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A LONGITUDINAL RECORD ANALYSIS ON RISK DETERMINANTS FOR DIABETES MELLITUS: IN AYDER REFERRAL HOSPITA TIGRAY REGION, ETHIOPIA

[1]Fekade Getabil, [2]Wudneh Ketema*,[3]Mengistu Amare

First Author

[1]Fekade Getabil , DebreBerhan University, College of Natural Sciences, Department of Statistics
feka_get2002@yahoo.com

Co Authors

[2]Wudneh Ketema*, DebreBerhan University, College of Natural Sciences, Department of Statistics
wudnehketema@gmail.com

[3]Mengistu Amare, Mekele University, College of Natural Sciences, Department of Statistics
mengistuamare68@gmail.com

***corresponding Author**

[2]Wudneh Ketema*, DebreBerhan University, College of Natural Sciences, Department of Statistics.
Wudnehketema@gmail.com

ABSTRACT

Background: *Diabetes mellitus (DM) is set of metabolic infections arranged by hypernym glucose levels that outcome from blemishes in either insulin emission or its adventure. This is characterized by long suffering disease with a high frequency and a growing anxiety in worldwide.*

Objectives: *The study mainly be situated on longitudinal analysis of diabetes mellitus risk factor by utilizing fasting blood glucose level and identify the associated risk factor of patients in Mekele and surrounding area, Tigray Ethiopia.*

Method: *This study used a retrospective data of DM patients demographic and health survey was conducted on patients from April, 2018 to February, 2020 by collaboration with Minster of health and other stockholders. The entire number of patient contained within this study was 210. The data analysis began with descriptive statistics followed by exploring structure of fasting blood glucose data set Using SAS 9.4. The study used linear mixed effect model to perform the final model fit, and a number of methods were used to conduct the model diagnosis.*

Result: *the final model fit indicates that patient from total of 210 DM patients were studied to analyze the longitudinal data. Time was one factor that significance affect to patient of FBG level (p-value<0.0001) and estimate (0.0247), the rate of change in logFBG level is 0.024per unit increase in time. This proposes that the extent of progress in logFBG level increments with time.*

Conclusion: *The result from this investigation revealed that visiting times, BP (diastolic), types of diagnosis (type1) and educational level (primary) had statistically significant effect on the longitudinal bio-marker and missing after imputation observed that time (duration of follow up), patients that are not hypertensive, type one diabetes were negatively significant effect factors for fasting glucose level count progression.*

Keywords*:* Diabetes mellitus, linear mixed model, longitudinal data analysis, FBG

Background

Diabetes mellitus is a social occasion of metabolic ailments portrayed by high glucose levels that result from gives up in either insulin emanation or its movement [1].

Diabetes mellitus is one of various constant diseases with multi-framework inconveniences [1]. It is an intricate, constant issue requiring perpetual therapeutic consideration with multifactorial danger decrease procedures outside glycemic ability to control. Long stretch disarrays consolidate cardiovascular disease, stroke, progressing kidney ailment, foot ulcers, mischief to the nerves, damage to the eyes and scholarly shortcoming [2].

The two sorts of diabetes are Type1 diabetes results from the pancreas' failure to convey enough insulin due to loss of beta cells [3]. This structure was recently alluded to as "insulin-subordinate diabetes mellitus" (IDDM) or "adolescent diabetes"[3]. Type2 begins with insulin resistance, a condition wherein cells disregard to respond to insulin appropriately [4]. This structure was as of late suggested to as "non-insulin-subordinate diabetes mellitus" (NIDDM) or "grown-up beginning diabetes" [4]. The most notable explanation is a mix of inordinate body weight and lacking activity [4]. Counteraction and treatment incorporate keeping up a strong eating routine, standard actual exercise, acustomary body weight, and keeping up a key good ways from usage of tobacco [5]. Control of circulatory strain and keeping up authentic foot and eye care are huge for people with the contamination. Type 1 diabetes must be managed with insulin imbuements [5].

Type 2 diabetes may be treated with solutions with or without insulin [6]. Insulin and some oral medications can cause low glucose [7]. Weight decrease operation in those with strength is once in a while a convincing measure in those with type 2 diabetes [8].

A few signs and side effects can check the beginning of diabetes despite the fact that they are not explicit to the illness [9]. Deferred high blood glucose can cause glucose maintenance in the point of convergence of the eye, which prompts changes in its shape, achieving vision changes. Long stretch vision adversity can moreover be achieved by retinopathy [10].

Like the rest of the world, sub-Saharan African countries are experiencing a growing inescapability of diabetes close by other non-communicable diseases [11]. The predominance of diabetes in sub-Saharan Africa is around 7%, like patterns being seen overall are quickly raising [12].In 2015, the IDF assessed that there were 14.2 million individuals with diabetes in sub-Saharan Africa. This number is relied upon to increment to 34.2 million patients by 2040. Pervasiveness is exceptionally shifted between nations, with predominance going from a low of 0.6% in Benin to a high of 18.2% in Reunion, off the shoreline of Madagascar [12]. The larger part (59%) of individuals with diabetes live in urban communities, despite the fact that the populace is overwhelmingly (61%) country. This district has additionally the most noteworthy extent of beforehand undiscovered diabetes; more than 66% (67%) of individuals with diabetes being ignorant they have the sickness **[13].**

The assessed predominance of diabetes (type 1 and type 2)joined, both analyzed and undiscovered in individuals matured 20–79 years has ascended from 151 million (4.6% of the worldwide populace at that point) to 463 million (9.3%) today [14]. Without adequate activity to address the pandemic, we foresee 578 million individuals (10.2% of the populace) will have diabetes by 2030. That number will leap to an amazing 700 million (10.9%) by 2045 **[14]**.

The predominance of diabetes in many territories of Ethiopia seems to have expanded from that assessed by the IDF in 2015 (for example 3.9%), that is higher variety in diabetes predominance across various territories of Ethiopia, 0.3% and 7.0% for the least and the most noteworthy pervasiveness individually (IDF, 2015).

The predominance of prediabetes in the current examination was discovered to be 15.9%. This is higher than the assessed Ethiopian public predominance of 6–8% [15] and this recommends that the pervasiveness of DM in the investigation zone may increment soon as there is a danger of movement of prediabetes condition to diabetic **[16].**

Diabetes can even now impact each day social cooperation’s from numerous points of view from all locales up to the world [17]. In this investigation the exploration group worries to survey the components that influence the FBG level of diabetic patients. The groups were likewise intrigued to gauge the pace of progress of FBG profile experienced by patients after some time. Under this inquire the FBG level data of diabetic patients were analyzed using longitudinal depends on the nature of the response or dependent variable, which contain repeated observation (response) for each individual and have continuous nature. When the response variable has approximate normal distribution (Gaussian), perhaps after transformation, as is often the case with continuous response. In this examination of longitudinal information, the mean profiles were assessed by direct blended impacts model.

Methodology and Data Source

All type I and type II DM patients' on follow up retrospectively in FBG level measurement from 23 April 2018 to February 2020 that will be conducted under repeated in three months.

Data Source and Description

For this study, data was obtained from Ayder Referral Hospital Diabetic Mellitus Outpatient Clinic follow up. All follow-up contains epidemiological, laboratory and clinical information of all Diabetic patients.

Longitudinal Data Analysis:

The objectives of longitudinal information examination are to analyze and think about reactions after some time. The characterizing highlight of a longitudinal information model is its capacity to contemplate changes after some time inside subjects and changes after sometime between gatherings. For instance longitudinal models can assess singular level subject-explicit relapse boundaries and populace level relapse boundaries. Longitudinal informational indexes vary from time arrangement informational indexes on the grounds that longitudinal information for the most part comprises of countless a short arrangement of time focuses. Be that as it may, time arrangement informational collections typically comprise of a solitary, long arrangement of time focuses **[18]**.

Most focused on point of statistical examination is to address varieties in the data. For longitudinal data; within- subject variety is in the estimations inside each subject, and between-subject variety is variety in the information between within-subjects. Modeling within-subject variation permits studying fluctuations over time, while modeling between-subject discrepancy allows understanding differences between subjects. In longitudinal studies the outcome variable can be continuous, binary or count. The data set can be incomplete (missing data/dropout) and subjects may be measured at different occasions.

Linear Mixed Model (LMM)

The study considered the changes in the FBG levels in diabetes patients on treatment over the period of study. By thinking about changes over the long time, the mixed effects model for longitudinal information examination approach has the additional preferences of noticing changes all the more precisely by expanding the force and legitimacy of estimating the change in FBG level. The statistical examination of the change in FBG level of diabetes patients over time was finished utilizing direct linear mixed effects models .Longitudinal data can be investigated utilizing different techniques, the methodology this work took was to fit linear mixed effect (LME) model. This displaying approach is truly adaptable enough to represent natural heterogeneity in the population, and can handle dropout and missing data, and can deal with dropout and missing information. It additionally considers within and between wellsprings of variety. A linear mixed model is an expansion of a linear regression model to show longitudinal data. This statistical technique used to assess repeated longitudinal measurements in continuous response variable in valid and flexible manner [19]. It tends to be utilized for information with inconsistent number of estimations per subjects **[19]**.

According to Verbeek and Molenbergs [20], linear mixed model is defined as:

$$Y_{ij}= \beta_{0i} + \beta_{1i}X_i + \cdots \beta_{pi}X_{pi} + \left(b_{0i} + b_i t_{ij}\right)Z_i + \varepsilon_{ij}$$

Where:-

- ✓ Y_{ij} *is* Outcome for subject i at time j = 1... n
- ✓ X_i, Z_i are fixed and random effect covariate
- ✓ The vectors ε and b are statistically independent , σ_e^2 *and* σ_b^2 are unknown scalar-value parameters called variance components
- ✓ bi~N(0,D),εi~N(0, $\sigma^2 I_{ni}$)

Estimating linear mixed model**:-**

Estimation the parameters is to more difficult in the linear mixed model b/c of not only we need to estimate but also unknown parameter in $bZ\&R$.

The qualification among ML and REML gets significant just when the quantity of fixed impacts is moderately enormous. All things considered, the examinations unequivocally favor REML. To start with, REML adapts substantially more viably with solid connections among the reactions for the subjects than does ML [21]. Second, REML gauges don't have the descending predisposition that ML gauges have on the grounds that REML assessors consider the levels of independence from the fixed impacts in the model. At long last, REML assessors are less delicate to exceptions in the information than ML assessors. Indeed, when the appraisals do shift generously **[21]**.

Results and Discussions

As presented in Table 1 Among the 210 patients 116 (55.24%) were females and the remaining 94 (44.76%) were males, from these patient about 90(42.86%) were living in rural area and 120(57.14%) were patients live in urban area, in case of marital status about 110 (52.38%) were married the remain 66(31.43%) and 34(16.9%) are single and other respectively. From the total patients 130(61.9%) has hypertensions, 80(38.1%) has not hypertensions and most of the patients diagnosis about 70% has type two diabetes the remain 31.9% were type one diabetes, most of the patients113 (54%) are exercised not perform and 97(46%) were performed, in case of medication about 106(50.46%) are NPH user and the romaine 35 and 13.6% are insulin and other respectively, from total patients above 52% are married.

Table 1: Summary of FBG Progress for categorical Covariate

Variable	Category	Frequency	percent
Sex	Male	116	55.24
	Female	94	44.76
Address	Rural	90	42.86
	Urban	120	57.14
Hyper	hypertensive	130	61.9
	Not hypertensive	80	38.1

Digno	Type1	67	31.9
	Type2	143	68.1
Alchol	Alcohol taking	93	44.29
	Not taking	117	55.7
Excirse	Perform	97	46.19
	Not perform	113	53.81
Gentc	Has g/family	99	47.14
	Hasn't g/family	111	52.86
Medica	Insulin	75	35.71
	NPH	106	50.48
	Other	29	13.81
Mstatus	Single	66	31.43
	Married	110	52.38
	Other	34	16.9
estatus	Illustrate	61	29.05
	Elementary	64	30.48
	Secondary	44	20.95
	Tertiary	41	19.52

Distribution of FBG Count

In order to choose appropriate longitudinal model and to analyze the longitudinal pattern of FBG count data, first we should checked the assumption of normality the data. The most formal approaches are conducting a statistical test of Normality and use graphical methods like QQ plot and Histogram with normal curve.

This is most-often done using either the Shapiro-Wilk Test or the Kolmogorov-Smirnov, which are both non-parametric tests that allow one to check the normality of this sample data.

Table 2 shown below the Shapiro-Wilk test and Kolmogorov test of p-value all months except month15 and month18 are the logarithm of FBG level count is greater than the alpha value(0.05), indicates the logFBG count satisfy the normality assumption.

Table 2: Test for each month using Shapiro and Kolmogorov test for log FBG

Test		Logm0	Logm3	Logm6	Logm9	Logm12	Logm15	Logm18	Log21
Shapiro wilk test	Statistics	0.98	0.98	0.97	0.983	0.98	0.79	0.977	0.988
	p-value	0.16	0.168	0.099	0.08	0.081	0.0099	0.012	0.34
Kolmogorov test	Statistics	0.06	0.063	0.0064	0.067	0.067	0.097	0.089	0.07
	p-value	0.12	0.126	0.01	0.09	0.0891	0.01	0.01	0.027

Generally the repeatedly measured FBG count of the patients were measured as a continuous and its log satisfy the assumption of normality, indicates that we need to use Gaussian longitudinal data analysis which is linear mixed eff ect model (LMM).

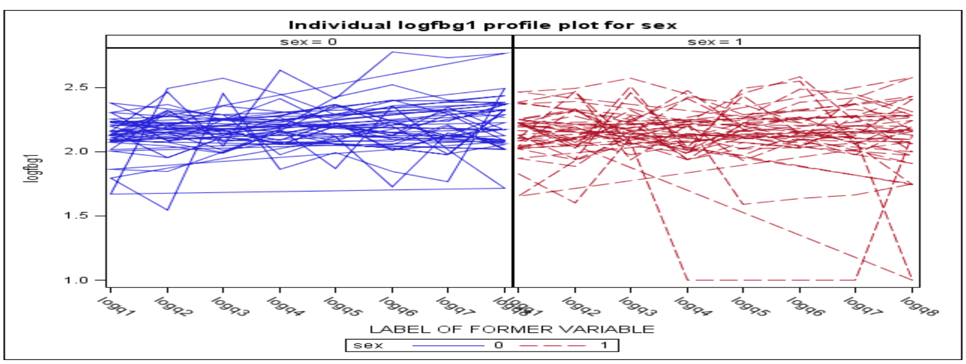

Figure 1: Exploring Individual Profile Plot by Sex

Figure1: shows the individual Profile plot for log FBG count of patient's for both male and female groups were displayed. The between patients variation is high at the end as compared with a baseline for both groups. Essentially, a few directions were more extreme while others were practically level, demonstrating the conceivable fluctuation in the incline of logFBG tallies. Hence, as a result of the inconstancy in the catch and slant of directions, utilizing a blended

model could fit the information well overall.

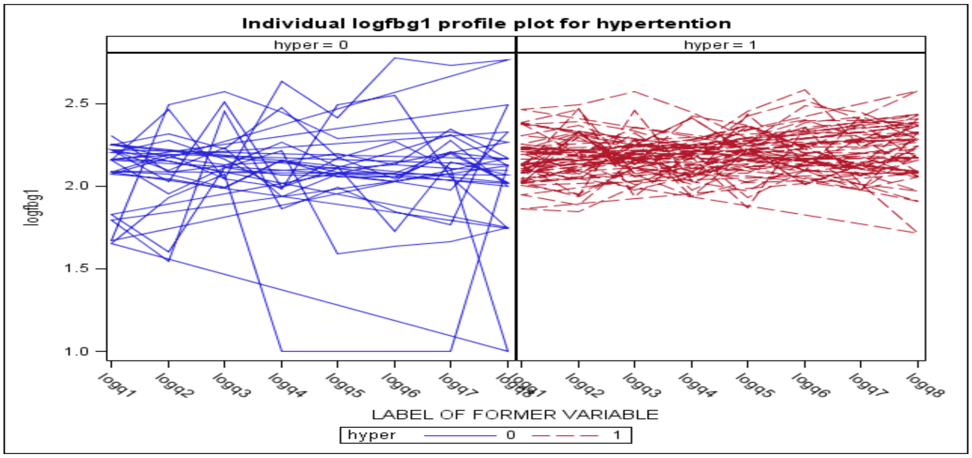

Figure 2: Individual Profile for Hypertension

Figure 2 indicates the individual profile of FBG plot of fasting blood glucose level there is high variability between and within for not hypertensive (hyper=0) at the end month of (month21) than at the begging month of (month1).generally the individual profile plot of fasting blood glucose level not hypertensive (hyper=1) have more variability than hypertensive (hyper=0).

Generally, individual profile plot of fasting blood glucose level for all variable we observed that, there is different variation at start and at the end.

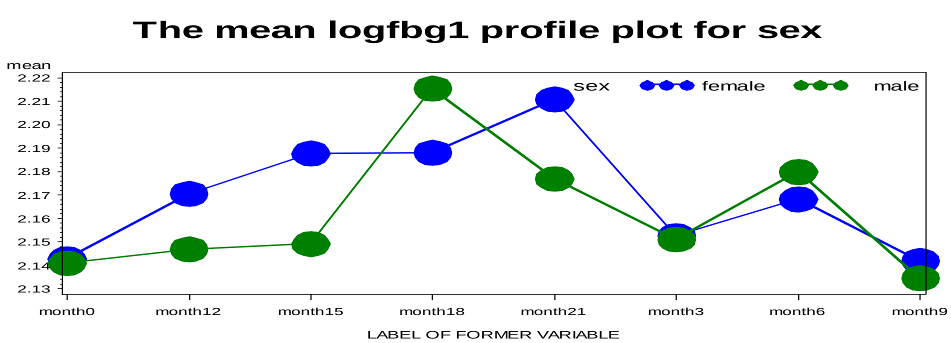

Figure 3: Exploring Mean Profile Plot of logFBG Count by Sex

The mean logFBG include increments in a high rate from standard till the sixth month and afterward it begins to increment after the ninth months since the mean profile plot of logFBG. By and large they don't show straight development design in the two gatherings.

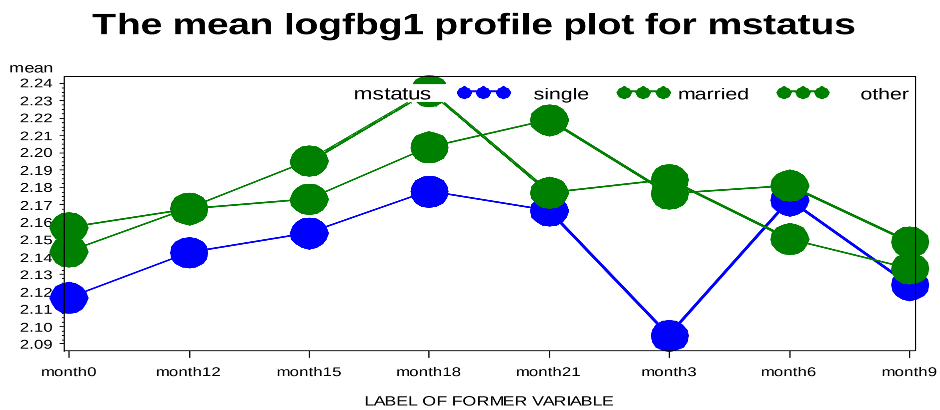

Figure 4: Mean Profile Plot of logFBG by Marital Status

From figure 4 the mean profile of the married patients seems higher than other patients from baseline up to time point month18, but after time point month18 it decreased, therefore is linear pattern of logFBG for marital status for increasing month.

Generally mean profile plot for each variable appears that there is a non-linear pattern for all as time increase; most of the mean profiles are increasing logFBG at the middle than the begging there fore they need to linear mixed model.

Discussion of the Results

The objective of this study was to identify the associated factor of diabetes in Tigray region, Ethiopia using longitudinal analysis.

For deciding the danger elements of the mortality of diabetes patients; a sum of 210 patients were remembered for the investigation that out of patients 116 (55.24%) were females and the remaining 94 (44.76%) were males, from these patient about 90(42.86%) were living in rural area and 120(57.14%) were patients live in urban area, in case of marital status about 110 (52.38%) were married the romaine 66(31.43%) and 34(16.9%) are single and other respectively.

From the respondents, Descriptive statistics revealed thatfemale patients were more exposed to diabetes than male patients; this result is similar with other study conducted in Ethiopia by **[22]**.

Next to the descriptions, the studies focus on longitudinal data analysis with linear mixed model. Type one DM of the variables main effect such as marital status, educational level, patient who perform exercises and BMI are significance effect for logFBG and solution for fixed effects of type2 DM. this result agrees with **[23]**, reported that there is high significances in those covariates.

In this Monograph covariates such as DBP patients, medication for NPH, and alcohol taking were significance effect on logFBG. From the overall final LMM, among the main effect time, DBP**[17]**, and diagnosis of type one DM and educational status primary were significant at 5% level of significance.

The result of solution fixed effect of missing after imputation showed that time (duration of follow up), patients that are not hypertensive, type one diabetes, m/status who had single and married, who were not educated and primary educated, has no genetic family and who used insulin respectively were significant independent factors for fasting glucose level count progression. But the variable sex, address, BMI, exercises and SBP used with the FBG levels of patients were not significant with a p value of 0.3304, 0.68, 0.135 and 0.34 respectively. Sex (p-value=0.3304)was no criticalness decrease among guys and females over the long run however it doesn't imply that FBG was not diminished over the long run by sex upheld by **[17], [24], [25].**

Conclusion

To summarize, a longitudinal report was used to show the FBG level of diabetes patients on treatment. This was done by reflectively following the clinical records of patients from April 2018 to February 2020 in the diabetes focus of Ayder Referral Hospital with respect to time.

DM patient data was analyzed by using exploratory data analysis. From the individual profile of FBG, there was fluctuation among subjects and inside subjects. The exploratory analysis result for the mean structure also suggested that on average, level of glucose fast was not a linear pattern over time and also from the mean profile, the FBG level of the patient's changes over time. Measured FBG count of the patients was measured as a continuous and its log satisfy the assumption of normality.

The study fit fixed effect model and random effect components by using the selected Toeplitz (Toep) and restricted maximum likelihood (REML) method of estimation. By using backward automatic variable selection method time, age, educational status and marital status of patient are significant at 25% level of significance. From the overall final (type one and type two) linear mixed-effects model demonstrated that time (term of treatment), circulatory strain (diastolic) and educational level (primary) and affected decidedly to the FBG level of patients and type one diabetes influenced negatively. Because of the missing value the other variables are not significance.

After handling missing value using multiple imputation the result of solution fixed effect of missing by imputation observed that time (duration of follow up), patients that are not hypertensive, type one diabetes were negative significant effect variables for fasting glucose level count progression and patients who single and married of marital status, patients who were not educated and primary educated and who used insulin were positive significance effect variable of FBG. Even if most of the variables were significant, the missing handling technique (mi) has better efficiency to represent the data the between-imputation change, within-imputation fluctuation and all out difference for joining total data deductions for every factor, alongside the levels of opportunity for the all-out fluctuation. The relative efficiency values, is greater than 99% in the variance information table indicates even if most of the variables were significant, the missing handling technique (mi) have better efficiency to represent the data.

Acronomy

ADA	America diabetes associated
AIC	Akaki information criteria
BIC	Bayesian information criteria
BMI	Body mass index
BP	Blood pressure
FBG	Fasting blood glucose
GLS	Generalized least square
IDF	International diabetes federation
LDA	Longitudinal data analysis
LME	Linear mixed effect
LMM	Linear mixed model

MLE	Maximum likelihood estimation
NMAR	Not missing at random
NPH	Natural protamine hagedom
RMLE	Restricted maximum likelihood estimate
WHO	World Health Organization

Conflict of interest

The authors have articulated that no contending interests exist.

Creators' commitment

WK had made generous commitment to origination and plan, or securing of information, or investigation and translation of the information; MA had been engaged with drafting the composition or amending it basically for significant scholarly substance; AW had given last endorsement of variant to be distributed

Subsidizing

The creators have no help or subsidizing to report.

Accessibility of information and material

The datasets utilized and isolated during the current assessment are accessible from the differentiating creator on sensible mentioning. Ethics underwriting and consent to share

Morals endorsement and agree to take an interest

Moral freedom was taken from Debre Berhan University; school Post Graduate coordination moral audit board and authority letter was composed by the division of insights to in Ayder Referral Hospital Tigray Region clinic so as to acquire the information from the emergency clinic before arranging and beginning information assortment. Official letter was given for concerned bodies and afterward privacy of the data was guaranteed from all perspectives.

Consent for publication

Not applicable.

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