Fasting Blood Glucose Level Progression And Its Associated Factors Among Diabetic Patients Attending Treatment In North Shewa Hospitals, Oromia, Ethiopia

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Abstract

**Background:** Diabetes describes a group of metabolic disorders characterized and identified by hyperglycemia without treatment. It includes defects in insulin secretion, insulin action, or both, and disturbances of carbohydrate, fat, and protein metabolism. The study aimed to assess fasting blood glucose level progression and its associated factors among diabetic patients attending insulin and metformin follow-up in Fiche and Chancho hospitals.

**Methods:** A retrospective study was conducted to obtain secondary data among diabetic patients attending treatment from September 2016 to August 2018 in the hospital. The linear-mixed effects model for longitudinal data was employed to measure the changes in fasting blood glucose level.

**Result:** The result of the study revealed that age, body mass index, systolic blood pressure, diastolic blood pressure, marital status, regime, and education level were significantly associated factors for the progression of fasting blood glucose levels among diabetic patients.

**Conclusion:** The study recommended that the progression of blood glucose level was higher among diabetic patients, and the health professionals, health sectors, and government should be paid an intervention on patients who had high systolic and diastolic blood pressure, who had high BMI, and older age patients.

1. **Introduction**

Diabetes is a complex, chronic illness requiring continuous medical care with multifactorial risk-reduction strategies beyond glycemic control. Ongoing patient self-management education and support are critical to preventing acute complications and reducing the risk of long-term complications (ADA, 2020). It is the most common chronic disease in nearly all countries and increases in numbers and significance, as changing lifestyles lead to reduced physical activity and increased obesity (Whiting et al. 2011).

Diabetes is found in every population globally and all regions, including rural parts of low- and middle-income countries (ADA, 2020). According to the 2016 World Health Organization report, high blood sugar level causes around 4 million deaths each year (WHO, 2016). The IDF estimates that the annual global health care spending on diabetes among adults was 850 billion dollars in 2017 (Cho, 2018). The current estimated numbers of people with diabetes by age group for 2010 and 2030. For developing countries, adult diabetes numbers are likely to increase by 69% from 2010 to 2030, compared to 20% for developed countries, whereas total adult populations are expected to increase by 36% and 2%, respectively (Whiting et al. 2011).

More than two-thirds of the rise in the prevalence of diabetes is expected in low-and middle-income countries, including those in sub-Saharan Africa (Wild et al. 2004). The prevalence of diabetes was estimated at 3.8% in 2010, projected to increase to 4.7% in 2030 in Africa among adults aged 20-79 years (Whiting et al. 2011). Around 19.4 million people were estimated to live with diabetes in 2019, projected to
increase to 47.1 million by 2045 (Saeedi et al. 2019). In Sub-Saharan Africa, this trend is emerging in a region grappling with high rates of infectious diseases like the highest global prevalence of HIV/AIDS, Tuberculosis, and Malaria (Hall et al. 2011) (Gill, 2009). The highest proportion of all deaths attributable to diabetes occurring before the age of 60 is in the Africa region, at 73.7% (Cho et al. 2018).

According to International Diabetes Federation (IDF) estimated that 19.8 million people have diabetes in Africa, and approximately 75% are still undiagnosed. Countries with the highest estimated numbers of persons with diabetes include Nigeria (3.9 million), South Africa (2.6 million), Ethiopia (1.9 million), and Tanzania (1.7 million) (IDF, 2013). African countries with diabetes prevalence more significant than 10% appeared to be upper-middle-income economies. In absolute terms, however, low-income countries in the region, such as Ethiopia, Tanzania, and the Democratic Republic of Congo, by their large populations, featured among Africa countries with the most significant number of people with diabetes (Peer et al. 2014). In Ethiopia, according to the national WHO STEPS, survey of 2015, the prevalence of diabetes mellitus was 3.2% (Gebreyes et al. 2018).

There are different studies done on diabetic patients in Ethiopia. A retrospective cohort study was done in the university of Gondar Comprehensive Specialized Hospital. The result showed that duration of follow-up, body mass index, alcohol use, diet, exercise, education status, residence, age, family history, and treatment type significantly influence the blood glucose level (Andargie and Zeru, 2018). Another retrospective cohort study was done at Haramaya University Specialized Hospital; the result revealed that variables such as age, body mass index, residence, early diet, and malnutrition status significantly affected the blood glucose level of patients (Zeru, 2018). Similarly, the fasting blood glucose data was collected from a retrospective study conducted in Jimma University Specialized Hospital diabetic clinic. The result obtained from the study was that variables like time of follow-up and weight significantly affect the level of blood glucose (Aniley et al. 2019).

Even though different studies were done on diabetic patients, many studies had used binary logistic regression by ignoring the follow-up time other than longitudinal models like the linear mixed model. For instance, a cross-sectional study was conducted in Adama hospital medical college (Yosef et al. 2021), in Debre Berhan (Habtewold et al. 2016), in Debre Tabor (Gebermariam et al. 2020), in North Showa Zone hospitals (Sahile et al. 2020), in Nikemte referral hospital (Fekadu et al. 2019), and Hossana town (Dereje et al. 2020). But as we all know, diabetic patients had follow-up time, and the data obtained should be analyzed using a longitudinal model. Therefore, this study aimed to assess fasting blood glucose level progression and its associated factors among diabetic patients attending insulin and metformin follow-up in fiche and Chancho hospitals. And also, the study addressed the following research questions: How do the average progressions of fasting blood glucose levels for diabetic patients following insulin and metformin change over time, and the factors that predict the progression of fasting blood glucose level.

2. Method

2.1 Study Area
The study was conducted in the two governmental Hospitals, Fiche and Chancho ART clinics. Fiche is located 112km north of Addis Ababa latitude of 9°48′N and longitude of 38°44′E and an elevation between 2,738 and 2,782 meters above sea level. Chancho is located about 40km north of Addis Ababa, with a latitude of 9° 18′ 29.1240″ N and longitude 38° 45′ 11.2320″ E.

2.2 Source of Population

The target population was obtained from the two hospitals attending treatment between 1st September 2016 and 30th August 2018. The data were extracted from the patient chart and identification card. Both contain epidemiological, laboratory, and clinical information of all Diabetic patients receiving treatments in follow-up.

2.3 Study Design

A retrospective study was conducted to obtain secondary data among diabetic patients attending treatment from September 2016 to August 2018 in the hospitals.

2.4 Eligibility Criteria

All Type I and Type II diabetic patients and placed under insulin and metformin attending follow-up in the study area. Patients of all ages who are the follow-up were included in the study. Patients who were both diabetic and hypertensive were included in the study. Patients who were out of the study period were excluded from the study.

2.5 Operational Definitions

Body mass index: Calculated from the patients’ weight (in kilograms) divided by their height (in meters) squared.

Diabetics Mellitus: According to the American Diabetes Association should be 5.0–7.2 mmol/l (90–130 mg/dL) before meals and less than 180 mg/dL (10 mmol/L) after meals.

Insulin: is a hormone produced naturally in humans and animals in the beta cells of the pancreas.

Mg/dL: It stands for milligram per decilitre. It is a measurement that indicates the amount of a particular substance (such as glucose) in a specific amount of blood.

2.6 Sampling Technique

The sampling technique, the recorded identification card of patients, was filtered first from their cards according to their entry to the follow-up. Then, patients were clarified using inclusion criteria, given a code for the remaining records, and selected each recorded card for the study using simple random sampling to get real, relevant, and detailed information from diabetic patients who follow up at hospitals.
2.7 Sample Size Determination

The sample size was calculated using single population proportion formula, taking into account the following premise: 95% confidence level, 5% margin of error, and progression of fasting blood glucose level was 5% (Gebermariam et al. 2020), design effect=0.05, and non-response rate=10%.

\[
n = \frac{(Z_{\alpha/2})^2pq}{d^2} = \frac{1.96^2(0.5)(0.5)}{0.05^2} = 384
\]

2.8 Data Collection Tools and Procedures

Medical records were reviewed by using a checklist. Both the inpatient and outpatients’ records were reviewed during the study. The data was collected from the patient’s identification card and charts.

2.9 Data quality assurance

The data collectors were familiar with medical cards review. The three-day training was given for data collectors and supervisors about the study’s objectives and the data collection process. Strict supervision was assumed to meanwhile, any doubt in the checklist was clarified.

2.10 Study Variables

The dependent variable was fasting blood glucose level for three years. The independent variables were age, BMI, systolic blood pressure, and diastolic blood pressure were continuous variables, whereas sex, functional status, residence, regimen, education level, and marital status were categorical variables (Table 1).

Table 1: Independent variable with their categories
| Variables                      | Categories (if any)                          |
|-------------------------------|----------------------------------------------|
| Sex                           | 0=male, 2=Female                             |
| Baseline Age (in years)       |                                              |
| Marital status                | 0=Married, 1=Others (single, widowed or Divorced) |
| Body Mass Index Kg/m²         |                                              |
| Observation time (in month)   |                                              |
| Residence                     | 1= Urban, 2= Rural                           |
| Education Level               | 1= Illiterate, 2= Primary, 3=Secondary, 4=Above Secondary |
| Functional status             | 1= Working, 2=Bedridden                      |
| Regime                        | 1= Insulin Agent 2=Oral Agent                |
| Systolic Blood Pressure (MmHg)|                                              |
| Diastolic Blood Pressure (MmHg)|                                              |
| Clinical Diagnosis            | 1=Type I 2=Type 2                            |

2.11 Statistical Data Analysis

2.11.1 Exploratory Data Analysis

To determine the evolution and balances of the data, the individual and mean profiles to time were plotted. The mean, the variance, and the correlation structures were also explored through graphical techniques. A random-effects model was chosen to define a covariance model in parallel to the fixed-effects model. After deciding the fixed effects, the study selected a set of random effects in the model.

2.11.2 Linear Mixed Model (LMM)

The study considered the changes in the fasting blood glucose (FBG) levels in diabetes patients on treatment throughout the study. Longitudinal data can be analyzed using various methods, but the approach employed in this study was to fit the linear mixed-effects (LME) model. This approach is pliant, considers the natural heterogeneity within the population, and can effectively handle drop-out and missing data. A general LME model can be written as (Laird and Ware 1982).
\[ y_i = X_i(t)\beta + Z_i(t)b_i + e_i \quad i = 1,2,3, \ldots n \]

\[ b_i \sim N(0, D) \quad e_i \sim N(0, R_i) \]

Where:

\[ b_i: N \sim (0, D) \]

\[ s: N(0, \Sigma) \]

\( Y_i \) - is \( n_i \) dimensional observed response.

\( \beta_i \) - is a \( p \) dimensional vector of fixed effect.

\( b_i \) - is a \( q \) dimensional vector of random effect.

\( X_{1i} \) - is a matrix of \( (s \times n_i \times p) \) fixed effect possibly time-varying covariates.

\( Z_{1i} \) - is a matrix of \( (s \times n_i \times q) \) random effect covariate.

\( e_i \) - is \( n_i \) dimensional vector within-group errors.

Statistical inference for a linear mixed model is typically based on the maximum likelihood method or the restricted maximum likelihood method (Laird and Ware 1982; Lindstrom and Bates 1988). The longitudinal study analysis using SAS version 9.4 was used for statistical analysis and graphics, and a 5% level of significance was used in statistical tests.

### 3. Result

#### 3.1 Description of the Data

Three hundred eighty-four patients admitted to the diabetic clinic in hospitals from 1st January 2016 to 30th August 2018 were included in the study. The mean age at baseline was 42.18 and a standard deviation of 15.78. The mean baseline fasting blood glucose level of diabetic patients was 179.9, with a standard deviation of 94.97. Diabetic patients' body mass index (BMI) mean was 23.67, and the standard deviation was 3.72 (Table 2).
A higher proportion of 204 (53.12%) of the patients was male. About 83.9% of patients had working functional status, and 68.9% of patients were married. Patients 34.6% were illiterate, 23.2% attained primary education, while 14.1% and 7% respondents attained secondary and higher education, respectively. More than half (58.3%) of patients lived in urban areas, and the remaining 31.9% lived in rural areas. Concerning medication type, 55.7% were used insulin, and the remaining 33.9% of patients had used oral agents. And finally, 55.9% were Type I diabetic patients, and 34.5% were Type II diabetic patients (Table 3).
### Table 3
Frequencies and percentage for categorical covariates at baseline

| Characteristics       | Category                             | N (%)          |
|-----------------------|--------------------------------------|----------------|
| Sex of patients       | Male                                 | 204(53.12%)    |
|                       | Female                               | 180(46.8%)     |
| Functional Status     | Working                              | 251(83.9%)     |
|                       | Bedridden                            | 18(6.3%)       |
| Marital Status        | Married                              | 206(68.9%)     |
|                       | Other (Single, widowed, divorced)    | 60(20.2%)      |
| Educational Level     | Illiterate                           | 103(34.6%)     |
|                       | Primary                              | 69(23.2%)      |
|                       | Secondary                            | 42(14.1%)      |
|                       | Above                                | 55(18.3%)      |
| Residence             | Urban                                | 175(58.3%)     |
|                       | Rural                                | 95(31.9%)      |
| Clinical Diagnosis    | Type I                               | 167(55.9%)     |
|                       | Type II                              | 102(34.3%)     |
| Regime                | Insulin Agent                        | 196(55.7%)     |
|                       | Oral Agent                           | 101(33.9%)     |

### 3.2 Descriptive statistics for fasting blood glucose level

The mean of fasting blood glucose of diabetic patients decreases through time points. The maximum mean for fasting blood glucose reached baseline with a value of 193.8. The number of observations drops from one to five and higher only at the baseline time point, the standard deviation higher at time point one, 102.0. The maximum fasting blood glucose level is 600 at the baseline time point, while the minimum fasting blood glucose is 456 from three to five-time points. Missing is considerably increasing through time is gone (Table 4).
Table 4
Descriptive Statistics of fasting blood glucose level

| Time | Baseline | 1   | 2   | 3   | 4   | 5   | 6   | 7   |
|------|----------|-----|-----|-----|-----|-----|-----|-----|
| N    | 384      | 284 | 291 | 288 | 288 | 272 | 244 | 204 |
| Mean of FBG | 193.8 | 192.1 | 189.4 | 180.4 | 178.2 | 174.6 | 173.4 | 169.3 |
| Std Dev | 102.0 | 89.1 | 91.25 | 83.8 | 87.6 | 88.3 | 89.9 | 85.0 |
| Maximum | 600 | 574 | 600 | 587 | 522 | 493 | 589 | 456 |
| Minimum | 22 | 32 | 29 | 31 | 28 | 31 | 44 | 46 |
| Missing | 0 | 16 | 9 | 12 | 12 | 28 | 56 | 96 |

### 3.3 Exploratory Data Analysis

#### 3.3.1 Mean profile plot

The mean profile plot for sex shown that the variability of the male patients lower than female patients, but at time five it was decreased, and at time point one, four and five female patients have higher variability and then at time point three they become equal and cross each other. And the plot for marital status had shown that there is higher variability in married patients than single widowed and divorced patients. For residence of patients the plot shown that there is higher variability in patients who lived in rural than patients who lived in urban. These all indicate the need for random intercept to correct the fact that patients started differently at different baseline FBG. In addition to random intercept, there is a need for random slope to allow subjects to have different slopes and account for the unstable between-subject variability at different time points (Figure 1).

#### 3.3.2 Profile for fasting blood glucose level by time

From Figure 2, the individual profiles of fasting blood glucose levels help identify the general trends within and between subjects that detect changes over time. There are changes among patients of fasting blood glucose level over follow-up time. The initial variability seems more significant than at the end of fasting blood glucose level for timely follow-up.

### 3.4 Associated factors that affect the progression of FBG

As shown in the result of Table 5, the average mean value fasting blood glucose level of patients was 112.03 by keeping the effect of other factors at zero. As one unit increased, the average rate of change in blood glucose levels was 11.23mg/dl per unit increased over time. There was a significant interaction between DM status and time ($p< 0.000$) such that the blood glucose levels of the patients increased over time. And the variable systolic blood pressure and diastolic blood pressures of patients have significantly affected the progression of FBG level in diabetic patients. Hence, as the age of a patient increased by a
year, change of FBG levels also increased by 4.17mg/dl keeping the other variables constant (p = 0.0439) and also for a unit change in BMI of patients increases the blood glucose level by 5.01mg/dl change in (p = 0.0281). The average rate of change of blood glucose level for illiterate patients was increased by 2.13 compared to the literate patients by, keeping the effect of the other variables constant. The mean rate of change of blood glucose level for married patients decreased by the value of 5.33mg/dl compared to that of other (single, widowed, divorced) patients. Patients use the treatment of insulin and oral agents. The mean change of blood glucose level of the patient who uses insulin by 2.01mg/dl decreased compared to the patient who used the oral treatment. The analysis revealed that the progression of FBG for patients is also affected by the marital status regime from the main effect. Furthermore, the interaction between age, systolic and diastolic blood pressure with time was also having a significant effect on the progression of FBG.

Table 5
The Parameter estimate for the reduced fixed effect linear mixed model for FBG

| Effect                          | Estimate | Std error | 95% CI       | P-value |
|---------------------------------|----------|-----------|--------------|---------|
| Intercept                       | 112.03   | 35.07     | 110.20 - 113.33 | < .0001 |
| Time                            | 11.23    | 9.96      | 5.541 - 12.687 | <.0001  |
| Body Mass Index                 | 5.01     | 0.95      | 1.981 - 6.114 | 0.0281* |
| Age                             | 4.17     | 0.09      | 2.544 - 5.254 | 0.0439* |
| Systolic blood pressure         | 6.06     | 0.15      | 5.087 - 8.515 | 0.0089* |
| Diastolic blood pressure        | 2.12     | 0.25      | 1.152 - 3.447 | 0.0062* |
| Marital Status (Married)        | 5.33     | 7.16      | 4.547 - 6.325 | 0.0125* |
| Regime (Insulin)                | 2.01     | 6.40      | 1.223 - 3.226 | 0.0378* |
| Education level (Above secondary)| 2.13    | 7.84      | 1.014 - 3.142 | 0.0053* |
| Time*Age                        | 3.034    | 0.02      | 2.054 - 2.458 | 0.0387* |
| Time*Systolic blood pressure    | 2.006    | 0.04      | 1.001 - 3.452 | 0.0073* |
| Time*Diastolic blood pressure   | 4.032    | 0.07      | 3.015 - 6.064 | 0.0024* |
| Time*Body Mass Index            | 3.274    | 0.22      | 2.451 - 5.785 | 0.0294* |
| Time*Regime                     | 2.235    | 1.62      | 2.147 - 3.145 | 0.0180* |

4. Discussion

The burden of diabetes mellitus and its associated modifiable risk factors are increasing in developing countries like Ethiopia (Animaw and Seyoum, 2017). A hospital-based retrospective study was conducted to assess fasting blood glucose level progression and its associated factors among diabetic patients.
attending insulin and metformin follow-up in Fiche and Chancho hospitals. From the total of three hundred eighty-four patients, 53.12% of the patients were male, and more than half of patients lived in an urban area; this in line with the study done by (Amare et al. 2021).

The rate of change of blood glucose level increased by 11.23mg/dl per unit increased over time. This result indicates that there is a significantly positive association between time and progression of blood glucose level. This result contradicts the study of (Andargie et al. 2018). The age of patients is also another factor for change of blood glucose level; this entails that a unit increase in age can increase the blood glucose level by 4.17mg/dl. This finding is similar to a study conducted in Ghana (Adampah et al. 2015). The patient’s BMI was found to be associated with the change in blood glucose level. This result revealed that with the increase of patients’ weight, they are more exposed to the risks of having diabetes; this is consistent with other studies (Andargie et al. 2018), (Dereje et al. 2020), and (Adampah et al. 2015).

There is a positive association between the progression of blood glucose level and marital status in the present study. It ultimately shows that married patients decreased by the value of 5.33 compared to single, widowed, divorced patients. This result is supported by (Amare et al. 2021). And the education level category result showed that being educated minimizes the associated factors that affect the progression of blood glucose level. This implies that literate patients manage disease better to understand the essential disease management and treatment plans. This finding was in line with the result of (Gebermariam et al. 2020; Fekadu et al. 2019; Amare et al. 2021 and Yosef et al. 2021).

Finally, patients who use insulin decreased as compared to an oral agent means that the insulin treatments has a significance contribution to the minimization of the blood glucose level of the diabetes mellitus patient as opposed to the patient who uses the treatment of oral. This finding is contradicted by (Sahile et al. 2020) and (Andargie et al. 2018). And the rising of both systolic and diastolic blood pressure was found to play a significance role in increasing the progression of blood glucose levels among diabetic patients, which is consistent with the studies (Dereje et al. 2020).

5. Conclusion

In the study, a longitudinal report was used to show the blood glucose level of diabetes patients on treatment. The study was conducted among diabetic patients from September 2016 to August 2018 in Fiche and Chancho Hospitals concerning time. From the mean profile, the blood glucose level of the patients decreased over time which was also confirmed with the model that the estimate of time was positive. Among the associated factors of fasting blood glucose level, age, body mass index (BMI), marital status, education level, systolic and diastolic blood pressure, and regime of patients were significant effects for the progression fasting blood glucose level (p<0.05). Hence, more attention was given to controlling the blood glucose level of the patients with these factors. From the study result, patients who were not educated, had higher BMI levels, were married, had high SBP and DBP, and used oral treatment were better not suited to control and reduce their fasting blood glucose level in their body.
over time. Finally, this study recommended that the progression of blood glucose level was higher among diabetic patients who had high systolic and diastolic blood pressure, who had high BMI, and older age patients. Therefore, special interventions must be paid for BMI, blood pressure level and older patients to control and reduce the consequence of progression of fasting blood glucose level among diabetes mellitus patients in the hospital, and further studies are recommended using additional covariate and deal with other longitudinal model like generalized linear mixed model.

**Abbreviations**

BMI: Body mass index

FBG: Fasting blood glucose level

**Declarations**

**Authors' contribution**

Yordanos Berihun had made substantial contributions to the conception and design, acquisition of data, or the analysis and interpretation, drafting the manuscript or revising it critically for important intellectual content; Berhanu Teshome and Buzuneh Ayano had given final approval of the version to be published.

**Data Availability**

The data used to support the findings of this study are available from the corresponding author on request.

**Ethics approval**

Ethical clearance was obtained from Salale University, research and publication director office.

**Competing interests**

The authors declare that they have no competing interests.

**Consent for publication**

Not applicable.

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**Figures**
Figure 1

Mean plot for sex, marital status and residence of patients with FBG over time.
Figure 2

Individual profile plot for Fasting blood glucose level