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Research article

Association Between Body Mass Index and Cardiac Parameters of Worcester Heart Attack Study

Rabindra Nath Das[1*], Sabyasachi Mukherjee[2] and Rajendra Nath Panda[3]

[1]*Department of Statistics, The University of Burdwan, Burdwan, West Bengal, India*

[2]*Department of Mathematics, NSHM Knowledge Campus, Durgapur, West Bengal, India*

[3]*Department of Statistics, The University of Kalyani, Kalyani, West Bengal, India*

Abstract

Objectives

The present report aims to identify the association between the body mass index and the cardiac parameters of the acute myocardial infarction (AMI) patients in the Worcester heart attack study (WHAS). Based on the separate analyses of body mass index (BMI), heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP), on the remaining other variables/ factors, many cardiac parameters (BMI) have (has) been identified which are (is) associated with the BMI (many cardiac parameters).

Background

The association of body mass index with the cardiac parameters is little known in the WHAS literature for the AMI patients.

Methods

All these four responses (BMI, SBP, DBP & HR) are continuous positive random variables with non-constant variances. So, they have been analyzed by the joint modeling of gamma and Log-normal models.

Results

Mean BMI increases with the decreased of age (*P<0.0001*), for male patient *(P=0.0597)* than female, and the AMI patients in the WHAS who have no complete heart block (AV3) *(P=0.0661)*. Mean BMI also increases with the increased of SBP *(P=0.0065)*, the AMI patients in the WHAS who have history of cardiovascular disease (CVD) *(P=0.0013)*, myocardial infarction type of Q-wave (MITYPE) *(P=0.0437)*, cohort year (YEAR) at 3=2001 *(P=0.0795)*. Variance of BMI is positively associated with the sex *(P<0.0001)*, and it increases for female AMI patients. DBP analysis shows that DBP variance increases with the increased of BMI *(P=0.0001)*. Note that mean DBP [SBP] is partially significant with BMI *(P=0.2170) [P=0.2080]*, while the mean and variance of HR are insignificant of BMI.

Conclusions

BMI is associated with many cardiac parameters such as SBP, DBP, AV3, CVD, MITYPE, and along with age, sex and cohort year. On the other hand, DBP or SBP is associated with BMI, but HR is independent of BMI. The present findings are completely new in the WHAS literature.

Keywords: Body mass index; Cardiac parameter; Heart rate; Joint generalized linear models; Myocardial infarction; Non-constant variance

Introduction

Recently, obesity and overweight have increased worldwide. At present, cardiovascular diseases (CVD) are recognized as a countrywide epidemic in India. The leading causes of death worldwide are stroke and coronary heart disease [1-3]. One of the most important cardio vascular disease risk factor is high body-mass index (BMI) [2-5]. Generally, diabetes, raised blood pressure, hypertension, cholesterol, tobacco use, overweight and dyslipidaemia are considered as the risk factors of CVD [4-6]. In the present days, for reducing obesity, weight managements are practiced by using mostly weight-loss drugs, whose efficacy are not approved in many cases [7,8]. Also, for very high obese individuals, surgical methods are recommended [9,10].

Many prospective studies have been conducted to identify the determinants of BMI and CVD [10-12]. Note that the BMI is a continuous random variable, while CVD is a categorical variable. Some authors have reduced the BMI into dichotomous variable in order to compare between the BMI and CVD. Consequently, many information on BMI have been lost. On the other hand, CVD is a categorical variable, which has already lost many information. In the earlier studies, the statistical tools (such as logistic regression, Chi-square test, simple correlation, analysis of variance, odds ratio) are not appropriate to identify the association between the BMI

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

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and CVD [10-13]. It is well known that the physiological data (such as BMI, CVD, SBP, DBP, HR) are generally heterogeneous. So, the statistical tools used in the earlier articles as mentioned above are not appropriate always [14,15]. In the earlier studies, both the responses CVD and BMI are considered as dichotomous. Based on our knowledge, there is a little study of WHAS data set for examining the association between the BMI and CVD (or equivalent variable) considering as continuous random variable. As these variables are positive physiological random variable, so they will be heterogeneous and non-normal. Consequently, they may belong to exponential family distribution, and their variance may have relationship with the mean. In these situations, these data should be analyzed either by gamma or Log-normal model [14-16].

The risk factors of a disease are determined in an epidemiology study. In case of the AMI patients in the WHAS data set, there is very little study of determining the risk factors of the cardiac parameters and BMI [13,20]. This report examines the following queries (or hypotheses): Is there any association between the BMI and the cardiac parameters? Is there any association between the systolic blood pressure (SBP), or diastolic blood pressure (DBP), or heart rate (HR) with the BMI? What are the effects of BMI on SBP, or DBP, or HR, or any other cardiac parameters? What are the effects of the cardiac parameters on the BMI? To examine these queries, the present report separately analyzes the four responses SBP, DBP, HR, and BMI, based on the remaining other variables. The association and the effects of the factors are determined in the present report, based on appropriate modeling of the WHAS multivariate data set (500 subjects with 21 covariates) [13]. All these four responses are continuous non-normal positive random variables with non-constant variances. Consequently, they have been analyzed by the joint modeling of gamma and Log-normal models [14-17]. For ready reference, a short description of both the gamma and Log-normal models are described in the Methodology Section.

Methodology

Joint Generalized Gamma & Log-Normal Liner Models

This report aims to identify the association of BMI with the cardiac parameters, and conversely. The considered responses are the BMI, SBP, DBP and HR which are all positive, continuous, non-normal with non-constant variances. These responses are to be modeled either by the gamma or Log-normal which are well described in [14-17]. In short, these two models can be reproduced as follows:

Let us consider the positive responses y_i's with variance σ_i^2, and it is assumed that these responses satisfy the following

$E(y_i) = \mu_i$ and $\mathrm{Var}(Y_i) = \sigma_i^2 \mu_i^2$

In order to stabilize the variance, generally, the log transformation, that is, $Z_i = \log(Y_i)$ can be used. Note that this transformation may not stabilize the variance always [18]. Then it is better to use the joint generalized linear models (JGLMs) for the mean and dispersion (suggested by Nelder and Lee [19]). The joint models (mean and dispersion) for the Log-normal distribution are suggested by Nelder and Lee [19] as given by

$E(Z_i) = \mu_{zi}$ and $\mathrm{Var}(Z_i) = \sigma_{zi}^2$,

$\mu_{zi} = x_i^t \beta$ and $\log(\sigma_{zi}^2) = g_i^t \gamma$,

where x_i^t and g_i^t are respectively, the row vectors associated with the mean parameters β and the dispersion parameters γ.

For the positive response y_i, the JGLMs (suggested by Nelder and Lee [19]) can be used when

$$E(y_i) = \mu_i \text{ and } Var(y_i) = \sigma_i^2 V(\mu_i),$$

where σ_i^2's are the dispersion parameters, and $V(\cdot)$ is the variance function, which has two parts. Note that, a part of $V(\mu_i)$ depends on the mean changes, and the σ_i^2 is independent of mean adjustment. Moreover, $V(\mu_i)$ characterizes the GLM family distribution. The GLM distribution, for example, is gamma if $V(\mu) = \mu^2$, Poisson if $V(\mu) = \mu$, and normal if $V(\mu) = 1$. According to Nelder and Lee [19], the JGLMs are

$$\eta_i = g(\mu_i) = x_i^t \beta \text{ and } \varepsilon_i = h(\sigma_i^2) = w_i^t \gamma,$$

where $g(\cdot)$ and $h(\cdot)$ are the GLM link functions for the mean and variance, respectively. Note that x_i^t, w_i^t are respectively, the row vectors associated with the mean and variance model. Maximum likelihood (ML) method is used to estimate the mean parameters, while the restricted ML (REML) is used to estimate the dispersion parameters [17,19].

Worcester Heart Attack Study Data, BMI Analysis & Interpretations

Worcester Heart Attack Study Data Description

This WHAS has been carried out by Prof. Robert J. Goldberg, Department of Cardiology at the University of Massachusetts Medical School. 500 individuals with 21 covariates have been studied in the WHAS [13]. This present data set is available at the following Wiley's FTP site: ftp//ftp.wiley.com/public/sci_tech_med/survival

A detailed data description along its aims are given in [13]. This data description is also reproduced in [20]. This patient population and the data collection method are not described in details here as it would increase the length of the paper. The present data set contains the AMI patients admitted to hospitals in the Worcester, Massachusetts Standard Metropolitan Statistical Area. The WHAS data set contains the following covariates: Sex (0=male, 1=female) (SEX), age at hospital admission (AGE), initial diastolic blood pressure (DBP), initial systolic blood pressure (SBP), body mass index (BMI), initial heart rate (HR), atrial fibrillation (0 = no, 1 = yes) (AFB), history of cardiovascular disease (0=no, 1=yes) (CVD), congestive heart complications (0=no, 1 =yes) (CHF), cardiogenic

shock (0=no, 1=yes) (SHO), myocardial infarction (MI) order (0= first, 1=recurrent) (MIORD), complete heart block (0=no, 1=yes) (AV3), cohort year (1=1997, 2=1999, 3=2001) (YEAR), MI type (0=non Q-wave, 1=Q-wave) (MITYPE), admission date in hospital (ADDATE), discharge date from hospital (DSDATE), last follow up date (LFDATE), hospital stay length (from admission to discharge) (HSL), status of discharge from hospital (0=alive, 1= dead) (SDFH), total follow-up length in days (from admission to last follow-up date) (TFLD), physical status at last follow-up (0= alive, 1= dead) (PSLF).

Dependent Variables

The present article focuses the association between the BMI and the cardiac parameter, and conversely of the WHAS data set. Therefore, the dependent variables are the BMI, DBP, SBP and HR. Analyses of DBP, SBP and HR are given in [20], and they are not reproduced herein. Only the analysis of BMI is given in this report. Interpretations of the association of DBP, or SBP, or HR with BMI are included in this report from [20].

Independent Variables

There are two sets of independent variables, namely, qualitative and quantitative in the WHAS data set. This data set contains fifteen categorical factors and six continuous variables. The levels of the factors are described in the data description.

The Body Mass Index (BMI) Analysis, Results and Interpretations

The dependent continuous non-normal random variable BMI has been modeled based on the remaining independent variables/ factors using both the Log-normal and the gamma models. The final models have been selected based on the smallest Akaike information criterion (AIC) value in each class. It is well-known that the AIC selects a model which minimizes the predicted additive errors and squared error loss [21]. One can verify that the selected Log-normal fit (Table 1) (AIC= 2936.00) reveals better results than the gamma fit (AIC=2939.905). The derived joint Log-normal model fit results are displayed in (Table 1).

Table 1 reveals the following results interpretations about BMI.

I. Age *(P<0.001)* is negatively associated with the mean BMI. It indicates that the BMI is higher at younger ages of the AMI patients of the WHAS data set, than the older ages. Note the minimum age of the WHAS patients is 30 year, while the maximum age is 104 year. In practice, the amount of consumed food of the AMI patients at younger ages is higher than the older ages.

II. Mean BMI is negatively associated with the sex (male = 0, female = 1) *(P=0.0597)*. It implies that the mean BMI is significantly higher for male WHAS patients than the female. Note that the average BMI (27.2689) of male is higher than female (25.6311).

III. The mean BMI is positively associated with the systolic blood pressure (SBP) *(P=0.0065)*, indicating that SBP is higher of the WHAS patients having higher BMI.

IV. The mean BMI is positively associated with the history of cardiovascular disease (0=no, 1=yes) (CVD) *(P=0.0013)*, indicating that the BMI is higher of the WHAS patients having CVD than without CVD.

V. The mean BMI is negatively associated with the complete heart block (0=no, 1=yes) (AV3) *(P=0.0661)*, indicating that the BMI is higher for the AMI patients of the WHAS data set with no AV3

Table 1: Mean & variance models of Log-normal fit results of body mass index (BMI)

Model	Covariate	Estimate	Standard error	t-value	P-value
Mean Model	Constant	3.4545	0.05463	63.234	< 0.001
	AGE	-0.0050	0.00056	-8.883	< 0.001
	SEX	-0.0344	0.01823	-1.887	0.0597
	Systolic BP (SBP)	0.0007	0.00024	2.734	0.0065
	History of Cardiovascular Disease (CVD)	0.0580	0.01791	3.240	0.0013
	Complete heart block (AV3)	-0.0917	0.04980	-1.842	0.0661
	MI Type (MITYPE)	0.0346	0.01713	2.022	0.0437
	Cohort year (YEAR)2	0.0219	0.01849	1.186	0.2362
	Cohort year (YEAR)3	0.0344	0.01958	1.757	0.0795
Dispersion Model	Constant	-4.145	0.3142	-13.192	< 0.0001
	Sex	0.664	0.1331	4.990	< 0.0001
	Systolic BP (SBP)	0.003	0.0021	1.422	0.1556
	Cardiogenic Shock (SHO)	-0.479	0.3396	-1.410	0.1592

Model fitting diagnostic plots, namely, residual and normal probability plots are examined for the fitted models in (Table 1). In Figure 1(a), the absolute residuals are plotted with respect to fitted values. It is absolutely a flat diagram with the running means, revealing that the variance is constant for the fitted models. Normal probability plot of the Log-normal fitted mean model (Table 1) is displayed by Figure 1(b), which does not show any lack of fit

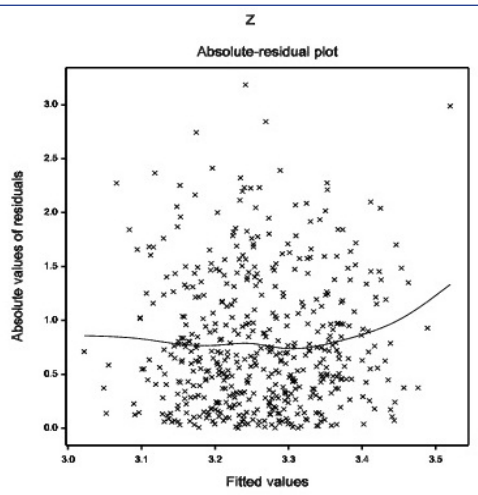

Figure- 1(a)

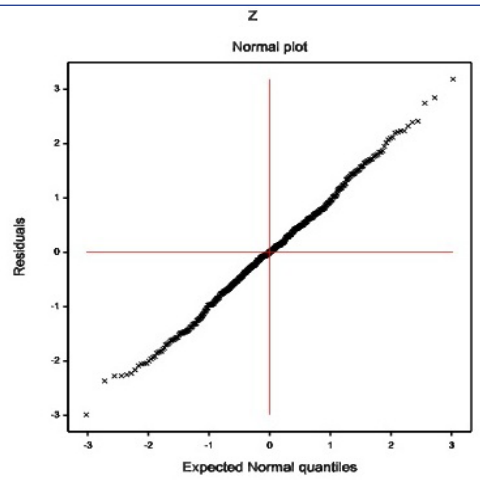

Figure- 1(b)

Figure 1: For the Log-normal fitted models of BMI (Table 1), the (a) absolute residuals plot with respect to fitted values, and the (b) normal probability plot of the mean model

than the patients with AV3.

VI. The mean BMI is positively associated with the MI type (0=non Q-wave, 1=Q-wave) (MITYPE) *(P<0.001)*, indicating that the AMI patients of WHAS data set with Q-wave MITYPE have higher BMI than the patients with non Q-wave.

VII. The mean BMI is positively associated (partially) with the cohort year(1=1997, 2=1999, 3=2001) (YEAR) *(P=0.0795)* at year 3=2001, indicating that the AMI patients of WHAS data set at year = 3 have higher BMI than the other cohort years. Note that in epidemiology, partially significant factors are treated as confounder, and they are important in the fitted model.

VIII. The variance of BMI is positively associated with the sex (male=0, female=1) *(P<0.0001)*, indicating that the female AMI patients of WHAS data set have higher BMI variance than the male. It implies that BMI of female patients are highly scattered. Note that the mean female BMI is lower than the male.

IX. BMI variance is positively associated (partially) with the SBP *(P=0.1556)* (as confounder), indicating that the BMI variance is higher of the AMI patients of WHAS data set having higher SBP.

X. BMI variance is negatively associated (partially) with the cardiogenic shock (0=no, 1=yes) (SHO) *(P=0.1592)* (as confounder), indicating that the BMI variance is higher of the AMI patients of WHAS data set having no cardiogenic shock.

XI. Table 1 [20] (here Table 2 as a ready reference) shows that DBP variance is positively associated with the BMI (P=0.001), indicating that the DBP variance increases with the increased of BMI.

XII. Table 1 [20] (here Table 2) shows that the mean DBP is positively associated (partially) with BMI *(p=0.217)* (as confounder), indicating that mean DBP increases with the increased of BMI.

XIII. Table 2 [20] (here Table 3 as a ready reference) shows that the mean SBP is positively associated (partially) with BMI (p=0.208) (as confounder), indicating that mean SBP increases with the increased of BMI.

Discussions and Concluding Remarks

The current article focuses the association between the BMI and the cardiac parameters, and conversely. Consequently, the BMI has been modeled on the remaining covariates of the AMI patients of WHAS data set. Note that the cardiac parameters DBP, SBP, and HR have been modeled for the same data set respectively, in Tables (1, 2 and 3) [20]. Analyses of these cardiac parameters have not shown here. For ready reference, analyses results of DBP and SBP are reproduced from [20] in Tables (2 and 3), respectively. As heart rate (for the WHAS data set) has not been predicted by BMI (Table 3) [20], so Table 3 [20] has not been reproduced here. Model fitting of the fitted models have been verified based on appropriate diagnostic plots. All the results and conclusions have been derived in this report based on the derived models in Tables (1, 2 and 3). The reported results can be verified using data set given in Wiley's FTP site: ftp//ftp.wiley.com/public/sci_tech_med/survival

To examine the factors associated with survival time and incidence rate of AMI patients of WHAS data set, a study has been given in [13]. Based on our knowledge, there is no study to examine the present hypothesis: Is there any association between the BMI and the cardiac parameters of WHAS data set, and conversely? This report derived many significant results, which are completely new in AMI literature of WHAS data set. As there was not any earlier study of BMI for the WHAS data set, it is not possible to compare the present results with the earlier studies.

This report has established the association between the BMI and the cardiac parameters [Table 1]. Two additional Tables (2 and 3) from [20], also show some association between the cardiac parameters

Table 2: Mean & variance models of Gamma fit results of diastolic blood pressure (DBP)

Model	Covariate	Estimate	Standard error	t-value	P-value
Mean Model	Constant	3.5001	0.09484	36.906	<0.001
	AGE	-0.0030	0.00072	-4.157	<0.001
	SEX	-0.0244	0.01829	-1.333	0.183
	Heart rate (HR)	0.0019	0.00037	5.302	<0.001
	Systolic BP (SBP)	0.0057	0.00029	19.639	<0.001
	Body mass index (BMI)	0.0024	0.00193	1.236	0.217
	Atrial Fibrillation (AFB)	0.0377	0.02093	1.803	0.072
	Cardiogenic Shock (SHO)	0.0712	0.03384	2.104	0.036
	Congestive Heart Complications (CHF)	-0.0541	0.01996	-2.712	0.007
	MI Order (MIORD)	-0.0415	0.02152	-1.930	0.054
	MI Type (MITYPE)	0.1059	0.01971	5.372	<0.001
Dispersion Model	Constant	-5.556	0.4063	-13.676	<0.001
	Systolic BP (SBP)	0.007	0.0020	3.323	0.001
	Body mass index (BMI)	0.042	0.0125	3.347	0.001
	Atrial Fibrillation (AFB)	-0.496	0.1819	-2.724	0.007
	Complete heart block (AV3)	-1.334	0.4741	-2.814	0.005
	MI Order (MIORD)	0.460	0.1393	3.300	0.001
	Cohort year (YEAR)2	0.480	0.1673	2.870	0.004
	Cohort year (YEAR)3	0.453	0.1815	2.497	0.013

Table 3: Mean & variance models of Log-normal fit results of systolic blood pressure (SBP)

Model	Covariate	Estimate	Standard error	t-value	P-value
Mean Model	Constant	4.3285	0.07441	58.17	< 0.001
	AGE	0.0015	0.00059	2.49	0.013
	SEX	0.0474	0.01567	3.03	0.002
	Heart rate (HR)	-0.0012	0.00032	-3.68	< 0.001
	Diastolic BP (DBP)	0.0071	0.00036	19.88	< 0.001
	Body mass index (BMI)	0.0019	0.00150	1.26	0.208
	History of Cardiovascular Disease (CVD)	0.0409	0.01611	2.54	0.011
	Atrial Fibrillation (AFB)	-0.0529	0.02069	-2.56	0.011
	Cardiogenic Shock (SHO)	-0.1761	0.04565	-3.86	< 0.001
	MI Type (MITYPE)	-0.0612	0.01676	-3.65	< 0.001
Dispersion Model	Constant	-4.166	0.1608	-25.907	< 0.001
	History of Cardiovascular Disease (CVD)	0.482	0.1514	3.182	0.002
	Cardiogenic Shock (SHO)	0.468	0.3328	1.407	0.160
	MI Order (MIORD)	-0.205	0.1394	-1.470	0.142
	Cohort year (YEAR)2	0.257	0.1584	1.619	0.106
	Cohort year (YEAR)3	0.526	0.1675	3.139	0.002

and the BMI. In Table 1, it is observed that the BMI is associated with the cardiac parameters such as systolic blood pressure, history of cardiovascular disease, complete heart block, cardiogenic shock, the myocardial infraction type (Table 1). On the other hand cardiac parameter DBP and SBP are respectively, associated with the BMI in Tables (2 and 3). In addition, age and sex are associated with the BMI (Table 1). The derived results in the current report, though not completely conclusive, are revealing—

The present results have been derived based on the following five statistical data analysis criteria: 1. Results have been selected based on comparison of two fitted Log-normal and gamma models. 2. Final model is selected based on diagnostic plots. 3. Final selected models have the smallest AIC. 4. Unknown parameter estimates have the small standard errors Tables (1, 2 and 3) 5. Based on appropriate response distribution, final model is selected. Therefore, the research should have greater faith in the present reported results.

The interpretations of the derived results are stated above. These results are related with the AMI patients for the WHAS data set. Similar study should be done for other types of cardiac patients. It will be better if the separate weights and heights are recorded for each patient. Future cardiac diseases researchers are advised to take the measurement of weight, height, hip and waist sizes of each subject, in addition to other interested covariates. This report recommends to all individuals that the BMI should not be high, as it is associated with the different cardiac parameters.

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