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Consequence of War on Diabetic Mellitus patients in Tigray region, Ethiopia: a longitudinal study

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Abstract

Background Studies of the world health organization indicated that Diabetes is on the rise. The occurrence of diabetes is steadily increasing everywhere, most markedly in the world's middle and low-income countries. The aim of this study is to explore the consequence of war on the sugar level of diabetic mellitus patients.

Methods A retrospective longitudinal study with a sample of 67 diabetic mellitus patients was used. As a result, longitudinal different models, which are generalized linear mixed effects and nonlinear mixed effect models were fitted on the continuous response variable, the Sugar Level of the diabetic patients.

Results The results depicted that Blood Sugar Level of the patients increases over time. Moreover, as age, weight, medication, total cholesterol, high density lipoprotein (HDL), creatinine and linear time effect increase, Blood Sugar Level increases significantly, whereas triglyceride and low density lipoprotein increase, Blood Sugar Level of the adult Diabetes mellitus patients decreases.

Conclusion The war has significant effect on the poor control of blood glucose level of the adult diabetic patients in Tigray region, Ethiopia. Due to the war, siege or blockages, in return there were rare of medicine, the patients were not taking their medicines on time, and they did not get enough insulin as well.

Keywords Diabetic Mellitus, Sugar level, War consequence, Generalized Linear Mixed Model, Nonlinear Mixed Model

Introduction

Diabetes Mellitus (DM) remains one of the foremost concerns in life insurance, and it is responsible for premature death since its first description by Aristaeus in the third century. Diabetes mellitus is a condition in which the amount of sugar in the blood is too high because the body cannot use it properly. Means that it is a serious, chronic disease that occurs either when the pancreas does not produce enough insulin (a hormone that regulates blood pressure or glucose), or when the body cannot effectively use the insulin it produces. It is an important component of non-communicable diseases, is undoubtedly rising problem globally means that the number of patients and the prevalence of diabetes have been gradually increasing over the earlier few periods[1].

Studies of the world health organization (WHO) indicated that Diabetes is on the rise. No extended a disease of primarily wealth nations, the occurrence of diabetes is steadily increasing everywhere, most markedly in the world's middle and low-income countries [2]. Unfortunately, in many settings the lack of effective policies to create supportive environments for healthy lifestyle and the

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lack of access to quality health care are not being pursued. When diabetes is uncontrolled, it has dire consequences for health and well-being. In addition, diabetes and its complications impact harshly on the finances of individuals and their families, and as well the economies of nations [3].

Similarly, to other developing countries, little is done to quantify the prevalence of chronic diseases and their risk factors in Ethiopia. Small-scale surveys of bank employees in Addis Ababa and Ethiopia medical patients at different times have revealed the existence of these diseases and their risk factors; besides an increasing trend of myocardial infraction admissions were also recorded from 1988 to 1997[4]. A burden of disease analysis carried out in rural Ethiopia found that chronic diseases have contributed to 245 of disability-adjusted life year (DALY) lost compared to 72% for other health problems including communicable diseases. Currently, in Ethiopia DM is emerging as one of the major chronic health problems [5]. According to the Ethiopian Ministry of health, 22nd report on health and health-related signs, hypertension without mention of heart was the 9th cause of death nationwide in 2003/04[6]. In Ethiopia, lack of evidence population based prevalence study exist but hospital based studies shown the occurrence of diabetes entrance has increased from 1.9% in 1970 to 9.5% in 1990 of all medical admissions, and it accounts for about 7% of all deaths beyond 55 years age in the medical wards of referral hospital [7].

According to WHO estimate, the number of diabetic cases in Ethiopia in 2000 was about 800,000 and proper to increase to 1.8 heap by 2030 [8]. Empirical dispassionate remarks by us and so forth, suggesting an unusually extreme percentage of seeming type 1 diabetic sufferer in northerly Ethiopia. It has long happened famous that any of the phenotypic type 1 diabetic inmates in northerly Ethiopia are very thin, mainly male and 'commonly discontinued insulin but infrequently developed ketoacidosis'. We and so forth have pretended that by way of these dispassionate notes and the obvious past and present undernutrition in the field, these victims can have starvation-connected diabetes-mellitus [9]. For infrequently, exceptional phenotypes of diabetes had been situated in northerly Ethiopia, nevertheless have scarcely been completely examined. In the main capital city (Addis Ababa) and surroundings, stated that juvenility diabetes expected 'typical type 1' and 'clinically identical to away'. Similarly, standard type 2 diabetes, frequently followed by being overweight, is further visualized or in general area [10]. However, in the remote and weak northerly regions most diabetic patients visualized are young, thin and obviously have type 1 diabetes. This has happened stated from Mekelle and also from Gondar, accompanying an even taller fraction in rural districts [9]. Interestingly, nevertheless, these young and thin northerly Ethiopia diabetic patients exceptionally, if always, endure diabetic ketoacidosis and commonly survive regardless of missing provisions of insulin [11]. A recent survey from country Ethiopia repeated rooted the life of unusually abundant numbers of young (peak age 25 to 29 age) insulin-medicated patients (45% of the diabetic state of the hospital) accompanying low BMI. Most of these victims were weak livelihood peasants or were unemployed [12].

Diabetes, their complications and diabetic related deaths are increasing from time to time. Diabetes can eventually cause a variety of disabling and life-threatening complications. By investigating its trends, the way to survive the patients, its longitudinal effects, increasing public awareness of the seriousness of diabetes and its complications, as well as promoting good self-management and treatment among those diagnosed with the disease is key in combating the adverse health effects and economic burden to society associated with this disease [13]. Due to the war in Tigray Region, Ethiopia, and blockages, almost all clinic centers were run out of medicine and pharmaceutical tools. As a result, chronic disease patients were suffering by shortage of medicines. Therefore, studying the war effect on the diabetic mellitus patients is very crucial, and it gives insight about the effect of the war on the overall trend of the Patients FBS level and combating of the different types of burdens.

This was a longitudinal study to investigate the consequence of war on the sugar Levels of diabetic mellitus patients who were under follow-up and identifying their significant risk factors. Investigating such problem on the patients is very essential for the treatment, early detection and care of the disease. Hence, this longitudinal study was undertaken. In the short term, healthcare expenditure could be saved. In the long term, people as well as the government can understand the bad effect of siege especially for the chronic disease patients, a better prognosis, maintenance or improvement in quality of life in patients with diabetes mellitus.

Methods and materials

Study area

Mekelle, the capital city of the Tigray Region in northern Ethiopia, is bordered by several districts within the region. Mekelle is located in the Latitude of 13.4967° N and Longitude of 39.4750° E. Mekelle is 2,084 m above sea level, about 109 square kilometers area, and is about 783 km north of Addis Ababa, the capital city of Ethiopia.

Study design, source of data, and period

Based on the FBS dataset, this study employed a longitudinal study design with institutionally based data analysis. The data collection was conducted in January–February of 2022. The main objective of this study is to show the effect of the Tigray conflict on the trend of Fasting Blood Sugar Levels of diabetic mellitus patients who were under follow-up and identifying their significant risk factors.

Sample and sampling procedure

This study was conducted in Ayder Comprehensive Specialized Hospital (ACSH), Mekelle town, Tigray Region, Ethiopia. The needed sample was recruited by probability sampling technique. Simple random sampling technique was used to select the sample. The needed sample size (n) was calculated using the Yamane's formula since this method is important in case when the total population size is known [14]. The total number of adult diabetic mellitus patients in the ACSH (study population) is 2500 (N = 2500), and the sample was given as follows.

$$n = \frac{N}{1 + Ne2}$$

where, N = total population size, e = margin of error (sampling error). The margin of error was taken to be 0.12. Therefore, the sample size is, $n = \frac{2500}{1+2500(e^2)} = 67$. As a result, the measurements of 67 adult diabetic mellitus patients of ACSH were taken for this study.

Variables and data measurements

The dependent variable for this study was a continuous variable, the monthly records of Fasting Blood Sugar, of diabetic mellitus patients who were under follow-up in the Ayder Comprehensive Specialized Hospital, Mekelle, Ethiopia. These records were obtained from the electronic medical records (EMR) (Smart care). The independent variables include demographic information such as patient's age, gender, weight, and other clinical related variables which may identify medical conditions/comorbidities; and risk factors such as time since initial diagnosis of diabetes, and so on. Consistent with longitudinal analysis techniques, patients were measured their Fasting sugar level monthly during the Tigray war, in the siege time. Since the measurements of each subject were repeated monthly, number of measurements of the subject's FBS level may not be equal as some of subjects miss their follow-up period because of different reasons as the people was within the war.

Generalized linear mixed effects models

The generalized linear mixed-effects model is particularly important in cases where some degree of linearity is preserved. This means that generalized linear mixed models can sometimes be nonlinear in a limited way [15]. Generalized linear mixed models are generalized linear models that include multivariate normal random effects in the linear predictor. The first papers to explicitly address this idea are in the frequentist and Bayesian frameworks. The term "generalized linear mixed model" seems to have been invented by [16, 17]. In GLMMs, the mean response model depends on both the covariates used and the unobserved random effects; it is the inclusion of the latter that produces a marginal correlation between repeated responses when averaging over the distribution of random effects. The generalized linear mixed model was given as follows:

$$\mathrm{h} - 1\{\mathrm{E}(\mathrm{Yij}|\mathbf{b}\mathrm{i})\} = \boldsymbol{X}\boldsymbol{ij}\boldsymbol{\beta} + \boldsymbol{zij}\boldsymbol{bi} + ei$$

For some known link function, $\mathrm{h}-1(\cdot)$. The conditional variance is assumed to be dependent on the conditional mean according to $\mathrm{Var}(\mathrm{Yij}|\mathbf{b}\mathrm{i}) = \phi\mathrm{v}\{\mathrm{E}(\mathrm{Yij}|\mathbf{b}\mathrm{i})\}$, where $\mathrm{v}\{\mathrm{E}(\mathrm{Yij}|\mathbf{b}\mathrm{i})\}$ is the known variance function and ϕ is a scale parameter which may be known or may need to be estimated. In GLMMs the regression parameters have "subject-specific" interpretations. They represented the effects of covariates on changes in an individual's possibly transformed mean response per unit change in the covariate, while controlling for all other covariates and the random effects [18].

Non-linear mixed-effects models

The non-linear mixed effect model is best accepted framework when the relationship between the response variable and predictors is inherently non-linear [18]. In such models, the mean response is non-linear in the regression parameters and the random effects. It is perceptive to fit these models in two stages: a model for intra-individual (within subject) variability joined with a model for inter-individual (between subjects) variability.

The first-stage model specifies the mean and covariance structure for a given individual (subject-specific mean and covariance). In the first stage, we assume that the mean response for the i^{th} individual at the j^{th} measurement can be expressed in terms of a non-linear regression function and random error as follows:

$$Yij = f\left(xij, \beta i\right) + eij$$

where e_{ij} is a random error term with $E(e_{ij}|\boldsymbol{\beta}_i) = 0$. In this model, the regression function depends on a non-linear way on a set of subject specific regression parameters, $\boldsymbol{\beta}_i$. Even though, the functional form, $f(\cdot)$, is the same for all subjects, differences between individuals in their longitudinal response paths are accommodated by allowing for different $\boldsymbol{\beta}_i$ (as well as differences in the covariates, $\boldsymbol{X}_{ij}$).

The first-stage model characterizes intra-individual variation in the response over time. In contrary, the second-stage models characterizes inter-individual variation in the regression parameters $\boldsymbol{\beta}_i$. For example, to account for inter-individual variation among the $\boldsymbol{\beta}_i$, it might be assumed that the $\boldsymbol{\beta}_i$ depend linearly on a set of covariates.

$$\beta i = Xi\beta + bi$$

where the random effects, $\boldsymbol{bi}$ assumed to have zero mean and covariance matrix, G, $\boldsymbol{bi} \sim N(\mathbf{0}, G)$. Where $d(\cdot)$ is an acknowledged vector-valued function. (b) indicated that we can model $\boldsymbol{\beta}_i$ as a non-linear function of $\boldsymbol{\beta}$. The two-stage specification of the non-linear mixed-effects model given above provides a very general and rich class of models for the analysis of longitudinal data [18]. A characteristic of non-linear mixed-effects models is that inference usually focuses on features or mechanisms that underlie the subject-specific longitudinal response trajectories and how these fluctuate across subjects in the population. By modeling the response at the individual level, the components of $\boldsymbol{\beta}$ describe the typical subject-specific effects of covariates on the mean response over time [18].

Before the model building and model extension, the missing values were imputed using non-monotone missing value multiple imputation mechanism. Multiple imputations (MI) were officially familiarized by [19], and the key principle of the MI procedure is replacing each missing value with a set of M plausible values which are drawn from the distribution of the given data set. The missing values were filled in M times to complete M complete data sets using the PROC MI procedure in SAS. The imputed data set was then analyzed using standard procedures for complete dataset.

In order to check the normality assumption of the random effects, histogram as well as scatter plot matrix of Empirical Bayes (EB) estimates of the random effects were given in Fig. 4 for GLMM. Since these parameters are expected to be stochastic, Bayesian methods were applied. Therefore, the obtained estimates are called Empirical Bayes (EB) estimates, which are the expected random effects, conditional on the observed data for that specific subject. In practice, histograms/ or scatterplots of EB estimates are used to show the normality assumption as well as to detect outlying profiles. On the other hand, random effects reflect how specific subjects' estimates deviate from the population average [20].

Results

Below Fig. 1 shown the sugar levels profile for some randomly selected adult diabetic mellitus patients over time. It can be observed that there seems much between as well as within subject's variability, and which is indicated that models that can accommodate such variabilities should be used. Moreover, it can be explained that the patients have different sugar levels at baseline as well as they have different progress of sugar level over time which implied that random slope might be required in the model (Fig. 1). As there are missing observations, the number of measurements per subject is different.

On the other hand, the overall mean structures with respect to categorical covariates gender and medication was depicted in figs. 2 and 3 with their standard error bars. The length of the bars of the standard error within the plots indicated the amount of the variability. As the bars have higher length, there is higher standard error, and then there could be higher variability. Although in some months seem to show no-increment, as a general the overall mean structure plot for gender (Fig. 2), and initially indicated that at baseline, both males and females have similar average sugar level, however, as time

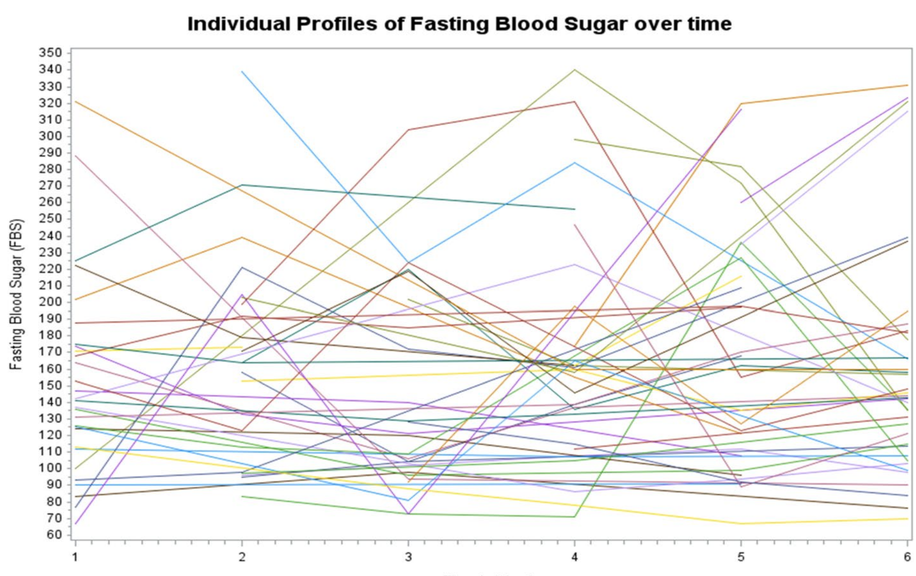

Fig. 1 Individual profile plot of sugar level over time

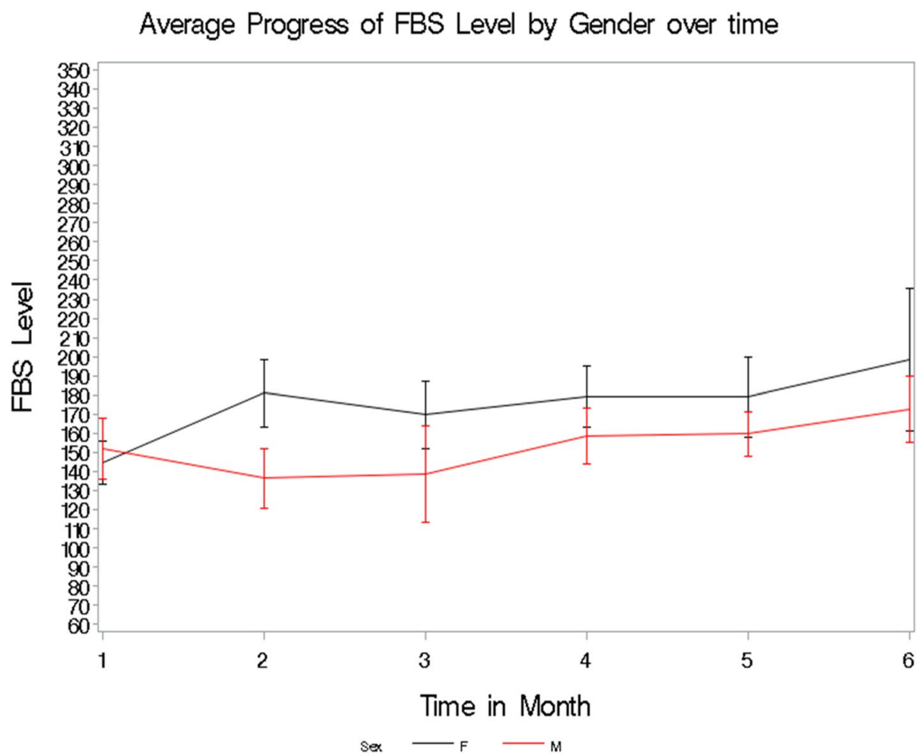

Fig. 2 Mean structure plot of FBS by Gender

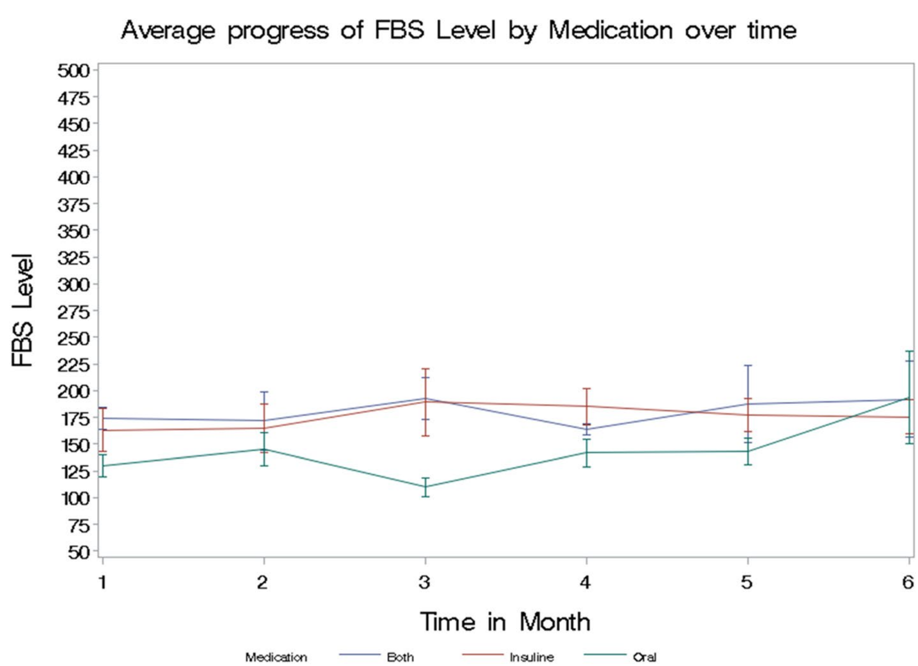

Fig. 3 Mean structure plot of FBS by Medication

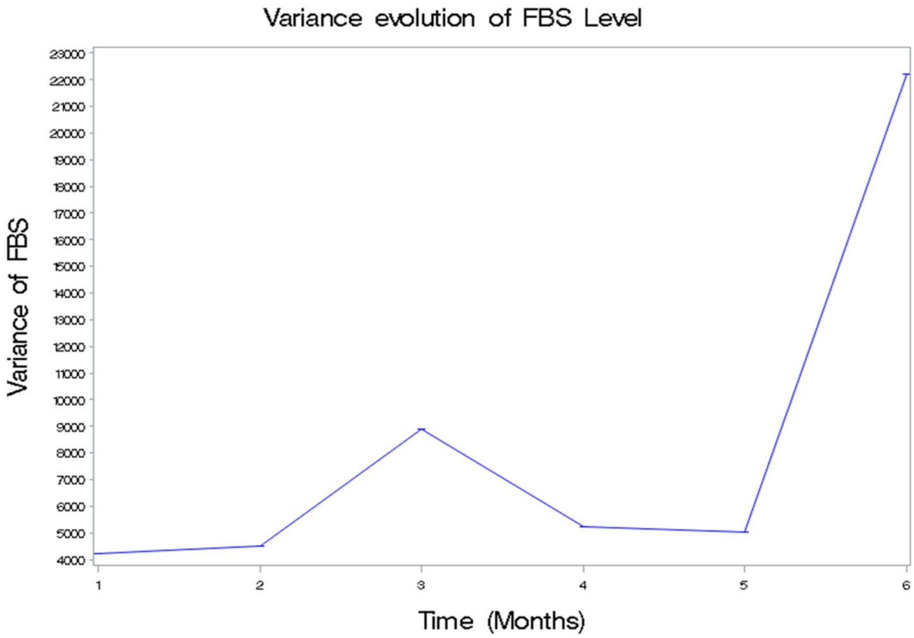

Fig. 4 Variance structure plot over time

increases, mean sugar level of females become higher than that of the males.

The mean structure plot of the sugar level by medication over 6 months was also shown below (Fig. 3). Starting from baseline, the average sugar level for the diabetic patients who took medication insulin is lower than those of who took medications oral and both over time(per month). In addition, the mean structure plot of fasting blood sugar versus time in month revealed that the progression of the FBS level might not follow linear time trend, but it might follow cubic time trend.

The variance structure plot was depicted in Fig. 4, and included the variance of FBS level versus time in months. The fluctuation (up and down) of the graph indicates the instability of the overall variance. As observed from the graph (Fig. 4), the variances for the observations measured at time 6 and at time 3 are very high compared to the other ones though the overall variance is considerably high. It was observed that the variance seems to fluctuate up to month five. However, after month five to month six, the variance increases fastly. This figure suggested that variance could not be constant, and this is the indication that the models to be used should consider the between as well as the within variabilities.

Table 1 represented the tests for the time trend which should be included in the model. It was observed from the table which represents the results of F_{meta}, that cubic time effect is adequate to explain the total within subject variability for each subject in the data. The p-value = 0.0787 for the quartic time effect showed that

Table 1 Model Checking

1.1. Checking for model extension			**1.2. Comparison of models to check whether random effect(s) are needed.**		**1.3. Comparison of Models to select the best on for parameter estimation.**		
			Model	**Log likelihood**	**Model**	**AIC**	**Log Likelihood(LL)**
Model	F-value	*P*-value	1: With no random effect	-58558.95	Generalized Linear Mixed Model (GLMM)	107060.0	-53519.0
Linear	24.012	<0.0001	2: With only random intercept	-58105.2	Nonlinear Mixed Model (NLMM)	116587	-58287.5
Quadratic	65.0527	<0.0001	3: With random intercept and random slope	-56624.1			
Cubic	53.9426	<0.0001	4: Random intercept and quadratic slope	-54935.45			
Quartic	41.1079	0.0787	5: With random intercept and cubic slope	-53518.95			

this quartic time has no significant effect if it would be included in the model. As a result, the highest time effect which includes in the model is the cubic time effect.

Tests for variance components of the random effects: In a number of situations, it may be interest of knowing whether variance components are equals to zero. Absence of any heterogeneity between measurements within a subject would be reflected in $\sigma = 0$. It could be of interest to test H_0: $\sigma^2 = 0$ versus H_A: $\sigma.^2 > 0$. Table 2

The above reported *p*-values are based on the N (0,1) approximation to the Z-statistic, i.e., this could not reflect to the correct sampling variability in the estimation of the variance components as these are estimated under the restriction of being positive. As a result, these classical p-values require correction, of course this correction depends on the type of model, sometimes needs simulation methods. In this case, the correction needs to reduce the reported *p*-values by halve [21]. After taking the correction, all the *p*-values become < 0.00005 which indicates highly significance. We can observe that the p-values are all very small, and indicated that the covariances are all different from zero.

As it can be observed from the histogram as well as the scatterplot matrix (Fig. 5), there are some patients with large values of FBS in both models estimates. The histograms as well as the scatter plots matrix seem to suggest that the normality assumption for the random effect is questionable.

Of course, we should realize that the precision of these random effects depend on many aspects, and can vary from subject to subject, and therefore, these plots do not necessarily reflect non-normality of the random effects.

Table 2 Variance–Covariance matrix and its estimates

Parameter	Variance–covariance	*P*-value	Parameter	Variance–covariance	*P*-value
b_{0i}	67,917	<.0001	b_{2i}	8195.51	<.0001
b_{1i},b_{0i}	−74,119	<.0001	b_{3i},b_{0i}	−1968.43	<.0001
b_{1i}	85,987	<.0001	b_{3i},b_{1i}	2389.01	<.0001
b_{2i},b_{0i}	21,928	<.0001	b_{3i},b_{2i}	−768.90	<.0001
b_{2i},b_{1i}	−26,157	<.0001	b_{3i}	74.0872	<.0001
Residual	2216.98	<.0001			

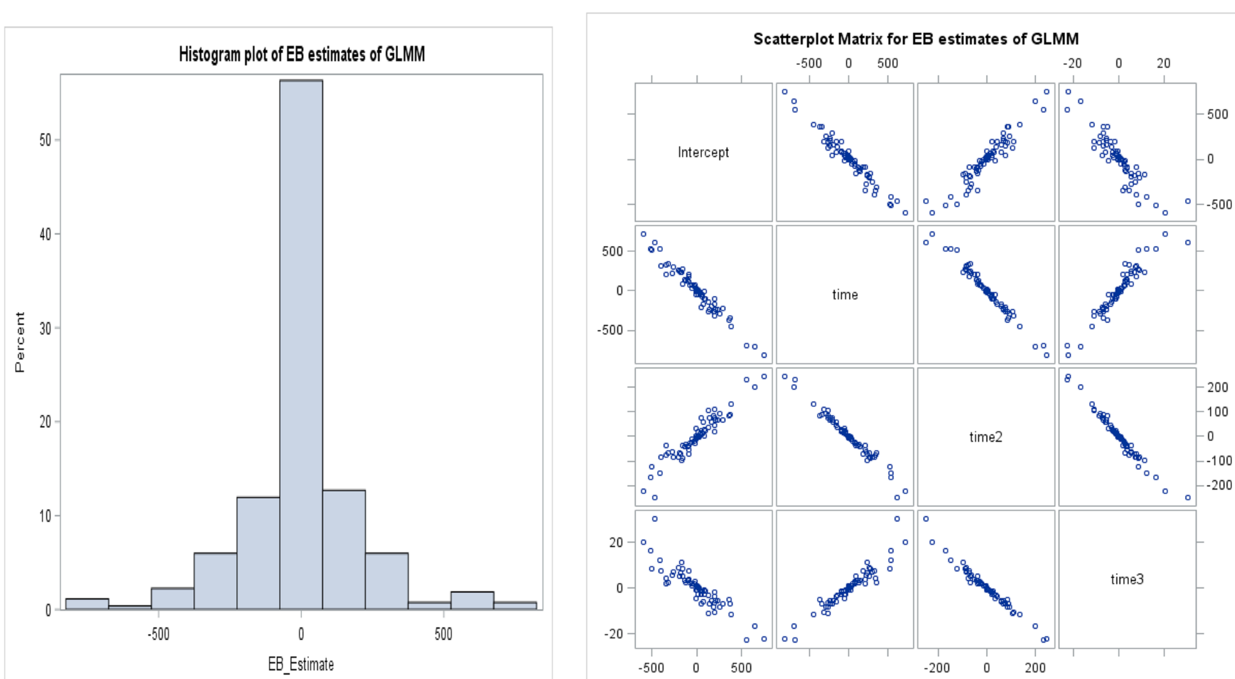

Fig. 5 Histogram and scatter plot of empirical Bayes (EB) estimates of GLMM

Although inferences about the fixed effects are very robust even with respect to model deviations, providing that the data set contains sufficient independent subjects, the normality assumption for the random effects may not be tested within the context of the generalized linear mixed model, but model extension are required. As a result of model extension, model comparisons were followed.

When a method comprises a subset of predictors from a more complex model, the difference in log likelihood forms a chi-square test statistic that can be tested against a chi-square distribution with degrees of freedom equal to the difference in the number of parameters between the full model and the reduced model. But, in some instances in iterative model building, one model is not necessarily a subset of another. In such cases, comparison of AIC values is useful, with lower values showing a better model. AIC used the log likelihood values from each model, but it adds a penalty for including unnecessary predictors to the model that might add little to the overall relationship. A summary of the generalized linear mixed model (GLMM) and nonlinear mixed model (NLMM) were given in Table 1 (Table 1.3). As it can be observed, the AIC = 107,060 for GLMM is smaller than that of the NLMM, AIC = 116,587. Although there is no statistical test to determine the significance of the difference in AIC values, the AIC value of GLMM is smaller than that of the NLMM (as is the log likelihood values). Therefore, GLMM is used as the final model, and parameter estimates were taken from it.

Inference on fixed effects

Ketone and other all interaction variables were excluded from the models in the variable selection stage since they were observed to be insignificant (Table 3). Age, weight, medication (insulin), cholesterol, TGA, HDL, LDL, Cr, and linear time in months have significant effect on the mean Sugar level of the DM patients, and the rest variables have not significant effect. An increment in age, it showed that there is significant increment in the average FBS value. Holding constant the other predictors, as age increases by one unit, the average value of FBS also increases by 1.719 mg/dL. An increase in the weight of the patients, there is significant increase in the mean value of FBS level of these patients. Holding constant the effect of the rest predictors, when weight increases by one kg, the average value of FBS level increases by 1.506 mg/dL. It was also observed that patients who took medication type of insulin tend to have higher increase in the average FBS levels over time as compared to the oral medication type. This means, the patients who took oral medication have lower average sugar level than the patients who took medication type of insulin. Furthermore, holding constant the effect of the other predictors, as the cholesterol value increases by one mg/dL, the mean value of sugar level of the DM patients increases by 1.232 mg/dL.

On the other hand, a unit increase in TGA tends to increase the mean value of sugar level by 0.243 mg/dL, fixing constant the effects of the other predictors. As the high density lipoprotein (HDL) increases by one mg/dL, the mean sugar level of the DM patients decreases by 1.13 mg/dL, however, when there is a unit increase in the low density lipoprotein (LDL), there is an increase in the average value of FBS level by 1.35 mg/dL. Additionally, the effect of Cr also revealed significant effect on the FBS level of the adult DM patients, and implied that patients who have abnormal Cr tend to have higher value of average FBS level as compared to those who have normal average value of Sugar level. It was also observed that there was a significant effect of time in month on the mean value of FBS level, which implied that fixing constant the effect of other predictors, when time increases, the mean value of the patients' FBS level increases. Figure 5

Table 3 Fixed effects parameter estimates of GLMM

Effect	Estimates	Std. err	*P*-value	Effect	Estimates	Std. err	*P*-value
Intercept	−183.50	52.445	0.0009*	TGA(mg/dL)	0.243	0.0233	< .0001*
Age(in years)	1.719	0.593	0.0037*	HDL(mg/dL)	−1.130	0.0659	< .0001*
Sex (F)	−2.855	8.939	0.7494	LDL(mg/dL)	1.350	0.110	< .0001*
Weight(in kg)	1.506	0.396	0.0001*	Cr(Abnormal)	53.855	19.512	< .0058*
Medication(Both)	12.939	14.730	0.3797	Comorbidities(No)	1.997	10.077	0.8429
Medication(Insulin)	22.812	9.587	0.0174*	Time(in month)	81.862	36.243	0.0272*
Cholesterol (mg/dL)	1.232	0.104	< .0001*	time2	−12.910	10.942	0.2423
time3	1.209	1.042	0.2499				

* Indicates significant at 5% level of significance. From medication oral (oral hypoglycemic agents), from Gender male, from the DM patients who have comorbidity (1) and from Cr normal, are reference categories

Inference on random effects

It was observed that there was a significant random intercept, random time slope, random quadratic time and random cubic time effects on the Sugar level of the adult diabetic patients. From the random effects results, a negative correlation was revealed between the intercept and time effect, and which implied that the patients those start with low FBS levels at baseline tend to have a larger increase over time. In addition to that, the individual patients' intercepts of the diabetic patients highly positively deviate from the average estimated intercept while the individual slopes of the patients highly negatively deviate from the average estimated slope. Furthermore, empirical Bayes estimates for the random effects were obtained in order to check for the presence of outlying observations. As shown in Fig. 4, it seems there are no potential outlying observations that may affect the obtained results. There were also revealed from the figures that there seems moderate to high correlations between the random effects.

Discussion

Using the diabetic patients' dataset, this study empirically explored and determined the potential risk factors that were linked to the Fasting Blood Sugar (FBS) level of the diabetic patients as well as the effect of time in the Ayder Comprehensive Specialized Hospital (ACSH), Mekelle town, Tigray Region, Ethiopia. Thus, the FBS level in the ACSH was examined over time, along with its related risk factors, using the GLM, and the NLM models analysis. Age and weight from the sociodemographic variables have significant effect on the control of blood glucose level. This is may be due to more sedentary lifestyle as the age goes up which is depicted similarly in different studies. As body weight increase by 1 kg, fasting blood glucose level increase by 1.5 mg/dl, and it coincided with the WHO's Global Report on Diabetics study [1].

The predictor variables creatinine, triacylglycerol and lipid profile, especially the HDL has significant effect on the fasting blood glucose level of the patients, which coincided with the study done in Addis Ababa, Ethiopia [4]. However, HDL is insignificant in the study which was done in the northern Ethiopia [6], and which opposed our study. Besides, the medication type of insulin as well as the cholesterol level of the patients has significant effect on the fasting blood glucose level, which showed the same result as the study done by [1, 4, and 6]. Moreover, the linear time also has clear significant effect, with which as the linear time increases, shows an increasing effect on the fasting blood glucose level of the diabetic patients.

Conclusion

We found that the average control of blood glucose level measured during the fasting state over six-month period was 164.98 mg/dl and it increase from month one through month six serially, which means the degree of blood glucose level was tends to have badly control as the patients stayed more with in the war and intensified siege. The reasons for this poor control of blood glucose level in our study may be; the scarcity of the medications which leads to decrease the dose or interruption their treatment, absence of electricity for keeping insulin in refrigerator, non-adherence to non-pharmacological treatment which are visible in the ground as a result of the war, siege and blockages.

From the study, other predictors like lipid profile and type of specific diabetic medications showed significant association with the control of blood glucose level of the participants. The total cholesterol level, triglyceride, low density lipoprotein has a negative association with the degree of blood glucose level. But having higher value of high density lipoprotein contributes for the good control of blood glucose level. This is an indication that diabetes mellitus patients with dyslipidemia has poor control of blood glucose level even during the stressful condition of war and siege and coincided with other different studies. To sum up, the average control of blood glucose level measured during the fasting state over six-month period was poorly control and it becomes worsened as the war and siege more intensified from month one through month six serially. Our study also showed that diabetes mellitus patients with dyslipidemia and chronic kidney disease had poor control of blood glucose level even during the stressful condition of war and siege.

Abbreviations

DM	Diabetic Mellitus
FBS	Fasting Blood Sugar
GLMM	Generalized Linear Mixed Model
NLMM	Nonlinear Mixed Model
WHO	World Health Organization
BMI	Body Mass Index
DALY	Disability-adjusted life year
EMR	Electronic Medical Records
MI	Multiple Imputations
SAS	Statistical Analysis System
LL	Likelihood; EB = Empirical Bayes
AIC	Akaike Information Criterion
TGA	Triglyceride
HDL	High Density Lipoprotein
LDL	Low Density Lipoprotein
Cr	Creatinine
mg/Dl	Milligrams per deciliter

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Authors' contributions

Mehari Gebre Teklezgi conceived the original idea of the study, designed the study, analyzed the data, statistical analysis, and drafted the manuscript. Dr.

Mengistu Berhe Tekle was involved with the conception of the study, interpretation, and revision of the manuscript. Gebru Gebremeskel Gebrerufael was involved in drafting, manuscript structure, and revision of the manuscript. Tesfu Solomon Yeebyo was involved designing the study and revision of the manuscript. All authors read and approved the final manuscript of this study.

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Data availability
The datasets used in this study is in the hand of the corresponding author Mehari Gebre Teklezgi (email: meharistat@gmail.com), and it can be provided if needed.

Declarations

Ethics approval and consent to participate
The need for the ethical approval was waived by the ethical review office (ERO) of College of Health Science, Mekelle University. Moreover, since the study relies on secondary data, and it was in the war time, no individual informed consent is needed. The individual informed consent was waived by the ethical review office (ERO) of College of Health Science, Mekelle University. The University's research regulations were followed in every way during conducting the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References
1. WHO, (2016). Global Report on Diabetics.
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010;33:S62–9.
3. Bommer C, Heesemann E, Sagalova V, Manne-Goehler J, Atun R, Bärnighausen T, Vollmer S. The global economic burden of diabetes in adults aged 20–79 years: a cost-of-illness study. Lancet Diabetes Endocrinol. 2017;5(6):423–30.
4. Frances T, Oli K. Chronic Non Infectious Diseases of Adults. The Ecology of Health and Disease in Ethiopia, Shama Books. 2006;21:702–12.
5. Tamiru, S. and Alemseged, F. (2010). Risk Factors for Cardiovascular Diseases among Diabetic Patients. In Southwest Ethiopia. Ethiop J Health Sci; 20: 121–128. (Tamiru and, Alemseged, 2010).
6. Ministry of Health, Ethiopia (2003/2004). Health and Health related Indicators in Ethiopia.
7. Gill, G. V., Tekle, A., Reja, A., Wile, D., English, P. J., Diver, M., ... & Tesfaye, S. (2011). Immunological and C-peptide studies of patients with diabetes in northern Ethiopia: existence of an unusual subgroup possibly related to malnutrition. Diabetologia, 54, 51–57.
8. Feleke Y, Enquselassie F. An Assessment of the Health Care System for Diabetes in Addis Ababa. Ethiopian Journal of Health Development. 2005;19:203–10.
9. G. V. Gill & A. Tekle & A. Reja & D. While & P. J. Englis h & M. Diver & A. J. K. Williams & S. Tesfaye (2011). Immunological and C-peptide studies of patients with diabetes in northern Ethiopia: existence of an unusual subgroup possibly related to malnutrition. 54:51–57. https://doi.org/10.1007/s00125-010-1921-7.
10. Lester FT. The clinical pattern of diabetes mellitus in Ethiopians. Diabetes Care. 1984;7:6–11.
11. Habtu E, Gill G, Tesfaye S. Characteristics of insulin requiring diabetes in rural northern Ethiopia—a possible link with malnutrition? Ethiopian Med J. 1999;37:263–7.
12. Derbachew Asfaw, Fikre Enquoselassie, and Cheru Atsmegiorgis (2015). Survival Analysis of Diabetes Mellitus Patients Using Parametric, Non-Parametric and SemiParametric Approaches: Addis Ababa, Ethiopia. Vol 7, no 1,: pp(20 -39).
13. Lin, X., Xu, Y., Pan, X., Xu, J., Ding, Y., Sun, X., ... & Shan, P. F. (2020). Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Scientific reports, 10(1), 1–11.
14. Israel, G. D. (1992). Determining sample size.
15. Verbeke G, Molenberghs G. Advanced Modeling Techniques. Diepenbeek: Course Note; Hasselt University; 2017.
16. Wong GY, Mason WM. The hierarchical logistic regression model for multilevel analysis. J Am Stat Assoc. 1985;80:513–24.
17. Gilmour AR, Anderson RD, Rae AL. The analysis of binomial data by a generalized linear mixed model. Biometrika. 1985;72:593–9.
18. Lee Y, Nelder JA, Pawitan Y. Generalized Linear Models with Random Effects: Unified Analysis via H-likelihood. Boca Raton, FL: Chapman & Hall/CRC; 2006.
19. Fitzmaurice, G., Davidian, M., Verbeke, G. and Molenberghs, G. (2008). Longitudinal Data Analysis. Department of Biostatistics, Harvard School of Public Health, Boston, MA, U.S.A.
20. Rubin DB. Multiple Imputation for Nonresponse in Surveys. New York: John Wiley & Sons; 1987.
21. Laird NM, Ware JH. Random effects models for longitudinal data. Biometrics. 1982;38:963–74.