

Editorial Article

# Serum Sodium Associations with Anaemia Patients

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It is well known that one of the most fundamental extracellular fluid electrolytes is serum sodium (SNa) that is important in keeping balance between extracellular fluid quantity and potentials across cell membranes of the human body [1, 2]. SNa's immitigability in condensation have been accepted to manifest as restlessness, headaches, confusion and nausea, while quick changes in Na condensation result in severe neurologic syndromes such as seizures and impaired mental status [2, 3]. Hyponatremia is usually defined as SNa condensations  $< 135$  mmol/L and it appears in the aged persons due to ruined water-excretory capacity concerned with normal aging [1, 4]. It is well known that dysnatremias [hyponatremia ( $< 135$  mmol/L) and hypernatremia ( $> 145$  mmol/L)] can gently attack many physiological functional processes and organ systems [3-5]. Electrolyte immitigable hyponatremia is usually noticed in anaemic patients ( $131.42 \pm 0.82$  meq/L vs.  $135.57 \pm 0.42$  meq/L;  $p$ -value $<0.0001$ ) [6-8]. It is reported that 25% of the global population is anemic, touching around two billion people worldwide with mortality of nearly 800,000 per year [9]. Rise of Na<sup>+</sup> / potassium (K<sup>+</sup>) ATPase intercourse in anemic subjects loses for the mechanism of adapting of the subjects with low oxygen level and its physiological effects in the cell, switching in membrane-bound enzymes directly affects the K<sup>+</sup> and Na<sup>+</sup> in the serum [10, 11]. However, the association of SNa with anaemic patients is not clear. This can be assured based on the suitable probabilistic SNa models with anaemic patients along with the other anaemia disease describing variables/ factors. Similarly, examining the suitable probabilistic models of hemoglobin/ iron deficiency/ Vitamin B12 deficiency etc., on SNa along with the other anaemia disease describing variables/ factors, one can be assured about the associations of SNa with anaemia disease.

This editorial report note inquires the following research queries.

- Is there any correlation/ association of SNa with anaemic patients? For the affirmative case, what is the most suitable SNa relationship model with anaemic patients?

- How do we develop the most likely SNa relationship model with anaemic disease patients?
- What are the effects of SNa on anaemic disease patients?

These above pointed research hypotheses are searched herein based on real data of 299 heart patients with 13 factors, and the data set is reported in the two articles [12, 13] that can be seen in the site <https://archive.ics.uci.edu/ml/datasets/Heart+failure+clinical+records>, the current study considers these 13 covariates/factors, which are:

- Sex (0=female, 1=male),
- Smoking habit (SMH) (0=no smoking, 1= smoking),
- Age,
- Diabetes status (DIS) of subjects (0= no diabetes, 1= diabetes),
- Anaemia status (ANS) of subjects (0= no anaemia, 1= anaemia),
- Creatinine phosphokinase (CRP),
- Ejection fraction (EJF),
- High blood pressure (HBP) of subjects (0= normal BP, 1=high BP),
- Serum creatinine (SEC),
- Time up to the end of the follow-up period (TTF),
- Serum sodium (SNa),
- Platelets count (PLC)
- Death event (DEE) (0=alive, 1=death).

The present considered heart disease data set is a physiological, multivariate type, non-constant variance and non-normal data set. The response variable in the current study is SNa, which is a non-normal continuous heteroscedastic variable. The response (SNa) variance is not stabilized by any appropriate transformation, so it can be modeled by joint generalized linear models (JGLMs), which is well described in the book by Lee, Nelder and Pawitan [14]. The obtained JGL mean and variance SNa gamma fitted models are as follows.

Gamma fitted SNa mean ( $\hat{\mu}$ ) model is

$\hat{\mu} = \text{exp. } (4.91 + 0.01 \text{ ANS} + 0.01 \text{ PLC} - 0.01 \text{ PLC} * \text{ANS} - 0.01 \text{ DEE} + 0.02 \text{ ANS} * \text{DEE} + 0.02 \text{ EJF} - 0.02 \text{ DIS} + 0.01 \text{ SMH} + 0.03 \text{ EJF} * \text{HBP} - 0.02 \text{ HBP} - 0.01 \text{ CRP} * \text{HBP} + 0.01 \text{ CRP} - 0.02 \text{ TTF} - 0.01 \text{ CRP} * \text{SMH} + 0.01 \text{ AGE} * \text{TTF} - 0.03 \text{ SEC} + 0.02 \text{ AGE} - 0.01 \text{ AGE} * \text{PLC} - 0.01 \text{ AGE} * \text{CRP} + 0.02 \text{ AGE} * \text{SEC} + 0.04 \text{ SEX} + 0.01 \text{ CRP} * \text{TTF} + 0.03 \text{ EJF} * \text{SEC} - 0.07 \text{ AGE} * \text{SEX} - 0.01 \text{ EJF} * \text{PLC})$ , and

The fitted SNa variance ( $\hat{\sigma}^2$ ) model is

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

The associations of SNa with anaemic subjects (ANS (0= no anaemia, 1= anaemia)) along with the other factors are presented by the above two mean ( $\hat{\mu}$ ) and variance ( $\hat{\sigma}^2$ ) equations of SNa. Here the response variable SNa is continuous, while the anaemia disease status (ANS) (0= no anaemia, 1= anaemia) is the only explanatory attribute factor related to anaemia disease, along with some other factors treated as the explanatory variables. Note that there are no extra variables/ factors related to anaemia disease such as hemoglobin/ iron deficiency/ Vitamin B12 deficiency etc. So, the present study focuses the associations of SNa with only anaemia disease status (ANS) from the above mean and variance equations of SNa.

From the above mean model, it is derived that mean SNa levels are partially inversely associated with the joint interaction effects of platelets count (PLC) and anaemia disease status (ANS) i.e. PLC\*ANS (P=0.11), while it is directly related with both the marginal effects PLC (P<0.01) (significantly) and ANS (P=0.11) (partially). This association indicates that the mean SNa levels are higher for non-anaemic subjects with higher PLC levels than anaemic subjects with lower PLC levels. Also, mean SNa levels are significantly directly related with PLC (P<0.01) levels, which implies that SNa levels increase as PLC levels increase. This is seen in practice. Again, mean SNa levels are partially directly related with ANS (0= no anaemia, 1= anaemia) (P=0.11), which can be treated as a confounder in the mean model. Note that in Epidemiology, partially significant effects are treated as a confounder.

Mean SNa is directly related with the joint interaction effects of ANS and death event (DEE) (0=alive, 1=death) i.e., ANS\*DEE (P<0.01), while it is inversely related with the marginal effect DEE (0=alive, 1=death) (P<0.01) and partially directly related with ANS (P=0.11). This indicates that mean SNa levels increase as the joint effect ANS\*DEE rises. Again, mean SNa levels are inversely related with the marginal effect DEE (survive =0, or died =1) (P=0.0001) that implies that mean SNa levels are higher for surviving study units than dead units.

Variance of SNa levels is directly related with the joint interaction effects of AGE and ANS i.e. AGE\*ANS (P=0.05), while it is partially directly related with the marginal effect AGE

(P=0.09) and inversely with ANS (0= no anaemia, 1= anaemia) (P=0.06). This indicates that SNa levels are more scattered for anaemic patients at older ages than non- anaemic study units at younger ages. Also, variance of SNa levels is partially inversely related with the marginal effect ANS (P=0.06), indicating that SNa levels are more scattered for non-anaemic study units than anaemic subjects without considering ages. Also, the factor AGE (P=0.09) is considered as a confounder in the variance model that indicates that SNa levels are more scattered at older ages than younger without considering the effects of ANS.

In the current editorial note, it is observed that mean SNa is related with the joint effects PLC\*ANS and ANS\*DEE, and also their marginal effects PLC, DEE, ANS. Again, variance of SNa is related with the joint effect AGE\*ANS and their marginal effects AGE and ANS. The associations of anaemic factors such as hemoglobin/ iron deficiency/ Vitamin B12 deficiency etc. are not discussed herein. The complete report along with all details results/ analysis will be submitted soon. The above findings of the mean and variance models are completely new in the anaemia disease literature. It is found that SNa has some complicated effects on anaemic patients. The medical treatment systems / research approaches should care on the SNa levels of the anaemic patients.

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### Conflict of interest

The authors confirm that this article content has no conflict of interest.

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