Editorial   **Open Access**

The Total Bilirubin Explanatory Factors of Liver Patients

Rabindra Nath Das*

Department of Statistics, University of Burdwan, West Bengal, India

Editorial

Bilirubin is a product formed when our body breaks down old red blood cells. It is a substance of heme catabolism that may have potent antioxidant and cytoprotective properties [1,2]. A little amount of bilirubin in our blood is normal (0.22 – 1 mg/dl), but a high level may be a sign of liver disease. Therefore, total bilirubin is a biochemical liver disease marker. Literature shows that a growing body with higher bilirubin levels is negatively correlated with insulin levels, the prevalence of diabetes and cardiovascular disease [3-5]. The report examines the explanatory factors of total bilirubin. The present hypotheses are: What are the risk and protective factors of liver disease based on total bilirubin? These hypotheses are examined based on a real data set given in [6,7].

The considered real data set was obtained from the North-East of Andhra Pradesh, India. The data set contains 579 subjects with 2 attribute characters, and 9 continuous variables. It is available in the site http://archive.ics.uci.edu/ml/machine-learning-databases/00225/". The two attribute characters are sex (male = 0, female =1), selected field used to split the data into two sets (liver patient=1, non-liver patient=2) (CLUSTER), and their proportions are displayed in (Table 1) [8]. Note that the data set contains 71.5% liver patients, and 28.5% non-liver patients. The nine continuous variables are age, total bilirubin (TB), direct bilirubin (DB), alkaline phosphatase (ALP), alanine aminotransferase (SGPT), aspartate aminotransferase (SGOT), total proteins (TP), albumin (ALB), and albumin and globulin ratio (A/G), and their mean, standard deviation, and normal ranges are given in (Table 1) [8]. Recently, the determinants of ALP are derived in [8]. The above data set has been analyzed based on both joint generalized linear Log-normal and Gamma models [9,10], as the response total bilirubin is heteroscedastic. It is observed that the joint Log-normal models give better results than Gamma fitted models, and the following results are reported based on the fitted joint Log-normal models.

The data set contains 11 explanatory variables/factors on 579 subjects. Total bilirubin (TB) is considered as the response variable, and the remaining others are considered as the explanatory variables. Based on the fitted joint Log-normal models, it is observed that sex (P=0.024) is inversely associated the mean TB. Therefore, total bilirubin is lower for female patients than male. It indicates that male liver patients are at higher risk than female patients. Total bilirubin is higher at older ages (P=0.0722). TB increases as ALP (P<0.0001) or direct bilirubin (DB) (P<0.0001) increases. The interaction effect of ALP & DB (ALP*DB) (P<0.0001) is inversely associated with the mean TB. It shows that even though the marginal effects of ALP & DB increases the mean TB, but their joint interaction effect decreases the mean TB. TB increases as the SGPT (P=0.1146) increases. Note that the SGOT is not associated with the mean TB, but the joint effect of SGPT & SGOT (SGPT*SGOT) (P=0.0331) is negatively associated with the mean TB. Total protein (TP) (P=0.1111) is negatively associated with the mean TB. It shows that total bilirubin is higher at lower value of TP. Also the interaction effect of DB & TP (DB*TP) (P=0.0227) is inversely

associated with the mean TB. It shows that if the interaction effect of DB & TP is lower, the mean TB is higher. The mean TB increases as the albumin (ALB) (P=0.0169) increases. Also the albumin and globulin ratio (A/G) (P=0.0359) is inversely associated with the mean TB. The variance of TB is inversely associated with the sex (P=0.0051). It shows that the variance TB is higher for male patients than female. TB variance increases as the DB (P<0.0001) or ALP (P=0.0327) increases. The summarized association of the explanatory variables/factors with total bilirubin is displayed in Table 1.

The association of total bilirubin with the other biochemical liver disease markers, and other explanatory factors/ variables is shown above Table 1. It is shown above that total bilirubin is positively associated with the direct bilirubin, alkaline phosphatase, alanine aminotransferase, and albumin, which are liver disease markers. So, care should be taken if one liver disease marker increases, the other should be increased. Note that their interaction effects have opposite roles. For confirmation that a patient is having liver disease, all liver disease's markers need to be tested. At older ages, care should be taken that liver diseases markers should be

Response	Associated with following	Association type	P-value
Mean Total Bilirubin (TB)	Sex	negative	P=0.0245
	Age	positive	P=0.0722
	Alkaline phosphatase (ALP)	positive	P<0.0001
	Direct bilirubin (DB)	positive	P<0.0001
	ALP*DB	negative	P<0.0001
	Alamine aminotransferase (SGPT)	positive	P=0.1146
	Aspartate aminotransferase (SGOT)	no	P=0.3394
	SGPT*SGOT	negative	P=0.0331
	Total protein (TP)	negative	P=0.1111
	DB*TP	negative	P=0.0227
	Albumin (ALB)	positive	P=0.0169
	Albumin and globulin ratio (A/G)	negative	P=0.0359
Variance of TB	Sex	negative	P=0.0051
	Direct bilirubin	positive	P<0.0001
	Alkaline phosphatase (ALP)	positive	P=0.0327

Table 1: Association of total bilirubin with different factors/ variables.

***Corresponding author:** Rabindra Nath Das, Department of Statistics, The University of Burdwan, West Bengal, India, E-mail: rabin.bwn@gmail.com

increased. Medical practitioners take care that interaction effects of liver disease markers have opposite role than the marginal effects of the markers. As a result it is difficult to identify a patient with liver disease.

Conflict of Interest

The author confirms that this article content has no conflict of interest.

References

1. Stocker R, Yamamoto Y, McDonagh AF, Glazer AN, Ames BN (1987) Bilirubin is an antioxidant of possible physiological importance. Science 235: 1043-1046.

2. Baranano DE, Rao M, Ferris CD, Snyder SH (2002) Biliverdin reductase: a major physiologic cytoprotectant. Proc Natl Acad Sci U SA 99: 16093-16098.

3. Lin LY, Kuo HK, Hwang JJ, Lai LP, Chiang FT, et al. (2009) Serum bilirubin is inversely associated with insulin resistance and metabolic syndrome among children and adolescents. Atherosclerosis 203: 563-568.

4. Tanaka M, Fukui M, Tomiyasu K, Akabame S, Nakano K, et al. (2009) Low serum bilirubin concentration is associated with coronary artery calcification (CAC). Atherosclerosis 206: 287-291.

5. Cheriyath P, Gorrepati VS, Peters I, Nookala V, Murphy ME, et al. (2010) High Total Bilirubin as a Protective Factor for Diabetes Mellitus: An Analysis of NHANES Data From 1999–2006. J Clin Med Res 2: 201-206.

6. Ramana BV, Babu MSP, Venkateswarlu NB (2011). A critical study of selected classification algorithms for liver disease diagnosis. Intern J Database Management Systems 3: 101-114.

7. Ramana BV, Babu MSP, Venkateswarlu NB (2012) Liver classification using modified rotation forest. International Journal of Engineering Research and Development 1: 17-24.

8. Das RN, Mukherjee S, Sharma I (2018) Alkaline Phosphatase Determinants of Liver Patients. J the Pancreas 19: 1-6.

9. Lee Y, Nelder JA, Pawitan Y (2006) Generalized linear models with random effects: unified analysis via H-likelihood. CRC Press.

10. Das RN, Lee Y (2008) Log-normal versus gamma models for analyzing data from quality-improvement experiments. Quality Engineering 21: 79-87.