

Role of Body Mass Index on Insulin and Glucose for Breast Cancer Women

Ishita Saha¹ and Rabindra Nath Das^{2*}

¹Department of Physiology, Calcutta Medical College and Hospital, Kolkata, West Bengal, India

²Department of Statistics, The University of Burdwan, Burdwan, West Bengal, India

*Corresponding Author: Rabindra Nath Das, Department of Statistics, The University of Burdwan, Burdwan, West Bengal, India.

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Body mass index ($BMI = \text{Weight}(\text{kg})/\text{Height}(\text{m}^2)$) is frequently treated as an important risk factor for many diseases. Generally, $BMI < 25 \text{ kg/m}^2$ is recommended as standard, otherwise it is treated as obesity. BMI is a composite measure, and it is used as the predictor of many diseases [1-3]. Practically, it is used as a measure of an individual index of fatness. It is commonly used as a risk factor for the promotion of many diseases such as cardiovascular diseases, diabetes, breast cancer (BC) etc [3-5]. The following inquires are investigated in the current editorial note:

- Is there any association of BMI with glucose and insulin for breast cancer women?
- If it is affirmative, what are the associations?
- What are the effects of BMI on glucose and insulin?

These above inquires are investigated in the report with the help a real data set of 116 (52 controls and 64 BC patients) women containing 10 study factors, which is available in the UCI Machine Learning Repository. The patient populations and the data collection method are well described in [6,7]. For ready reference, the 10 study factors are displayed as follows:

- Age (years),
- BMI (kg/m^2),
- Insulin ($\mu\text{U/mL}$),
- Glucose (mg/dL),
- Homeostasis model assessment score insulin resistance (HOMA-IR),
- Adiponectin ($\mu\text{g/mL}$),
- Resistin (ng/mL),
- Monocyte chemoattractant protein-1 (MCP-1) (pg/dL),
- Leptin (ng/mL),
- Patient type (TYOP) (1 = Healthy controls; 2 = Breast cancer patients).

The above data set contains two diabetes markers such as glucose and insulin. The above inquires should be investigated in two ways such as modeling of BMI on diabetes markers, along with the remaining factors, and also modeling of each diabetes marker on BMI, along with the remaining factors. Note that BMI, glucose and insulin are all continuous variables.

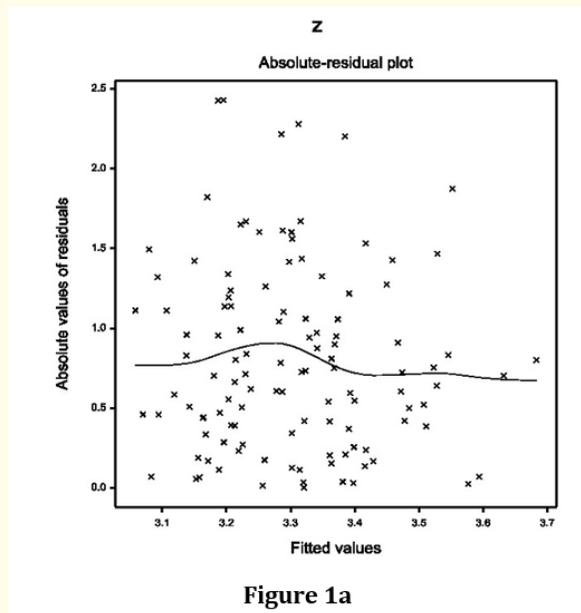
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Let us investigate the BMI modeling on glucose, insulin and the rest other factors of the data set. Note that BMI, glucose and insulin are all continuous positive, heterogenous and non-normally distributed variable, which can be modeled applying joint generalized linear models (JGLMs) using both the Log-normal and Gamma distributions [8-10]. JGL Log-normal BMI fit is better than the Gamma, which is displayed in table 1 and its fitting test is presented in figure 1. Figure 1a presents the absolute residuals plot with respect to BMI predicted values, which is almost a flat straight line, indicating that that variance is constant with the running means. Figure 1b displays the normal probability plot of mean BMI Log-normal fitted model in table 1. These two plots do not present any lack of fit. Hence, Log-normal fitted BMI model (Table 1) is closely to its true model. Detailed analysis of BMI is given in [11]. Mean and dispersion models of BMI are as follows:

Model	Covariates	Log-normal				Gamma			
		Estimate	s.e.	t-value	P-Value	Estimate	s.e.	t-value	P-Value
Mean	Constant	3.0370	0.0836	36.31	< 0.0001	3.0460	0.0837	36.40	< 0.0001
	Glucose	0.0015	0.0008	1.80	0.0753	0.0016	0.0009	1.85	0.0670
	Insulin	0.0123	0.0032	3.85	0.0002	0.0121	0.0032	3.82	0.0002
	HOMA-IR	-0.0421	0.0104	-4.08	< 0.0001	-0.0421	0.0102	-4.13	< 0.0001
	Leptin	0.0053	0.0006	8.23	< 0.0001	0.0052	0.0007	8.10	< 0.0001
	Adiponectin	-0.0068	0.0018	-3.74	0.0003	-0.0068	0.0019	-3.66	0.0004
	MCP-1	0.0001	0.0001	3.87	0.0002	0.0001	0.0001	3.73	0.0003
	TYOP	-0.0708	0.0276	-2.57	0.0116	-0.0699	0.0277	-2.52	0.0130
Dispersion	Constant	-4.445	0.7261	-6.12	< 0.0001	-4.358	0.7167	-6.08	< 0.0001
	Age	0.015	0.0107	1.37	0.1751	0.013	0.0108	1.27	0.2085
	Resistin	-0.019	0.0132	-1.47	0.1450	-0.020	0.0134	-1.51	0.1344
	Insulin	-0.018	0.0156	-1.18	0.2413	-0.019	0.0157	-1.22	0.2239
AIC= 613.9					AIC=615.062				

Table 1: Outcomes for joint mean and dispersion model analysis for BMI under Log-Normal and Gamma fit.



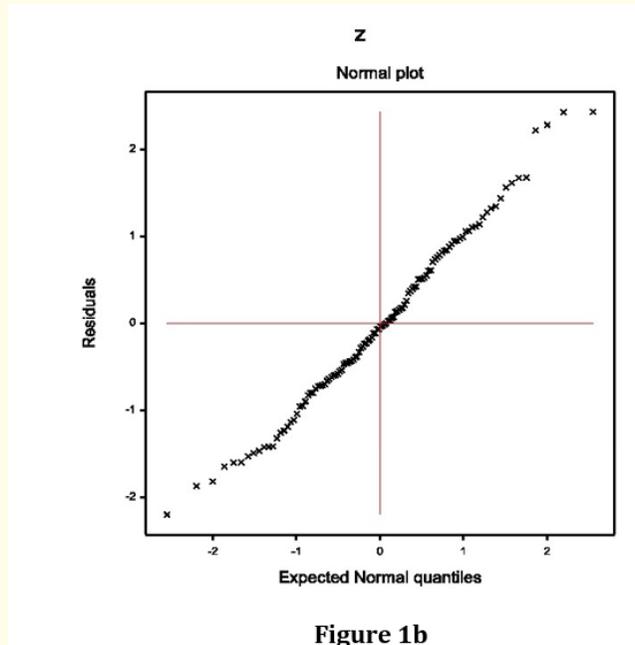


Figure 1: For the BMI joint lognormal fitted model in table 1, the (a) absolute residuals plot corresponding to the fitted values, and (b) the mean BMI normal probability plot.

Fitted Log-normal BMI mean ($\hat{Z} = \text{Log}(\text{BMI})$ model (From table 1) is

$$\hat{Z} = 3.0370 + 0.0123 \text{ Insulin} + 0.0015 \text{ Glucose} - 0.0421 \text{ HOMA-IR} - 0.0068 \text{ Adiponectin} + 0.0053 \text{ Leptin} + 0.0001 \text{ MCP-1} - 0.0708 \text{ TYOP},$$

and the BMI fitted Log-normal variance ($\hat{\sigma}^2$) model is

$$\hat{\sigma}^2 = \exp. (-4.445 - 0.019 \text{ Resistin} + 0.015 \text{ Age} - 0.018 \text{ Insulin}).$$

From the above mean and dispersion models, and also from table 1, the following associations of BMI with glucose and insulin can be reported:

- The mean BMI is directly associated with glucose (P = 0.0753), concluding that BMI rises as glucose level increases.
- Mean BMI is directly associated with insulin (P = 0.0002), indicating that BMI increases as insulin rises.
- Variance of BMI is partially inversely associated with insulin (P = 0.2413), interpreting that BMI variance rises as insulin decreases. In BMI variance model, insulin acts as a confounder, which is important in epidemiological studies.

On the other hand, the associations of insulin (separately glucose) with BMI can be investigated from its respective JGLMs. From the insulin JGLMs, the following associations of insulin with BMI can be noted [12]:

- Mean insulin is directly associated with BMI ($P < 0.0001$), concluding that insulin rises as BMI increases. This is also supported in BMI modeling (Table 1).
- Mean insulin is inversely associated with the joint interaction effect of BMI and HOMA-IR (BMI*HOMA-IR) ($P < 0.0001$), concluding that insulin rises as BMI*HOMA-IR decreases. Note that insulin is directly associated with HOMA-IR ($P < 0.0001$) and as well as BMI ($P < 0.0001$), but their joint interaction effect BMI*HOMA-IR is inversely associated with insulin. This shows that even both BMI and HOMA-IR increase, but insulin may not increase significantly.

Note that for this data set, glucose JGLMs do not show any association between glucose and BMI [12], while BMI mean model shows the positive association between them (Table 1). But it is frequently observed that glucose is positively associated with BMI, and conversely [13]. The report has focused the associations of BMI with glucose, insulin and BMI*HOMA-IR in both mean and dispersion models. Further studies may give more information. Breast cancer patients should care on BMI along with insulin, glucose and HOMA-IR regularly.

Conflict of Interest

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

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