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Creatinine ratio's association with HbA1c and Lipid profile parameters

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ABSTRACT

Objectives: This study tries to find the associations of Creatinine ratio (Cr) with HbA1c and lipid profile parameters based on a real dataset.

Materials & Methods: A real data set has been considered with 1000 individuals, this data set can be found at https://data.mendeley.com/datasets/wj9rwkp9c2/1. Using statistical joint generalized linear models, the creatinine ratio probabilistic model has been derived.

Results: From the fitted Log-normal model, the mean Cr is positively associated with Urea (P=0.0004) and is indifferent to HbA1c (P=0.9299), but it is positively associated with the joint interaction effect (JIE) of HbA1c and Urea, i.e., of HbA1c*Urea (P=0.0197). Mean Cr is indifferent to Chol (P=0.8158), while it is positively associated with the JIE of HbA1c*Chol (P=0.0001). Mean Cr is negatively associated with HDL (P=0.0417), TG (P=0.0045), the JIE of HbA1c*HDL (P<0.0001), and the JIE of HbA1c*TG (P=0.0030). Mean Cr is positively associated with the JIE HDL*Chol (P=0.0003). Mean Cr is indifferent to LDL (P=0.3080), while it is negatively associated with the JIE of Chol and LDL, i.e., of Chol*LDL (P=0.0240). Variance of Cr is positively associated with both the marginal effects BMI (P=0.0185) and Chol (P=0.0092), but it is negatively associated with the JIE of BMI*Chol (P=0.0079). Variance of Cr is positively associated with TG (P=0.0061) and Urea (P<0.0001).

Conclusions: On the basis of the above real data set, it is established that creatinine ratio maintains a complex relationship with HbA1c and lipid profile parameters along with their joint interaction effects.

KEYWORDS

Creatinine ratio (Cr), Hemoglobin A1c (HbA1c), Lipid profile parameters, joint generalized linear models (JGLMs).

Introduction

Kidney disease is a condition where the kidneys are not functioning properly and are losing their ability to function. One of the most early and important indicators of kidney function is urea to creatinine ratio (UCR). Generally, in a blood test report, high level of UCR is an initial indication that kidneys are not working optimally,

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probably this happens because of prerenal issues, such as, dehydration (low blood volume), heart failure, shock, or, kidney disease, or high protein intake. Besides that, low levels of UCR indicates liver disease, malnutrition/low protein intake, kidney conditions like rhabdomyolysis (muscle breakdown), overhydration, etc. Out of the other common markers of kidney disease, like albuminuria, estimated glomerular filtration rate (eGFR), Cystatin C, β-trace protein, kidney injury molecule-1 (KIM-1), etc., creatinine is widely used as an indicator that helps to detect and monitor the health of the kidneys. It is known that the amount of creatinine, a waste product that is produced during muscle tissue's normal breakdown, in the blood is determined by a blood test called serum creatinine.

Some studies indicated that low serum creatinine is a risk factor of type 2 diabetes [1–4]. For example, out of 8,570 non diabetic Japanese men aged 40-55 years, 877 men developed type 2 diabetes for lower levels of serum creatinine [1]. Article [2] mentioned for 2,676 non diabetic subjects aged 18 to 75 years, with stable and normal renal function shown that serum creatinine reflects body muscle mass, and a decrease in serum creatinine may be considered a risk factor for type 2 diabetes. Similarly, in a case of a chinese population, a study has been conducted among 201,298 individuals with age $\geq$ 20 years, 3,389 patients developed diabetes risk and indicated that lower serum creatinine is independently connected with rising risk of type 2 diabetes [3]. Based on 1,017 morbidly obese patients, a cross sectional study has been performed and established that lower levels of serum creatinine may be a predictor of type 2 diabetes [4]. Few articles based on diabetic nephropathy [5, 6], have shown their interest to find the relationship between renal function test parameters, most likely, serum urea and serum creatinine and blood glucose level in diabetic patients. Article [7] is based on a single-center cross-sectional study and observed the association between serum creatinine and lipid profile parameters like, total cholesterol, triglyceride, HDL, LDL, etc. for old age patient ($>$ 60 years old). Another study has been performed with 159 individuals having cardiovascular disease to determine the correlation between the parameters of lipid profile and renal function tests [8].

Article [9] is based on the association between blood urea nitrogen (BUN) to creatinine ratio and incident type 2 diabetes mellitus (T2DM) and observed that to identify and prevent the incident of T2DM, BUN to creatinine ratio (BCR) can be used as a valuable diagnostic tool for the individuals having varying degrees of renal dysfunction. For a group of 12,999 T2DM patients Liu F. et al. [10] established a positive association between BCR and risk of Coronary Artery Disease (CAD), also pointed out that BCR is an independent risk factor for CAD patient with T2DM. If Urea to creatinine ratio (UCR) is high for the patients who are hospitalized due to some infection, then it often indicates a long-term all cause mortality, but it can't be taken as an indicator of transient acute kidney injury (ACI) [11]. Peng R. et al. [12], shown that lower BCR implies high risk of total and ischemic stroke. Higher age female patients ($\geq$ 65 years) may have gastrointestinal tract bleeding, heart failure, ACI and lower serum albumin levels if they have high levels of UCR. Also, this study showed that elevated UCR level may ensure higher death rates within hospitals, readmission in hospital once again within 30-days or the patients need to stay in hospital for more days. In addition, they established that chronic kidney disease (CKD) patients who have already been admitted in hospital for treatment may experience poor clinical outcomes if their UCR level gets higher [13]. Article [14] clearly mentioned the distinction between blood urea nitrogen:creatinine ratio (BCR) and urea:creatinine ratio

(UCR), and discussed the association of BCR/UCR with gastrointestinal (GI) bleed, ACI, heart failure. BCR/UCR is higher for the individuals having an upper GI bleed than those who have a lower GI bleed [15–20]. Glomerular filtration rate (GFR), the best overall indicator of kidney function, measures how well the kidneys filter blood. In the case of AKI, reduction of GFR levels is sometimes an indication of increasing levels of BCR/UCR [14]. The association of UCR and malnutrition identified by [21] and shown that UCR increased with worse nutritional state, also UCR can be used as a marker of malnutrition. Few articles have considered blood urea in terms of blood urea nitrogen (BUN) [22, 23]. Patients having Acute heart failure (AHF), may give higher attention to their blood urea/creatinine ratio (BUN/creatinine ratio) than BUN or creatinine alone. High levels of BUN/creatinine ratio is correlated with higher death rate for AHF patients [22]. For chronic ambulatory heart failure patients urea to creatinine ratio (BUN/creatinine ratio) is highly connected with declines in eGFR [23]. Insufficient protein consumption, reduced urea synthesis (indication of liver problem), increased urinary urea excretion, rhabdomyolysis, etc., can happen due to low BUN/creatinine ratio [24].

The earlier studies use simple correlation, regression analysis and machine learning etc, to establish their claim. Exact model selection criterion or any appropriate model diagnostics are not clearly discussed in their study to validate their results. So, this may lead to some doubts and debates. The current report aims to find the following research hypothesis on the basis of an appropriate probabilistic modeling.

- Is there any association of blood urea to creatinine ratio (UCR or, simply Cr) with HbA1c and lipid profile parameters, such as, cholesterol, Triglycerides, HDL, LDL, VLDL, and other biochemical factors/variables for diabetic patients?
- What is the way to develop the most probable Cr relationship model?
- What are the effects of Cr on the diabetic patients and other explanatory factors?

To find the answers of the above hypotheses, the following sections of this article are classified as - materials and methods, statistical analysis and results, discussions, and conclusions. The blood urea to creatinine ratio (Cr) probabilistic model is shown in Table 1 on the basis of a real data set, discussed in the materials section. The probabilistic Cr mean and dispersion models are developed by joint generalized linear models (JGLMs), described in the methods section. The obtained outcomes of Cr analysis are presented in the results section, and these outcomes are clearly illustrated in the discussions section. Depending on the derived Cr mean and variance models, the current report has earned some information, which are presented in the conclusions section.

Materials & Methods

Materials

The Cr probabilistic model is obtained herein from a data set containing 1000 observations (including 565 male and 435 female) collected from the laboratory of Medical City Hospital and (the Specializes Center for Endocrinology and Diabetes-Al-Kindy Teaching Hospital) [25]. The data set can be found in the

site (https://data.mendeley.com/datasets/wj9rwkp9c2/1). Some articles have been already published on this data set, interested researchers are requested to read these for detailed description [26, 27].

The present study considers 12 interested characters out of which 10 are continuous variables, and the rest 2 are attributes. The 10 continuous variables are Age (AGE), Urea, Creatinine ratio (Cr), HbA1c, Cholesterol (Chol), Triglycerides (TG), HDL, LDL, VLDL, and BMI, while the other 2 attribute characters are the subject's Gender (1=Male, 2=Female), CLASS (1=Non-Diabetic, 2=Predict-Diabetic & Diabetic). This study contained 103 non-diabetic and 897 predict-diabetic & diabetic individuals out of 1000 individuals.

Blood urea test measures the whole urea molecule in blood, whereas blood urea nitrogen (BUN) test measures the nitrogen content of urea in the blood [24]. In this study, the aimed response, creatinine ratio is considered as blood urea to creatinine ratio (or urea/creatinine ratio, or urea:creatinine ratio, or UCR), simply denoted by Cr, since it is not clearly defined in the dataset [25], whether Cr is a blood sample or urine sample. It is also noted that both UCR and BUN/creatinine ratio (BCR) represents the relationship between urea and creatinine levels in blood. HbA1c or Hemoglobin A1c, a valuable marker of diabetes. HbA1c blood test indicates the average blood sugar (glucose) levels for the last 2-3 months [28]. For more information about the significance of HbA1c, readers are requested to read the articles [29–31]. Lipid profile test, a fasting blood test, measures the various kinds of lipids or fats (such as, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, VLDL cholesterol, Non-HDL cholesterol). Usually, this test is very much necessary to check the risk of developing heart attacks, strokes and other cardiovascular diseases [32, 33].

Methods

The aimed response random variable in this current study is creatinine ratio (Cr), which is to be modeled with the HbA1c, lipid profile parameters, and the remaining variables/factors. It is observed that the response Cr is heteroscedastic and non-normally distributed random variable. As a result, it is not possible to stabilize the variance of Cr with any suitable transformation, and this is the ideal situation to model it using joint generalized linear models (JGLMs) under both Log-normal and Gamma distribution [34–37]. For more details about JGLMs, interested readers may go through the book of Lee, Nelder and Pawitan [34]. JGLMs under both the Log-normal and Gamma distribution are briefly given herein.

JGLMs for Log-normal distribution:

For the positive response $\mathbf{Y}_{\mathrm{i}}$(=Cr) with E($\mathbf{Y}_{\mathrm{i}}$ = Cr)= μ_{i} (mean) and Var($\mathbf{Y}_{\mathrm{i}}$ = Cr)= $\boldsymbol{\sigma}_{\mathrm{i}}^2$ μ_{i}^2 = $\boldsymbol{\sigma}_{\mathrm{i}}^2$ $\boldsymbol{V}(\mu_{\mathrm{i}})$ say, where $\boldsymbol{\sigma}_{\mathrm{i}}^2$'s are dispersion parameters, and $\boldsymbol{V}(.)$ reveals the variance function. To stabilized the variance Var($\mathbf{Z}_{\mathrm{i}}$) $\approx$ $\boldsymbol{\sigma}_{\mathrm{i}}^2$, usually, the log transformation $\mathbf{Z}_{\mathrm{i}}$ = log ($\mathbf{Y}_{\mathrm{i}}$=Cr) is applied. But the variance may not always be stabilized [37]. For developing an improved model, JGLMs for the mean and dispersion are considered. For the response Cr, assuming Log-normal distribution, JGL mean and dispersion models (with $\mathbf{Z}_{\mathrm{i}}$ = log ($\mathbf{Y}_{\mathrm{i}}$ = Cr)) are as follows:

E($\mathbf{Z}_{\mathrm{i}}$) = μ_{zi} and Var($\mathbf{Z}_{\mathrm{i}}$) = $\boldsymbol{\sigma}_{\mathrm{zi}}^2$,

$\mu_{zi} = \mathbf{x}_i^t\ \boldsymbol{\beta}$, and $\log(\boldsymbol{\sigma}_{zi}^2) = \mathbf{g}_i^t\ \boldsymbol{\gamma}$,

$\mathbf{x}_i^t\ \boldsymbol{\beta}$ and $\mathbf{g}_i^t\ \boldsymbol{\gamma}$ are the explanatory variables/factors vectors of Cr connected with the mean regression coefficients and dispersion regression coefficients $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$, respectively.

JGLMs for Gamma distribution:

For the above stated $\mathbf{Y}_i$'s(=Cr), the variance has two components such as $\boldsymbol{V}(\mu_i)$ (depends on the mean parameters) and $\boldsymbol{\sigma}_i^2$ (independent of μ_i's). The variance function $\boldsymbol{V}(.)$ reveals the GLM family distributions. For example, if $\boldsymbol{V}(\mu) = \mu$, it is Poisson, gamma if $\boldsymbol{V}(\mu) = \mu^2$, and normal if $\boldsymbol{V}(\mu) = 1$ etc. Gamma JGLMs means and dispersion models of Cr are as follows:

$\boldsymbol{\eta}_i = g(\boldsymbol{\mu}_i) = \mathbf{x}_i^t\ \boldsymbol{\beta}$ and $\boldsymbol{\epsilon}_i = h(\boldsymbol{\sigma}_i^{\boldsymbol{2}}) = \mathbf{w}_i^t\ \boldsymbol{\gamma}$,

where g(.) and h(.) are the GLM link functions connected for the mean and dispersion linear predictors respectively, and $\mathbf{x}_i^t\ \boldsymbol{\beta}$ and $\mathbf{w}_i^t\ \boldsymbol{\gamma}$, are the explanatory factor vectors of Cr attached with the mean and dispersion parameters respectively. To estimate the mean parameters, maximum likelihood (ML) method is applied, while the restricted ML (REML) method is used for estimating the dispersion parameters, which are clearly discussed in the book of Lee, Nelder and Pawitan [34].

Statistical Analysis & Results

Statistical Analysis

The response Cr is modeled by JGLMs with both the Log-normal and Gamma distributions. Here Cr is considered as the dependent (response) variable, and the remaining 11 variables/factors are considered as the Cr's explanatory variables. Final Cr model has been selected on the basis of the smallest Akaike information criterion (AIC) value (within each class), that reduces both the squared error loss and predicted additive errors [38, p. 203-204]. By following the AIC rule, JGLMs Log-normal fit (AIC = 8370.167) is better than gamma fit (AIC = 8388.329).

Some partially significant effects such as AGE*HbA1c (P=0.1553) (for Gamma fit P=0.1088), AGE*Chol (P=0.0764) (for Gamma fit P=0.0673), TG*Gender 2 (P=0.0636) (for Gamma fit P=0.0519), AGE*Gender 2 (P=0.1239) (for Gamma fit P=0.1135), Urea*VLDL (P=0.1352) (for Gamma fit P=0.0698) are added in the selected Log-normal mean model (Table 1). The partially significant effects ($< 16\%$) are termed as confounders in Epidemiology, and they are very much important in this field. Also some partial or insignificant effects are sometimes highly important for better fitting [39]. For this reason, TG*VLDL (P=0.1691) (for Gamma fit P=0.1875), AGE*VLDL (P=0.1648) (for Gamma fit P=0.4256), and TG*CLASS 2 (P=0.2009) (for Gamma fit P=0.0872) are included in the mean model. The other partial or insignificant effects such as AGE (P=0.7234), HbA1c (P=0.9299), Chol (P=0.8158) are included in the mean model due to Nelder's marginality rule [39], namely that, if an interaction effect (for example AGE*HbA1c) is significant or partially significant, so all its related lower-order effects (for example AGE, HbA1c) should be included in the model even insignificant. In both the fitted models there are many discrepancies

found, such as AIC values, values of the estimates, standard errors, P-values etc. [40]. Log-normal fitted models give better fit, and Table 1 carries the analysis results for both the models.

The derived Cr's probabilistic model (Table 1) is a data derived model. So, proper model checking tools are highly recommended to validate the model, and based on this data generated probabilistic model, all the valid interpretations are drawn. For the joint Log-normal fitted Cr models (Table 1), model verification graphical analysis is displayed in Figure 1. Figure 1 (a) presents the absolute residuals for the Log-normal fitted Cr model (Table 1) against the fitted values, which is almost a flat line, indicating that variance is constant with the running means. Figure 1 (b) displays the normal probability plot for the Log-normal fitted Cr mean model (Table 1) that does not show any lack of fit. These two Figures 1 (a) and 1 (b) do not show any Cr fitted model's (Table 1) discrepancy. From these two figures, it can be concluded that Log-normal Cr model fit is appropriate, and this can be taken as an approximation of the unknown Cr model.

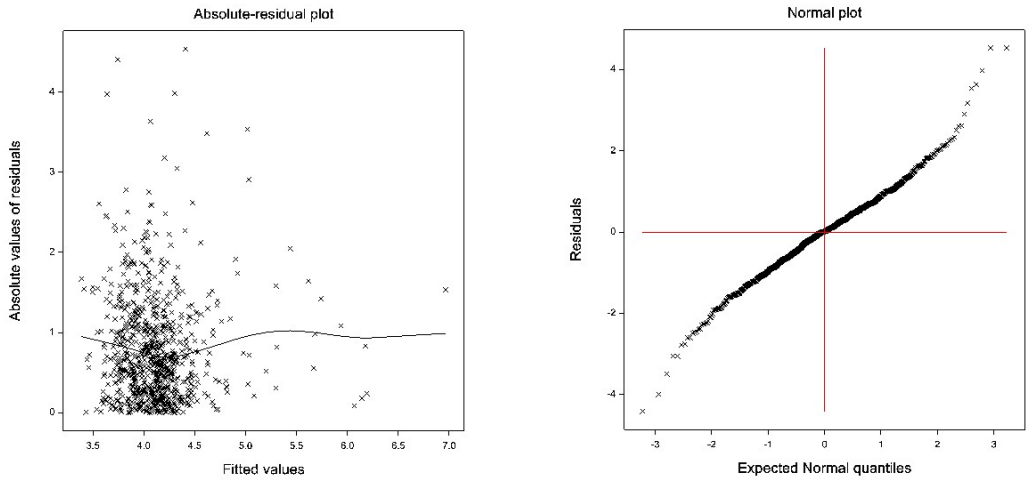

Figure 1 (a) Figure 1 (b)

Figure 1. For the joint Log-normal fitted models of Creatinine ratio (Cr) (Table 1), the (a) absolute residuals plot with the fitted values, and (b) the normal probability plot for the mean model

Results

Based on the AIC criterion, the Log-normal fitted model is better than the Gamma fit. The derived Cr mean model shows that mean Cr is positively associated with Urea (P=0.0004) and is indifferent to HbA1c (P=0.9299), while it is positively associated with their joint interaction effect (JIE), i.e., of HbA1c*Urea (P=0.0197). Mean Cr is indifferent to both the marginal effects HbA1c (P=0.9299) and Chol (P=0.8158), while it is positively associated with the JIE of HbA1c*Chol (P=0.0001). Mean Cr is negatively associated with HDL (P=0.0417) and the JIE of HbA1c*HDL (P<0.0001). Again, mean Cr is negatively associated with TG (P=0.0045) and the JIE of HbA1c*TG (P=0.0030). Mean Cr is indifferent to both the marginal effects AGE (P=0.7234) and HbA1c (P=0.9299), while it is partially negatively associated

with their JIE of AGE*HbA1c (P=0.1553). Mean Cr is negatively associated with TG (P=0.0045) and positively associated with the subject's CLASS (1=Non-Diabetic, 2=Predict-Diabetic & Diabetic) (P=0.0151), while it is positively associated with their JIE, i.e., of TG*CLASS 2 (P=0.2009) (partially) and it is negatively associated with the JIE of AGE*CLASS 2 (P=0.0030).

Mean Cr is negatively associated with HDL (P=0.0417) and indifferent to Chol (P=0.8158), while it is positively associated with their JIE, i.e., of HDL*Chol (P=0.0003). Mean Cr is indifferent to both the marginal effects LDL (P=0.3080) and Chol (P=0.8158), while it is negatively associated with the JIE of Chol*LDL (P=0.0240). Mean Cr is positively associated with Urea (P=0.0004), while it is negatively associated with the JIE of Urea*Chol (P=0.0980) (partially). Mean Cr is indifferent to both the marginal effects AGE (P=0.7234) and Chol (P=0.8158), while it is partially negatively associated with the JIE of AGE*Chol (P=0.0764).

Mean Cr is negatively associated with both the marginal effects HDL (P=0.0417) and TG (P=0.0045), while it is positively associated with their JIE, i.e., of HDL*TG (P=0.0001). Mean Cr is negatively associated with TG (P=0.0045) and indifferent to LDL (P=0.3080), while it is positively associated with their JIE LDL*TG (P=0.0003). Mean Cr is positively associated with VLDL (P=0.0001), while it is partially negatively associated with the JIE TG*VLDL (P=0.1691). Mean Cr is negatively associated with BMI (P=0.0001) and TG (P=0.0045), while it is positively associated with the JIE of BMI*TG (P=0.0371). Mean Cr is negatively associated with TG (P=0.0045), the subject's Gender (1=Male, 2=Female) (P=0.0006) and their JIE, TG*Gender 2 (P=0.0636) (partially).

Mean Cr is negatively associated with HDL (P=0.0417) and indifferent to AGE (P=0.7234), while it is positively associated with their JIE, i.e., of AGE*HDL (P=0.0456). Mean Cr is positively associated with VLDL (P=0.0001) and indifferent to AGE (P=0.7234), while it is partially negatively associated with their JIE AGE*VLDL (P=0.1648). Mean Cr is positively associated with both the marginal effects VLDL (P=0.0001) and Urea (P=0.0004), while it is partially negatively associated with the JIE of Urea*VLDL (P=0.1352).

Mean Cr is positively associated with Urea (P=0.0004) and negatively associated with the subject's Gender (P=0.0006), while it is positively associated with their JIE, i.e., of Urea*Gender 2 (P=0.0164). Mean Cr is indifferent to AGE (P=0.7234) and negatively associated with the subject's Gender (P=0.0006), while it is partially positively associated with the JIE of AGE*Gender 2 (P=0.1239). Mean Cr is negatively associated with BMI (P=0.0001) and indifferent to AGE (P=0.7234), while it is positively associated with their JIE, AGE*BMI (P=0.0012).

Variance of Cr is negatively associated with both the marginal effects AGE (P=0.0018) and the subject's CLASS (1=Non-Diabetic, 2=Predict-Diabetic & Diabetic) (P<0.0001), while it is positively associated with the JIE of AGE*CLASS 2 (P=0.0055). Variance of Cr is negatively associated with VLDL (P=0.0048) and the subject's CLASS (P<0.0001), while it is positively associated with their JIE, i.e., of VLDL*CLASS 2 (P=0.0447).

Variance of Cr is positively associated with both the marginal effects BMI

(P=0.0185) and Chol (P=0.0092), while it is negatively associated with the JIE of BMI*Chol (P=0.0079). Variance of Cr is negatively associated with VLDL (P=0.0048) and HDL (P=0.0077), while it is positively associated with their JIE, VLDL*HDL (P=0.0015). Variance of Cr is negatively associated with AGE (P=0.0018) and HDL (P=0.0077), while it is positively associated with their JIE, i.e., of AGE*HDL (P=0.0228). Variance of Cr is positively associated with TG (P=0.0061) and Urea (P<0.0001).

Log-normal fitted Cr mean ($\hat{\mu}_{\mathbf{z}}$) model (Table 1) is $\hat{\mu}_{\mathbf{z}}$= 4.5232 – 0.3997 Gender 2 – 0.0021 AGE – 0.0026 HbA1c – 0.0007 Age*HbA1c – 0.0441 BMI + 0.0007 AGE*BMI + 0.0828 Urea + 0.0053 HbA1c*Urea – 0.2183 HDL – 0.0111 Chol + 0.0114 HbA1c*Chol – 0.0268 HbA1c*HDL + 0.0262 LDL + 0.0273 HDL*Chol – 0.1608 TG + 0.0561 HDL*TG + 0.0234 LDL*TG – 0.0014 AGE*Chol – 0.0090 Chol*LDL + 0.0227 Urea*Gender 2 – 0.0258 TG*Gender 2 + 0.0032 AGE*Gender 2 + 0.0043 AGE*HDL + 0.4432 CLASS 2 – 0.0107 AGE*CLASS 2 – 0.0060 Urea*Chol + 0.0037 BMI*TG – 0.0097 HbA1c*TG + 0.0421 VLDL – 0.0022 TG*VLDL – 0.0003 AGE*VLDL – 0.0026 Urea*VLDL + 0.0539 TG*CLASS 2, and fitted Cr variance ($\hat{\boldsymbol{\sigma}}^2_{\mathbf{z}}$) model is $\hat{\boldsymbol{\sigma}}^2_{\mathbf{z}}$= exp.(–1.41 + 0.1226 Urea – 0.685 VLDL – 3.483 CLASS 2 + 0.0997 TG – 0.0672 AGE – 1.801 HDL + 0.0279 AGE*HDL + 0.0900 BMI + 0.570 Chol – 0.0193 BMI*Chol + 0.2041 VLDL*HDL + 0.0484 AGE*CLASS 2 + 0.463 VLDL*CLASS 2).

From the above Cr mean ($\hat{\mu}_{\mathbf{z}}$) and variance ($\hat{\boldsymbol{\sigma}}^2_{\mathbf{z}}$) models, it is noted that mean Cr is expressed by Gender, AGE, HbA1c, Age*HbA1c, BMI, AGE*BMI, Urea, HbA1c*Urea, HDL, Chol, HbA1c*Chol, HbA1c*HDL, LDL, HDL*Chol, TG, HDL*TG, LDL*TG, AGE*Chol, Chol*LDL, Urea*Gender, TG*Gender, AGE*Gender, AGE*HDL, CLASS, AGE*CLASS, Urea*Chol, BMI*TG, HbA1c*TG, VLDL, TG*VLDL, AGE*VLDL, Urea*VLDL, and TG*CLASS, while the Cr's variance is expressed by Urea, VLDL, CLASS, TG, AGE, HDL, AGE*HDL, BMI, Chol, BMI*Chol, VLDL*HDL, AGE*CLASS, and VLDL*CLASS.

Discussions

Table 1 represents the Cr analysis outcomes for Log-normal and Gamma fitted models. The Log-normal fitted Cr mean and variance models are displayed above. Some discrepancies are identified between the fitted Log-normal and Gamma models, which are clearly discussed in [40]. Note that the considered data set contains two diabetes disease factors/parameters such as HbA1c and CLASS (1=Non-Diabetic, 2=Predict-Diabetic & Diabetic). Also, it contains several parameters related to lipid profile, which are Chol, TG, HDL, LDL, VLDL. The given data set is a multivariate form. So, a simple correlation study is not enough to find the relationship. Again, since the data set is heteroscedastic, multiple regression analysis is not a suitable method. Herein, appropriate data analysis models (Log-normal and Gamma) are derived. Depending on the derived models, creatinine ratio's association with HbA1c and the parameters of lipid profile are discussed.

From the Cr fitted mean Log-normal model (Table 1), it is derived that mean Cr is positively associated with Urea (P=0.0004) and is indifferent to HbA1c (P=0.9299), while it is positively associated with their joint interaction effect (JIE) of HbA1c*Urea (P=0.0197). This indicates that Cr levels increase as the joint effect of Urea and

HbA1c, i.e, HbA1c*Urea increases. The marginal effects Urea and HbA1c are unimportant as their joint effect HbA1c*Urea is significant. It shows that Cr is associated with Urea along with HbA1c and HbA1c*Urea. Again, mean Cr is indifferent to both the marginal effects HbA1c (P=0.9299) and Chol (P=0.8158), while it is positively associated with their JIE of HbA1c*Chol (P=0.0001). This means that Cr levels increase as the joint effect of HbA1c and Chol, i.e., HbA1c*Chol increases. Also, mean Cr is negatively associated with HDL (P=0.0417) and indifferent to HbA1c (P=0.9299), but it is negatively associated with their JIE of HbA1c*HDL (P<0.0001). It implies that Cr levels increase as the joint effect HbA1c*HDL decreases. Mean Cr is indifferent to HbA1c (P=0.9299) while it is negatively associated with TG (P=0.0045), and their JIE of HbA1c*TG (P=0.0030). This shows that the levels of Cr increase as the joint effect HbA1c*TG decreases. Again, mean Cr is indifferent to both the marginal effects AGE (P=0.7234) and HbA1c (P=0.9299), while it is negatively associated with their JIE, i.e., of AGE*HbA1c (P=0.1553) (partially). This implies that Cr levels may not be higher for the old age patients having high levels of HbA1c. This indicates that Cr levels increase as the joint effect of AGE and HbA1c, i.e., AGE*HbA1c decreases.

Again, mean Cr is negatively associated with TG (P=0.0045) and positively associated with the subject's CLASS (1=Non-Diabetic, 2=Predict-Diabetic & Diabetic) (P=0.0151), while it is positively associated with their JIE of TG*CLASS 2 (P=0.2009) (partially). This means that Cr level may be higher for the Predict-Diabetic and Diabetic patients who have high levels of TG. Mean Cr is indifferent to AGE (P=0.7234), but it is negatively associated with the JIE of AGE and CLASS, i.e., AGE*CLASS 2 (P=0.0030). It shows that old age Predict-Diabetic and Diabetic patients may have lower Cr levels. From the derived Cr variance model (Table 1), it is observed that variance of Cr is negatively associated with both the marginal effects AGE (P=0.0018) and the subject's CLASS (1=Non-Diabetic, 2=Predict-Diabetic & Diabetic) (P<0.0001), while it is positively associated with their JIE of AGE*CLASS 2 (P=0.0055). It implies that Cr level's scatteredness increases for the old age Predict-Diabetic and Diabetic patients. Also, the variance of Cr is negatively associated with VLDL (P=0.0048), while it is positively associated with the JIE of VLDL and CLASS, i.e., VLDL*CLASS 2 (P=0.0447). It means that Cr levels are highly scattered for Predict-Diabetic and Diabetic patients with higher VLDL levels than Non-Diabetic patients with lower VLDL levels.

From the Cr fitted mean Log-normal model (Table 1), it is derived that mean Cr is negatively associated with HDL (P=0.0417) and indifferent to Chol (P=0.8158), while it is positively associated with their JIE of HDL*Chol (P=0.0003). This shows that Cr levels increase as the joint effect HDL*Chol increases. Again, mean Cr is indifferent to LDL (P=0.3080), while it is negatively associated with the JIE of Chol and LDL, i.e., Chol*LDL (P=0.0240). This indicates that Cr levels increase as the joint effect Chol*LDL decreases. Also, mean Cr is positively associated with Urea (P=0.0004), but it is partially negatively associated with the JIE of Urea*Chol (P=0.0980). This means that Cr levels may increase as the joint effect Urea*Chol decreases. Mean Cr is indifferent to both the marginal effects AGE (P=0.7234) and Chol (P=0.8158), but it is negatively associated with their JIE, i.e., of AGE*Chol (P=0.0764) (partially). It implies that old age patients along with high levels of Chol may have lower levels of Cr. This indicates that Cr levels may increase as the joint effect AGE*Chol decreases. Variance of Cr is positively associated with both

the marginal effects BMI (P=0.0185) and Chol (P=0.0092), while it is negatively associated with the JIE of BMI*Chol (P=0.0079). This means that scatteredness of Cr levels increases as the joint effect BMI*Chol decreases.

From the Cr fitted mean Log-normal model (Table 1), it is derived that mean Cr is negatively associated with both the marginal effects HDL (P=0.0417) and TG (P=0.0045), while it is positively associated with their JIE of HDL*TG (P=0.0001). It indicates that the levels of Cr increase as the joint effect HDL*TG increases. Also, mean Cr is indifferent to LDL (P=0.3080), but it is positively associated with the JIE of LDL and TG, i.e., LDL*TG (P=0.0003). It implies that the levels of Cr increase as the joint effect LDL*TG increases. Again, Mean Cr is positively associated with VLDL (P=0.0001), while it is negatively associated with the JIE of TG and VLDL, i.e., TG*VLDL (P=0.1691) (partially). It means that the levels of Cr may increase as the joint effect TG*VLDL decreases. Mean Cr is negatively associated with BMI (P=0.0001), while it is positively associated with the JIE of BMI and TG, i.e., BMI*TG (P=0.0371). It indicates that the levels of Cr increase as the joint effect BMI*TG increases. Mean Cr is negatively associated with the subject's Gender (1=Male, 2=Female) (P=0.0006) and the JIE of TG and Gender 2, i.e., TG*Gender 2 (P=0.0636) (partially). This implies that Cr levels are higher for male patients with lower levels of TG than female patients with higher levels of TG. Variance of Cr is positively associated with TG (P=0.0061), indicating that Cr level's scatteredness increases as the level of TG increases.

From the Cr fitted mean Log-normal model (Table 1), it is derived that mean Cr is negatively associated with HDL (P=0.0417) and indifferent to AGE (P=0.7234), but it is positively associated with their JIE of AGE*HDL (P=0.0456). This shows that Cr levels increase as the joint effect of AGE and HDL, i.e., AGE*HDL increases. This implies that old age patients along with high levels of HDL may have high levels of Cr. Also, from the fitted variance model, it is observed that variance of Cr is negatively associated with AGE (P=0.0018) and HDL (P=0.0077), while it is positively associated with their JIE of AGE*HDL (P=0.0228). This indicates that scatteredness of Cr levels increase as the joint effect AGE*HDL increases. Again, mean Cr is positively associated with VLDL (P=0.0001), while it is negatively associated with the JIE of AGE and VLDL, i.e., AGE*VLDL (P=0.1648) (partially). This means that Cr levels increase as the joint effect AGE*VLDL decreases, implying that Cr levels may lower for the old age patients with high levels of VLDL. Mean Cr is positively associated with both the marginal effects VLDL (P=0.0001) and Urea (P=0.0004), while it is negatively associated with the JIE of Urea*VLDL (P=0.1352) (partially). It indicates that Cr levels may increase as the joint effect Urea*VLDL decreases. Also, variance of Cr is negatively associated with VLDL (P=0.0048) and HDL (P=0.0077), while it is positively associated with their JIE of VLDL*HDL (P=0.0015). This indicates that scatteredness of Cr levels increases as the joint effect VLDL*HDL increases.

In addition, there are some factors except HbA1c and lipid profile parameters are also connected with the mean and variance of Cr levels. Mean Cr is positively associated with Urea (P=0.0004) and negatively associated with the subject's Gender (1=Male, 2=Female) (P=0.0006), while it is positively associated with their JIE of Urea*Gender 2 (P=0.0164). It means that Cr levels are higher for the female patients along with high Urea levels than male patients with low levels of Urea. Also, variance of Cr is positively associated with Urea (P<0.0001), indicating that Cr level's scat-

teredness increases as the levels of Urea increases. Again, it is observed that mean Cr is indifferent to AGE (P=0.7234) and negatively associated with the subject's Gender (P=0.0006), while it is positively associated with their JIE of AGE*Gender 2 (P=0.1239) (partially). This indicates that Cr levels are higher for the old age female patients than young male patients. Also, Mean Cr is negatively associated with BMI (P=0.0001), while it is positively associated with the JIE of AGE and BMI, i.e., AGE*BMI (P=0.0012). This implies that Cr level increases as the joint effect AGE*BMI increases, that means old age patients with high BMI levels may have high levels of Cr.

Conclusions

This report tries to develop the relationships of Cr with HbA1c, lipid profile parameters, age, gender, urea, and bmi for the normal and diabetic patients based on a real dataset with 1000 individuals with appropriate statistical joint modeling. The fitted Cr probabilistic model has been selected after comparing the AIC values of fitted Log-normal and Gamma JGLMs, small standard error of the estimates (Table 1) and model diagnostic plots. Some clear discrepancies are located from Table 1. So, researchers should give high attention to model selection.

It is seen that fitted Log-normal model is better than Gamma model fit depending on AIC rule and using the appropriate Log-normal fitted Cr probabilistic model, the above interpretations are presented in the discussions section. The obtained outputs based on this probabilistic model with different patients and factors though not fully conclusive, but revealing. Advanced statistical modeling along with appropriate model diagnostics are used to find all the outputs, so these are very much valid for all similar kinds of data sets. The findings will be helpful for common people, doctors and researchers. This data set [25] does not contain any information about kidney patients and other markers of diabetes, kidney disease and cardiovascular disease. Future researchers may give attention to such parameters for better studies. So, it is expected that the outcomes of this study may give good direction in the field of treatment system and research area for the society.

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Model	Covariates	LOG-NORMAL FIT				GAMMA FIT			
		estimate	*s.e.*	$t(966)$	P-value	estimate	*s.e.*	$t(966)$	P-value
Mean	Constant	4.5232	0.3413	13.252	<0.0001	4.5709	0.3395	13.463	<0.0001
	Gender 2	-0.3997	0.1154	-3.462	0.0006	-0.3492	0.1151	-3.035	0.0025
	AGE	-0.0021	0.0060	-0.354	0.7234	-0.0037	0.0060	-0.618	0.5367
	HbA1c	-0.0026	0.0298	-0.088	0.9299	0.0132	0.0296	0.446	0.6557
	AGE*HbA1c	-0.0007	0.0005	-1.422	0.1553	-0.0008	0.0005	-1.605	0.1088
	BMI	-0.0441	0.0110	-3.994	0.0001	-0.0419	0.0111	-3.778	0.0002
	AGE*BMI	0.0007	0.0002	3.247	0.0012	0.0006	0.0002	3.084	0.0021
	Urea	0.0828	0.0234	3.539	0.0004	0.0985	0.0229	4.296	<0.0001
	HbA1c*Urea	0.0053	0.0023	2.335	0.0197	0.0042	0.0022	1.879	0.0605
	HDL	-0.2183	0.1071	-2.039	0.0417	-0.2905	0.1041	-2.791	0.0054
	Chol	-0.0111	0.0478	-0.233	0.8158	-0.0174	0.0471	-0.369	0.7122
	HbA1c*Chol	0.0114	0.0029	3.926	0.0001	0.0118	0.0029	4.053	0.0001
	HbA1c*HDL	-0.0268	0.0059	-4.560	<0.0001	-0.0290	0.0059	-4.891	<0.0001
	LDL	0.0262	0.0257	1.020	0.3080	0.0268	0.0255	1.051	0.2935
	HDL*Chol	0.0273	0.0075	3.659	0.0003	0.0303	0.0075	4.027	0.0001
	TG	-0.1608	0.0565	-2.847	0.0045	-0.1649	0.0545	-3.022	0.0026
	HDL*TG	0.0561	0.0138	4.066	0.0001	0.0668	0.0137	4.859	<0.0001
	LDL*TG	0.0234	0.0064	3.671	0.0003	0.0273	0.0062	4.435	<0.0001
	AGE*Chol	-0.0014	0.0008	-1.774	0.0764	-0.0015	0.0008	-1.832	0.0673
	Chol*LDL	-0.0090	0.0040	-2.260	0.0240	-0.0106	0.0039	-2.719	0.0067
	Urea*Gender 2	0.0227	0.0094	2.404	0.0164	0.0109	0.0094	1.169	0.2427
	TG*Gender 2	-0.0258	0.0139	-1.857	0.0636	-0.0263	0.0135	-1.946	0.0519
	AGE*Gender 2	0.0032	0.0021	1.540	0.1239	0.0033	0.0021	1.584	0.1135
	AGE*HDL	0.0043	0.0021	2.002	0.0456	0.0052	0.0021	2.461	0.0140
	CLASS 2	0.4432	0.1821	2.434	0.0151	0.2943	0.1812	1.624	0.1047
	AGE*CLASS 2	-0.0107	0.0036	-2.975	0.0030	-0.0085	0.0036	-2.359	0.0185
	Urea*Chol	-0.0060	0.0036	-1.656	0.0980	-0.0050	0.0036	-1.401	0.1615
	BMI*TG	0.0037	0.0017	2.087	0.0371	0.0035	0.0017	2.026	0.0430
	HbA1c*TG	-0.0097	0.0033	-2.977	0.0030	-0.0125	0.0032	-3.856	0.0001
	VLDL	0.0421	0.0105	4.024	0.0001	0.0346	0.0100	3.471	0.0005
	TG*VLDL	-0.0022	0.0016	-1.376	0.1691	-0.0020	0.0015	-1.319	0.1875
	AGE*VLDL	-0.0003	0.0002	-1.390	0.1648	-0.0002	0.0002	-0.797	0.4256
	Urea*VLDL	-0.0026	0.0017	-1.495	0.1352	-0.0030	0.0017	-1.815	0.0698
	TG*CLASS 2	0.0539	0.0421	1.280	0.2009	0.0691	0.0404	1.712	0.0872
Dispersion	Constant	-1.41	1.60	-0.88	0.3791	-2.84	1.59	-1.79	0.0738
	Urea	0.1226	0.0157	7.82	<0.0001	0.1155	0.0150	7.70	<0.0001
	VLDL	-0.685	0.242	-2.83	0.0048	-0.684	0.242	-2.82	0.0049
	CLASS 2	-3.483	0.826	-4.22	<0.0001	-2.679	0.814	-3.29	0.0010
	TG	0.0997	0.0363	2.75	0.0061	0.0808	0.0361	2.24	0.0253
	AGE	-0.0672	0.0215	-3.13	0.0018	-0.0512	0.0212	-2.42	0.0157
	HDL	-1.801	0.675	-2.67	0.0077	-1.732	0.674	-2.57	0.0103
	AGE*HDL	0.0279	0.0122	2.28	0.0228	0.0263	0.0122	2.15	0.0318
	BMI	0.0900	0.0381	2.36	0.0185	0.1163	0.0378	3.08	0.0021
	Chol	0.570	0.219	2.61	0.0092	0.665	0.217	3.07	0.0022
	BMI*Chol	-0.0193	0.0073	-2.66	0.0079	-0.0231	0.0072	-3.20	0.0014
	VLDL*HDL	0.2041	0.0643	3.18	0.0015	0.2184	0.0640	3.41	0.0007
	AGE*CLASS 2	0.0484	0.0174	2.78	0.0055	0.0331	0.0172	1.93	0.0539
	VLDL*CLASS 2	0.463	0.231	2.01	0.0447	0.443	0.231	1.92	0.0552
AIC		8370.167				8388.329			

Table 1. Results for mean and dispersion models for Creatinine ratio (Cr) from Log-normal & Gamma fit.

References

[1] Harita N, Hayashi T, Sato KK, et al. (2009). Lower Serum Creatinine Is a New Risk Factor of Type 2 Diabetes. Diabetes Care, 32:424–426.

[2] Moon JS, et al. (2013). Variation in Serum Creatinine Level Is Correlated to Risk of Type 2 Diabetes. Endocrinol Metab, 28:207-213.

[3] Li R, et al. (2023). Association between serum creatinine and type 2 diabetes in the Chinese population: a retrospective cohort study. Scientific Reports, 13:6806.

[4] Hjelmesæth et al. (2010). Low serum creatinine is associated with type 2 diabetes in morbidly obese women and men: a cross-sectional study. BMC Endocrine Disorders, 10:6.

[5] Ullah W, Nazir A, Israr H, et al. (2023). Assessment of Serum Urea and Creatinine Levels in Diabetic Patients. BioScientific Review (BSR) Volume 5 Issue 3, ISSN(P): 2663-4198 ISSN(E): 2663-4201.

[6] Yosa D, Wibowo A (2019). Correlation between blood urea and creatinine level in patients with diabetes melitus at the ministry of marine and fishery clinic, Indonesia. The 6th International Conference on Public Health Best Western Premier Hotel, Solo, Indonesia, 576.

[7] Purwowiyoto SL, et al. (2022). Correlation Between Lipid Profile and Kidney Function in Ambulatory Heart Failure Patient. Mutiara Medika: Jurnal Kedokteran dan Kesehatan, Vol 22 No 1 Page 1-5.

[8] Baqi HR, Rostam SR K (2020). The Correlation Between Lipid Profile and Renal Function Tests in Patients with Cardiovascular Disease in Erbil city, Kurdistan Region of Iraq, Kurdistan. Journal of Applied Research, Volume 5, Issue 2, 52.

[9] Yin X, Wang Y, Jiang J, Zhong F, Zhang Q. (2024). Association of blood urea nitrogen to creatinine ratio with incident type 2 diabetes mellitus: A retrospective cohort study in the Chinese population. Medicine; 103:30(e39003).

[10] Liu F, et al. (2022). Elevated blood urea nitrogen-to-creatinine ratio increased the risk of Coronary Artery Disease in patients living with type 2 diabetes mellitus. BMC Endocrine Disorders 22:50.

[11] Slikke EC, Star BS, Jager VD, et al. (2020). A high urea-to-creatinine ratio predicts long-term mortality independent of acute kidney injury among patients hospitalized with an infection, www.nature.com/scientificreports/, 10:15649.

[12] Peng R, Liu K, Li W, et al. (2021). Blood urea nitrogen, blood urea nitrogen to creatinine ratio and incident stroke: The Dongfeng-Tongji cohort. Atherosclerosis, 333, 1–8.

[13] Brookes EM, Power DA (2022). Elevated serum urea-to-creatinine ratio is associated with adverse inpatient clinical outcomes in non-end stage chronic kidney disease, www.nature.com/scientificreports, 12:20827.

[14] Higgins C (2016). Urea and creatinine concentration, the urea:creatinine ratio, acutecaretesting.org, Radiometer Medical ApS, 2700 Brønshøj, Denmark.

[15] Snook JA et al. (1986). Value of a simple biochemical ratio in distinguishing upper and lower sites of gastrointestinal haemorrhage. Lancet; 1, 8489:1064-65.

[16] Felber S et al. (1988). The BUN/creatinine ratio in localizing gastrointestinal bleeding in pediatric patients. J Pediatr Gestroenterol Nutr; 7, 5: 685-87.

[17] Olsen LH et al. (1991). Stools containing altered blood- plasma urea: creatinine ratio as a simple test for the source of bleeding. Br J Surg; 78, 1: 71-73.

[18] Ernst AA et al. (1999). Usefulness of the blood urea nitrogen/ creatinine ratio in gastrointestinal bleeding. Am J Emerg Med; 17, 1: 70-72.

[19] Sittichanbuncha Y et al. (2013). How to differentiate sites of gastrointestinal bleeding in patients with hematochezia by using clinical factors? Gastroenterol Res Pract : 265076.

[20] Kim KS et al. (2015). Availability of blood urea nitrogen/ creatinine ratio in gastrointestinal bleeding with melena in children. Pediatr Gastroenterol Hepatol Nutr; 18, 1: 30-38.

[21] Tufan F, et al.(2014). Urea to creatinine ratio: a forgotten marker of poor nutritional state in patients undergoing hemodialysis treatment, The Aging Male, 18:1, 49-53.

[22] Sakr et al. (2023). The prognostic role of urea-to-creatinine ratio in patients with acute

heart failure syndrome: a case–control study. The Egyptian Heart Journal, 75:78.
[23] Sood MM, et al. (2015). The Urea-to-Creatinine Ratio Is Predictive of Worsening Kidney Function in Ambulatory Heart Failure Patients. Journal of Cardiac Failure Volume 21, Issue 5, Pages 412-418.
[24] Walker HK, Hall WD, Hurst JW (1990). Clinical Methods: The History, Physical, and laboratory Examinations. 3rd edition. Chapter 193 - BUN and Creatinine by Adrian O. Hosten. National Library of Medicine, National Center for Biotechnology Information.
[25] Rashid, Ahlam (2020), "Diabetes Dataset", Mendeley Data, V1, doi: 10.17632/wj9rwkp9c2.1.
[26] Almahdawi A, Al-Taie A, S.Naama Z (2022). Diabetes Prediction Using Machine Learning. Conference Paper· December 2022 DOI: 10.1109/IT-ELA57378.2022.10107919.
[27] Chaudhuri I, Shah A MD, Kamrujjaman MD (2024). Novel Risk Factors for Diabetes: A Comprehensive Analysis for Enhanced Disease Diagnosis. International Journal of Ground Sediment & Water. Vol. 19. 1355-1382.
[28] Eyth E, Naik R. Hemoglobin A1C. [Updated 2023 Mar 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK549816/
[29] Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. Biomark Insights. 2016 Jul 3;11:95-104. doi: 10.4137/BMI.S38440. PMID: 27398023; PMCID: PMC4933534.
[30] Bennett CM et al. (2007). HbA1c as a screening tool for detection of Type 2 diabetes: a systematic review. DIABETICMedicine. DOI: 10.1111/j.1464-5491.2007.02106.x.
[31] Lind M et al. (2008). A systematic review of HbA1c variables used in the study of diabetic complications. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2, 282—293.
[32] Pancholia AK et al. (2024). Laboratory evaluation of lipid parameters in clinical practice, Indian Heart Journal, Volume 76, Supplement 1, Pages S29-S32, ISSN 0019-4832.
[33] Onwe PE et al. (2015). Lipid Profile and the Growing Concern on Lipid Related Diseases. IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS). e-ISSN: 2278-3008, p-ISSN:2319-7676. Volume 10, Issue 5 Ver. III, PP 22-27.
[34] Lee Y, Nelder JA, Pawitan Y (2017). Generalized Linear Models with Random Effects (Unified Analysis via H–likelihood) (Second Edition). London: Chapman & Hall.
[35] Das RN, Lee Y (2009). Log-normal versus gamma models for analyzing data from quality-improvement experiments. Quality Engineering 21: 79-87.
[36] Qu Y, Tan M, Rybicki L (2000). A unified approach to estimating association measures via a joint generalized linear model for paired binary data. Communications in Statistics – Theory and Methods 29: 143-156.
[37] Lesperance ML, Park S (2003). GLMs for the analysis of robust designs with dynamic characteristics. Journal Quality Technology 35: 253-263.
[38] Hastie T, Tibshirani R, Friedman J (2001). The Elements of Statistical Learning, Springer-Verlag.
[39] Nelder JA (1994). The statistics of linear models: back to basics. Statistics and Computing 4: 221-234.
[40] Das RN (2012). Discrepancy in fitting between log-normal and gamma models: An illustration. Model Assisted Statistics and Applications 7: 23-32.