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Editorial

Functional Relationship of Serum Sodium with Heart Patients

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Serum sodium (SNa) is one of the principal extracellular fluid electrolytes that is necessary for balancing extracellular fluid volume and potentials across cell membranes.[1,2] SNa's imbalances in concentrations have been recognized to manifest as headaches, nausea, restlessness, and confusion, while rapid changes in Na concentrations result in acute neurologic symptoms such as impaired mental status and seizures.[2,3] Hyponatremia is generally defined as SNa concentrations <135 mmol/L and is prevalent in the elderly due to impaired water-excretory capacity related to normal aging.[1,4] Note that dysnatremias (hyponatremia (<135 mmol/L) and hypernatremia (>145 mmol/L)) can severely affect many physiological functions and organ systems.[3-5] Electrolyte imbalance hyponatremia is most often observed in heart failure patients admitted to hospitals.[6-8] Many research articles focus on the prognostic value of blood Na levels in heart failure subjects, which have shown that hyponatremia is connected with a highly lower blood pressure (BP) value, which is also freely connected with higher-risk.[9] Most researchers define hyponatremia as SNa <135 mmol/L, while some define it using quartiles, and a linear relationship has been identified between the risk of short- and long-term total mortality, in-hospital cardiovascular morbidity and mortality, and SNa <140 mmol/L. Again, some researchers have reported a U-curve for values between 140 and 145 mmol/L.[10-13] However, the association or correlation of SNa with heart disease patients is not clear. It can be ensured based on the exact probabilistic model of SNa with heart disease status, along with the other illustrative factors and variables of the heart disease. Again, this type of association or relationship can be obtained based on the models of blood pressure (systolic and diastolic), heart rate, ejection fraction, SNa, and other explanatory variables or factors of the heart disease.

The present editorial note investigates the following research hypotheses:

• Is there any relationship or association between SNa and heart disease patients? If it is affirmative, what is the most probable SNa relationship or association model with heart disease patients?
• How do we derive the most probable SNa relationship or association model with heart disease patients?
• What are the functional relationships between SNa and heart disease patients?

These above research hypotheses are investigated herein based on a real data set of 299 heart patients with 13 covariates, and the data set is described in the two articles,[14] which can be found on the website https://archive.ics.uci.edu/ml/datasets/Heart+failure+clinical+records.[15] In this study, there are 13 covariates, which are:

Gender/Sex	0=female, 1=male
Age	
Diabetes status (DIS) of subjects	0=No diabetes, 1=Diabetes
Creatinine phosphokinase (CRP)	
Anaemia status (ANS) of subjects	0=No anemia, 1=Anemia
High blood pressure (HBP) of subjects	0=Normal BP, 1=High BP
Ejection fraction (EJF)	
Serum creatinine (SEC)	
Serum sodium (SNa)	7 (1.4)
Time up to the end of the follow-up period (TTF)	
Platelet count (PLC)	
Smoking habit (SMH)	0=No smoking, 1=Smoking
Death event (DEE)	0=Alive, 1=Death

The above considered physiological data set is multivariate, non-normal, and heteroscedastic. The response in the present study is SNa, which is a non-constant-variance continuous variable. The variance of the dependent variable SNa is not stabilized by any suitable transformation; therefore, it is modeled by joint

generalized linear models (JGLMs) that are clearly described in the book by Lee, Nelder, and Pawitan.[16] The derived mean and variance of the SNa gamma-fitted models are as follows:

Gamma-fitted SNa mean (μ) model is

μ=exp. (4.91+0.02 EJF –0.02 DIS +0.03 EJF*HBP –0.02 HBP +0.01 PLC +0.01 ANS +0.01 SMH –0.01 PLC) *ANS –0.01 CRP*SMH –0.01 CRP*HBP +0.01 CRP –0.01 DEE –0.02 TTF +0.02 ANS*DEE +0.01 AGE*TTF +0.02 AGE –0.03 SEC –0.01 AGE*PLC +0.02 AGE*SEC –0.01 AGE*CRP +0.04 SEX –0.0001 EJF*PLC +0.03 EJF*SEC –0.07 AGE*SEX +0.01 CRP*TTF),

and the fitted SNa variance (σ^2) model is

σ^2=exp. (-4.28+0.01 CRP*DIS –0.89 DIS –0.01 CRP –0.08 EJF +0.07 EJF*DEE +1.14 SEC*DIS +1.83 DEE –0.06AGE*DEE +0.02 AGE –1.94 ANS +0.03 EJF*SEX –0.41 SEX –0.01 PLC –0.53 SEC*SEX –0.18 SEC -1.31 SMH +1.04 SEC*SMH –0.02 TTF +0.03 AGE*ANS +0.01 EJF*TTF).

These two above gamma-fitted equations present, respectively, the SNa's mean (μ) and the variance (σ^2) models. Note that there are two cardiac parameters, such as the HBP of subjects (0=normal BP, 1=high BP), and the EJF, while high blood pressure is an attribute or categorical character and the ejection fraction is a continuous variable. On the other hand, serum sodium, the response variable, is a continuous variable. The present editorial note examines the associations of SNa with high blood pressure and ejection fraction, along with the other remaining variables or factors, through the mean and variance models as in the above equations.

From the above mean model, it is observed that mean SNa is positively partially correlated or connected with the joint interaction effects of HBP (0=normal BP, 1=high BP) and EJF, i.e., HBP*EJF (p=0.14), while both the marginal effects of EJF (p=0.62) and HBP (p=0.82) are insignificant. This association indicates that higher SNa levels increase the subject's BP levels along with the EJF, while SNa is insignificant to both the HBP and EJF. It is well-known that higher SNa levels increase BP levels.[11,13,14] But the present analysis shows that higher SNa levels increase BP levels, along with the joint effect of EJF. Note that in epidemiology, partially significant effects are treated as confounders.

Mean SNa levels are inversely connected with the joint interaction effects of CRP and HBP (0=normal BP, 1=high BP), i.e., CRP*HBP (p<0.01), while they are directly connected with the marginal effect of CRP (p<0.05) and insignificant to HBP. This implies that mean SNa levels are higher for subjects with normal BP, along with higher CRP levels. Again, mean SNa levels are directly connected with the marginal effect of CRP (p<0.05), which implies that SNa levels increase as CRP levels increase.

Mean SNa levels are significantly inversely associated with the joint interaction effects of EJF and PLC, i.e., EJF*PLC (p=0.04), while they are directly connected with the marginal effect PLC (p<0.01) and insignificant to EJF (p=0.62). This association implies that the mean SNa levels are higher at the lower joint effect of EJF and PLC. Also, mean SNa levels are directly significantly connected with PLC (p<0.01) levels, which implies that SNa levels increase as PLC levels increase, which is observed in practice.

Mean SNa levels are directly connected with the joint interaction effects of EJF and SEC, i.e., EJF*SEC (p<0.01), while they are inversely connected with the marginal effect of SEC (p<0.01) and insignificant to EJF. This indicates that mean SNa levels increase as the joint effect of EJF and SEC increases. In addition, mean SNa levels are inversely connected with the marginal effect of SEC (p<0.01), which indicates that SNa levels increase as SEC levels decrease, which is also observed in practice.

SNa variance is directly partially related to the joint interaction effects of EJF and gender, or SEX (0=female, 1=male), i.e., EJF*SEX (p=0.10), while it is inversely connected with the marginal effect of EJF (p<0.01) and insignificant to SEX (0=female, 1=male) (p=0.62). This association implies that SNa levels are more scattered for male subjects with higher EJF levels than females with lower EJF. Also, SNa level's variance is inversely connected with the marginal effect of EJF (p<0.01), implying that SNa levels are more scattered if EJF levels decrease, indifferent to sex.

SNa variance is directly connected with the joint interaction effects of EJF and time up to the end of the follow-up period (TTF), i.e., EJF*TTF (p<0.01), while it is inversely connected with both the marginal effects of EJF (p<0.01) and TTF (p<0.01). This implies that SNa levels are more scattered when the joint effect of EJF and TTF increases. SNa level's variance is inversely connected with the marginal effect of TTF (p<0.01), indicating that SNa levels are more scattered when TTF decreases, indifferent to EJF.

SNa variance is directly connected with the joint interaction effects of EJF and DEE (0=alive, 1=death), i.e., EJF*DEE (p<0.01), while it is inversely connected with the marginal effect EJF (p<0.01) and directly partially connected with DEE (survive=0 or died=1) (p=0.14). This indicates that SNa levels are more scattered for the dead patients with higher EJF than the surviving patients. It is noted that DDE acts as a confounder in the variance model.

It is derived herein that mean SNa is connected with HBP*EJF, CRP*HBP, EJF*PLC, and EJF*SEC, while the variance of SNa is connected with EJF*SEX, EJF*TTF, and EJF*DEE along with their marginal effects. Herein, only the relationship of SNa is examined with the cardiac parameters. Similarly, the relationship between the cardiac parameters EJF, BP, or heart rate is to be examined with SNa. Herein, these associations have not been examined. The full report, along with all details and analysis, will be submitted soon. All the findings of the mean and variance models are completely new in the heart disease literature. It is observed herein that SNa has many complicated functional effects on cardiac parameters or heart subjects; therefore, the medical treatment process and research methods should focus on the subjects SNa levels.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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