLP algorithm-based future health prediction algorithm could help physicians and patients make further decisions based on their health conditions. The future work will concentrate on forecasting survival rate of the patients after hyponatremia with various health parameters.

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