Clinical Journal of Diabetes Care and Control
ISSN: 2642-0872

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Research Article *Volume 4 Issue 1*

The Effects of Glucose on Gestational Diabetes Women

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Received Date: April 30, 2021; **Published Date:** July 22, 2021

Abstract

The current paper studies the effects of glucose on different biochemical parameters of pregnant women. It is identified herein that mean glucose levels are negatively connected with skin thickness (ST) (P=0.0016), while they are positively connected with the joint interaction effect of blood pressure (BP) and ST (i.e. BP*ST) (P=0.0388), but they are insignificant with BP (P=0.2228). Mean glucose levels are positively connected with insulin (P<0.0001), body mass index (BMI) (P=0.0020) and age (P<0.0001), while they are negatively connected with the joint interaction effects Insulin*BMI (P=0.0085) and Insulin*Age (P=0.0004). Mean glucose levels are higher for pregnant diabetes women (P<0.0001) than non-diabetic. Variance of glucose levels is negatively connected with the interaction effect of ST*Insulin (P=0.0040), while it is insignificant of both ST (P=0.1237) and Insulin (P=0.2168).Variance of glucose levels is positively linked with age (P=0.0013), while it is partially positively connected with BMI (P=0.0989), and it is insignificant of diabetes pedigree function (DPF) (P=0.1480). This report shows a very complicated functional relationship of glucose with the biochemical parameters. Pregnant women should care for her glucose levels along with her BMI, insulin levels and ST.

Keywords: Glucose; Type-I diabetes; Type-II diabetes

Abbreviations: BMI: Body Mass Index; DPF: Diabetes Pedigree Function; GD: Gestational Diabetes; JGLMs: Joint Generalized Linear Models; NCV: Non-Constant Variance; ST: Skin Thickness; ML: Maximum likelihood.

Introduction

The mismanagement or condition that the human body cannot properly use the insulin is known as diabetes. When the human body cannot keep insulin levels properly, diabetes is one such mismanagement that damages all other body components [1-3]. In practice, three types of diabetes such as Type-I, Type-II and gestational, which are observed in the real field. In practice, Type-I diabetes is observed in early life when the pancreas yields a small amount of insulin, or it does not yield insulin, due to some unusualness. This is acquainted as juvenile, or insulin-dependent diabetes [4-6]. The medical treatment does not recover Type-I diabetes, and it attempts to administer blood sugar levels with insulin, diet and lifestyle to obstruct complexity. For pregnant women, it is frequently audited that they have higher glucose levels during pregnancy, which is known as gestational diabetes. Afterwards, gestational diabetes can be reduced to Type-II diabetes with high probability [7-10].

The present study is based on pregnant women, which is a gestational diabetes mellitus (GDM) study. Note that GDM is observed in practice around 5% of pregnancies, but it depends on many demographic and biochemical factors of the study unit [11,12]. It is thought that the number of pregnancies may be affected by GDM that imposes a greater risk for both mother and neonate. It is little known about the effects of glucose level on different biochemical parameters and demographic factors. The current article attempts to derive the linkages of glucose levels with other biochemical parameters and demographic factors for pregnant females at least 21 years old of Pima Indian heritage. The article is arranged as follows. The next section presents materials and methods, and the subsequent sections are statistical and graphical analysis, results and discussion, conclusions.

Materials and Methods

Materials

The current study is based on a real data set of 768 Pima Indian heritage women with minimum 21 years old. The dataset was initially surveyed by the National Institute of Diabetes and Digestive and Kidney Diseases. The data set is available in the UCI Machine Learning Repository. For immediate applications, the 9 study characters are restated as follows. Study women age (in years), patient type(1=non-diabetic, 2= diabetic), blood pressure (BP) (diastolic BP (mm Hg)),pregnancies (number of times pregnancy), skin thickness (ST) (triceps skin fold thickness (mm)), glucose level (plasma glucose concentration over 2 hours in an oral glucose tolerance test), insulin level (2-hour serum insulin (mu U/ml)), diabetes pedigree function (DPF) (a function which scores likelihood of diabetes based on family history)), body mass index (BMI) (weight in kg/(height in m)^2).

Statistical Methods

The considered pregnant women diabetes data are a physiological data set, which is heteroscedastic. Furthermore, the response glucose level is positive and continuous. Unequal variance data set can be modeled by adopting appropriate transformation, when it is stabilized under the transformation. For most of the heteroscedastic data sets, variance is not stabilized using suitable transformation [13]. Generally, a positive homogeneous and continuous random response variable can be modeled either by a gamma, or lognormal model [14]. For a heterogeneous dependent random variable modeling, joint generalized linear models (JGLM) using lognormal and gamma models can be adopted [15]. JGLMs is well illustrated in the book by Lee, et al. [16]. For immediate reference, JGLMs is very shortly discussed in this section.

JGL lognormal Models: Here Glucose level = y_i say, is the interested continuous and positive dependent variable with unequal variance ($\sigma_{i_2}^2$), and mean $\mu_i = E(y_i)$, maintaining $Var(y_i) = \sigma_i^2 \mu_i^2 = \sigma_i^2 V(\mu_i)$ say, where V(.) is termed as variance function. In practice, the log transformation $z_i = \log$ (Glucose level=y_i) is frequently used to stabilize the variance, which may not be stabilized always [13]. For deriving an appropriate model, JGLMs for the mean and dispersion are generally adopted. Considering the dependent variable Glucose level distribution as lognormal, the JGLMs of the mean and dispersion model (dependent variable Glucose level= y_i, with $z_i = \log$(Glucose level=y_i)) are given by
$E(z_i) = \mu_{zi} = x_i^t \beta$, $Var(z_i) = \sigma_{zi}^2$, and $\log(\sigma_{zi}^2) = g_i^t \gamma$,
Where x_i^t and g_i^t are the vectors of independent variables linked with the regression coefficients β and γ, respectively.

JGL Gamma Models: For the dependent variable glucose level=y_i as mentioned above, whose variance has two portions such that σ_i^2 (free of mean changes) and $V(\mu_i)$ (depends on the mean changes), while V (.) is considered as the variance function that identifies the GLM family distribution. For instance, if $V(\mu) = \mu$, it is Poisson, and it is gamma, or Normal according as $V(\mu) = \mu^2$, or $V(\mu) = 1$, etc.
Mean & dispersion JGLMs for Glucose level under gamma distribution are expressed by

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

where $g(\cdot)$ & $h(\cdot)$ are the GLM link functions for the mean & dispersion linear predictors respectively, and x_i^t, w_i^t are the vectors of dependent variables linked with the mean and dispersion parameters respectively. Maximum likelihood (ML) method is used to estimate mean parameters, while the restricted ML (REML) method is applied to estimate dispersion parameters [16].

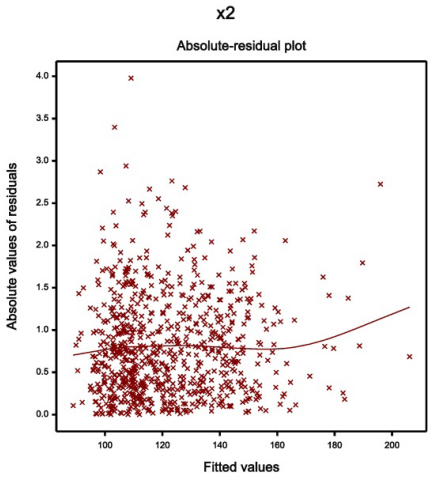
Statistical & Graphical Analysis

The dependent variable glucose level is modeled on the remaining dependent variables applying JGLMs under both the gamma and lognormal distribution. Here BMI, age, BP, ST, DPF, insulin, number of times pregnancy, types of sample units are treated as the independent variables. Here the dependent, or response variable glucose level is identified as heteroscedastic, so it has been modeled using JGLMs under both the distributions. The final glucose level JGLM has been taken based on the lowest Akaike information criterion (AIC) value (within each class) that minimizes both the predicted additive errors and squared error loss [17; p.203-204].Following the AIC criterion, the JGL gamma model (AIC=6991.420) gives better fit than log-normal fit (AIC=6996) as the AIC difference is greater than one which is significant. The final glucose level lognormal and gamma JGLMs analysis findings are reported in Table 1.

Model	Covariate	Gamma Fit				Log-Normal Fit			
		Estimate	s.e.	t(758)	P-Value	Estimate	s.e.	t(758)	P-Value
Mean	Constant	4.4135	0.0423	104.11	<0.0001	4.4100	0.0429	102.78	<0.0001
	BP (x3)	0.0006	0.0005	1.22	0.2228	0.0005	0.0005	1.09	0.2760
	ST (x4)	-0.0059	0.0019	-3.17	0.0016	-0.0059	0.0019	-3.15	0.0017
	BP*ST	0.0001	0.0001	2.07	0.0388	0.0001	0.0001	2.04	0.0417
	Insulin (x5)	0.0018	0.0003	5.58	<0.0001	0.0018	0.0003	5.59	<0.0001
	BMI (x6)	0.0035	0.0011	3.10	0.0020	0.0033	0.0011	2.93	0.0035
	Insulin*BMI	-0.0001	0.0001	-2.64	0.0085	-0.0001	0.0001	-2.55	0.0110
	Age (x8)	0.0044	0.0008	5.3	<0.0001	0.0041	0.0008	4.87	<0.0001
	Insulin*Age	-0.0001	0.0001	-3.55	0.0004	-0.0001	0.0001	-3.47	0.0005
	Type of Patient	0.1887	0.0157	11.97	<0.0001	0.1888	0.0158	11.91	<0.0001
Dispersion	Constant	-4.2422	0.2789	-15.206	<0.0001	-4.2433	0.2792	-15.195	<0.0001
	ST (x4)	0.0062	0.0040	1.541	0.1237	0.0058	0.0040	1.447	0.1483
	Insulin (x5)	0.0018	0.0014	1.236	0.2168	0.0018	0.0015	1.245	0.2135
	ST*Insulin	-0.0001	0.0001	-2.887	0.0040	-0.0001	0.0001	-2.859	0.0044
	BMI (x6)	0.0131	0.0080	1.652	0.0989	0.0122	0.0079	1.535	0.1252
	Age (x8)	0.0150	0.0046	3.228	0.0013	0.0168	0.0046	3.607	0.0003
	DPF (x7)	0.2326	0.1606	1.448	0.1480	0.2251	0.1603	1.404	0.1607
	AIC	6991.420				6996			

Table 1: Joint Log-normal and gamma model fittings of glucose levels.

The derived glucose level JGL gamma probabilistic model Table 1 is a data developed model which is tested using model diagnostic tools in Figure 1. For the fitted JGL gamma fitted glucose model Table 1, graphical diagnostic analysis is displayed in Figure 1. Figure 1(a) reveals the absolute residuals plot for the gamma fitted glucose level against the fitted values that is exactly flat straight line, concluding that variance is constant with the running means. Figure 1(b) displays the normal probability plot for the gamma fitted glucose mean model Table 1 that does not show any discrepancy of fit. Therefore, Figure 1 shows that the final gamma fitted glucose level model Table 1 is very close to its unknown true model.



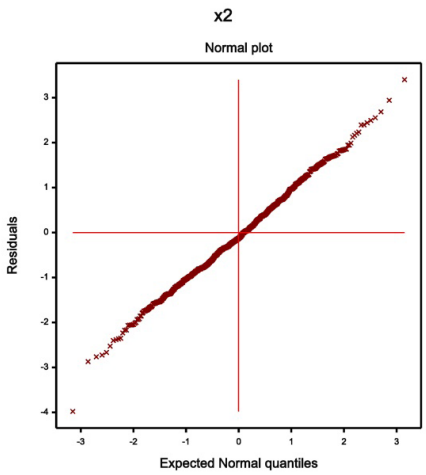


Figure 1(a) **Figure 1(b)**

Figure1: For the joint glucose fitted gamma model Table 1, the (a) absolute residuals plot against the glucose fitted values, and (b) the mean normal model of glucose probability plot.

Results and Discussion

Following Table 1, it is derived herein that mean glucose levels are negatively connected with ST (P=0.0016), while they are positively connected with the joint interaction effect of BP and ST (i.e. BP*ST) (P=0.0388), but they are insignificant with BP (P=0.2228).Mean glucose levels are positively connected with insulin (P<0.0001), BMI (P=0.0020) and age (P<0.0001), while they are negatively connected with the joint interaction effects Insulin*BMI (P=0.0085) and Insulin*Age (P=0.0004). Mean glucose levels are higher for pregnant diabetes women (P<0.0001) than non-diabetic. Variance of glucose levels is negatively connected with the interaction effect of ST*Insulin (P=0.0040), while it is insignificant of both ST (P=0.1237) and Insulin (P=0.2168).Variance of glucose levels is positively linked with age (P=0.0013), while it is partially positively connected with BMI (P=0.0989), and it is insignificant of DPF (P=0.1480). Some insignificant factors such as BP (in mean model), ST, Insulin (dispersion model) are included due to marginality rule given by Nelder [17], which states that if any higher order interaction effect is confounded, then all lower-order effects should be included in the model. Note that DPF is included in the model for better fitting [18]. In Epidemiology, a partially significant factor DPF (P=0.1480) is known as confounder.

Gamma fitted glucose mean () model from Table 1 is

= exp (4.4135 + 0.0006 BP -0.0059 ST + 0.0001 BP*ST + 0.0018 Insulin + 0.0035BMI - 0.0001 Insulin*BMI + 0.0044 Age - 0.0001 Insulin*Age + 0.1887 Type of patients),

and the gamma fitted glucose variance () model from Table 1 is

= exp (–4.2422 +0.0062 ST + 0.0018 Insulin -0.0001 ST*Insulin +0.0131BMI+ 0.015Age + 0.2326 DPF).

The effects of glucose on gestational diabetes women can be obtained by deriving an appropriate model of glucose on the remaining eight explanatory factors such as BMI, age, BP, ST, DPF, insulin, number of times pregnancy, types of patients. Both the JGL gamma and log-normal models are derived in Table 1. It is observed that the JGL gamma model is better fit than log-normal. Based on glucose level JGL gamma fit in Table 1, the above results are reported. From the gamma fitted JGL glucose level fit, the following can be easily reported.

Mean glucose levels are directly connected with the type of patients (1= non-diabetic, 2=diabetic) (P<0.0001), interpreting that they are always higher for gestational diabetes women than normal, which is observed in the real fields. The present analysis shows the real fact. Mean glucose levels are negatively connected with ST (P=0.0016), concluding that they are higher for pregnant women with thin ST level than others. But they are positively connected with the joint interaction effect BP*ST (P=0.0388), concluding that mean glucose levels are increasing if the joint effect of both BP and ST is increasing. Note that BP is not associated with mean glucose levels. Mean glucose levels are positively connected with age (P<0.0001), or BMI (P=0.0020), concluding that they are increasing as the age, or BMI is increasing. Generally, insulin level is negatively connected with the glucose level, but herein mean glucose levels are positively connected with insulin (P<0.0001), while they are negatively connected with the joint interaction effects Insulin*BMI (P=0.0085) and Insulin*Age (P=0.0004). These conclude that for higher joint effects of Insulin*BMI, or Insulin*Age, glucose levels are decreasing. Even though the marginal effect of Insulin is positively connected with the glucose levels, while the joint effects of Insulin*BMI and Insulin*Age are negatively connected with them. These current results are very special for pregnant diabetes women. For type 2 diabetes patients, it is seen that insulin is negatively connected with glucose levels, while the two interaction effects Insulin*Age and Insulin*BMI may, or may not be observed.

From Table 1, it is observed that the variance of glucose levels is negatively connected with the interaction effect ST*Insulin (P=0.004), implying that pregnant women with the higher interaction effect ST*Insulin should have very small scatteredness of glucose level. That is, the women with higher ST*Insulin level should have almost the same glucose level, which is normal level. In the mean model, it is observed that pregnant women with thick ST and higher insulin level should have lower glucose level. In other words, pregnant women with higher ST*Insulin effect should be non-diabetic. Variance of glucose levels is positively connected with age (P=0.0013), or BMI (P=0.0989), concluding that glucose levels are highly scattered for older, or obesity pregnant women. It implies that older, or obesity pregnant women may be diabetic, which is also supported by the mean model also.

The present findings support many practical situations which are frequently observed in the real society. There are very few articles which have focused the glucose level associations for pregnant women based on mean and dispersion modeling. So, the present results are not compared with the previous articles. Note that the number of pregnancies is independent of glucose level.

Conclusions

The present paper has presented the results based on comparison of two models such that log-normal and gamma fits. In addition, the final model has been chosen based on AIC criterion value, and model testing plots. Moreover, the standard errors of the estimates are very small for both the models, concluding that estimates are stable. Therefore, the research should have greater faith in the reported

results. One can verify the reported results based on the given data set. For similar data sets, the same results as reported herein should be reproduced, which is not tested herein as we have no similar data set. This report shows a very complicated functional relationship of glucose with the biochemical parameters. Both the mean and dispersion models can provide many interesting relationships, which are completely new to the researchers and practitioners. Therefore, patients, practitioners and researchers will be benefited from the report. Pregnant women should care for her glucose levels along with her BMI, insulin levels and ST.

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