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Research Article

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Predictors of glycemic control among patients with Type 2 diabetes in North West Ethiopia: A longitudinal study

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Abstract

Background: Type 2 diabetes mellitus patients with hyperglycemia for a long period are significant causes of mortality and morbidity worldwide. Studying the predictors of glycemic control helps to minimize deaths and the development of acute and chronic diabetes complication. Hence, this study aims to assess predictors of glycemic control among patients with Type 2 diabetes in Ethiopia.

Methods: A retrospective cohort study was conducted among type 2 Diabetes mellitus (T2DM) patients enrolled between December 2011 and December 2012 at Debre Markos and Felege Hiwot Referral Hospital. A total of 191 T2DM patients were included in the study meets the eligibility criteria. A generalized linear mixed model was employed.

Results: The prevalence of good glycemic control among type 2 diabetes patients was 58.4% whereas 23.25% of the variation was explained in the fitted model due to adding the random effects. The significance predictors of glycemic control among patients with Type 2 diabetes at 95% confidence level were reside in rural(0.454, 0.614)), patients age 38-50, 51-59 and 60-66 years(1.267,1.776), (1.057,1.476) and (1.004, 1.403), respectively, Proteinuria Positive (1.211, 1.546), diastolic blood pressure ≥ 90 (1.101, 1.522), systolic blood pressure ≥ 140 (1.352, 1.895), creatinine (0.415, 0.660), duration per visit (0.913, 0.987), duration since diagnosis (0.985, 0.998), weight 78-88(0.603, 0.881).

Conclusion: The level of glycemic control among type 2 diabetes patients was poor. Type 2 diabetes mellitus patients having higher age of the patient, higher weight, reside in rural, longer duration of T2DM since diagnosis, longer duration of type 2DM per visit, increase creatinine, positive protein urea, diastolic blood pressure ≥ 90 , and systolic blood pressure ≥ 140 were significant predictors of poor glycemic control among type 2 DM patients. During diabetic

patients follow up, clinicians should give appropriate attention to these significant variables for good glycemic control since it is the main goal of diabetes management.

Keywords: Type2 diabetes mellitus; Glycemic control; Adjusted Odd Ratio; Generalized Linear Mixed Model, logit link.

Introduction

Diabetes mellitus is a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbance in carbohydrate, fat and protein metabolism resulting from a defect in insulin secretion, insulin action or both(1).

Globally IDF reported that the prevalence of diabetes was estimated to be 8.8% (7.2-11.3%) in 2017 affecting 424.9 (346.4-545.4) million adults aged 20–79, including 212.4 million who are undiagnosed. In the African Region with 69.2%, undiagnosed diabetes has a prevalence of 3.3% (2)whereas in Ethiopia the number is estimated at 1 to 10 million in 2015(3).

Diabetes mellitus has emerged as one of the rapidly increasing non-communicable disease and a major public health challenge in developing countries like Ethiopia with a consequence of Chronicity and complications like disability and premature death(4)due to long-term effects of untreated diabetes mellitus(5, 6). Hence, diabetes mellitus patients with hyperglycemia in a long period are significant causes of mortality and morbidity worldwide. Glycemic control remains the major focus of type 2 diabetes management (7, 8). Studies showed that good glycemic control reduces the risk of diabetic-related complications and death (9, 10).

Studies in Ethiopia showed that Poor glycemic control was associated with rural residence(11), duration with diabetics(12-16), duration of diabetic's treatment(11-14), drug regimen of oral anti-diabetics or insulin treatment (15, 17), and body weight (10). Besides, drug regimen of more than one oral agent, diabetic complications and co-morbidities were associated with poor glycemic control (18).

Prior studies are cross-sectional study and have not accounted for fluctuations of glycemic control over time. Hence, this study aimed to identify predictors of glycemic control among patients with Type 2 diabetes using a longitudinal data analysis approach. This account for glycemic control variation among patients and thus maximized the amount of information that can be drawn from the data.

Results

Characteristics of study participants

The result of this study showed that the level of good glycemic control among type 2 diabetic patients was 58.4%. The incidences of hypertension, retinopathy, nephropathy, neuropathy, stroke, CHD, and PAD were 63.5%, 13.5%, 19.8%, 15.6%, 4.2%, 9.9% and 2.6% cases per 100-person year of observation respectively.

The proportion of good and poor glycemic control of type 2 diabetes patients fluctuated over time. Relatively, the proportion of good glycemic control of type 2 diabetic patients progressively rose (Figure 1).

Demographic variables

The proportion of good glycemic control of both female and male T2DM patients fluctuated over time. Besides, the proportion of good glycemic control of both female and male T2DM patients steadily rose. Relatively, the proportion of good glycemic control of female T2DM patients was slightly more than male T2DM patients (Figure 2).

The proportion of good glycemic control of T2DM patients who reside in rural and urban fluctuated over time. The proportion of good glycemic control of T2DM patients who reside in urban steadily rose (Figure 3). Generally, type 2 Diabetic patients who reside in rural are 47.2% less likely to have good glycemic control as compared with those who reside in urban (AOR=0.528, 95%CI(0.454, 0.614))(Table 1).

The proportion of good glycemic control of T2DM patients whose age in years are <51, 51-59, 60-66, and >66 fluctuated over time. Relatively, the proportion of good glycemic control of T2DM patients whose age are <51, 51-59 and 60-66 steadily rose (Figure 8). To be precise, type 2 Diabetic patients whose age are 38-50, 51-59 and 60-66 years are about 50%, 24.9% and 18.7% more likely to have good glycemic control as compared with those whose ages are 67-80 years, (AOR=1.500, 95%CI(1.267, 1.776)), (AOR=1.249, 95%CI(1.057, 1.476)) and (AOR=1.187, 95%CI(1.004, 1.403)), respectively (Table 1).

Clinical variables

The proportion of good glycemic control of T2DM patients who had taken more than one oral agent, insulin alone or insulin plus oral agent and one oral agent fluctuated over time. The

proportion of good glycemic control of T2DM patients who had taken more than one oral agent, insulin alone or insulin plus oral agent and one oral agent steadily rose. Relatively, the proportion of good glycemic control of T2DM patients who had taken more than one oral agent, insulin alone or insulin plus oral agent and one oral agent slightly one more than another respectively(Figure 4).

Type 2 Diabetic patients whose duration since diagnosis is increased by one month are about 0.8% less likely to have good glycemic control (AOR=0.992, 95%CI (0.985, 0.998))(Table 1).

Type 2 Diabetic patients whose duration per visit is increased by one month are about 5.1% less likely to have good glycemic control (AOR=0.949, 95%CI (0.913, 0.987)) (Table 1).

Type 2 Diabetic patients whose weight is 78-87kg are 27.1% less likely to have good glycemic control as compared with those whose weight is 58-69kg(AOR=0.729,95%CI (0.603, 0.881))(Table 1).

Physiological characteristics

The proportion of good glycemic control of negative and positive proteinuria of T2DM patients fluctuated over time. The proportion of good glycemic control of negative proteinuria of T2DM patients steadily rose (Figure 5). In the main, type 2 Diabetic patients whose proteinuria is negative are 36.8% more likely to have good glycemic control as compared with those whose Proteinuria is positive (AOR=1.368, 95%CI(1.211,1.546))(Table 1).

The proportion of good glycemic control of T2DM patients whose diastolic blood pressure was <90 mmHg and $\geq$ 90 mmHg fluctuated over time. The proportion of good glycemic control of T2DM patients whose diastolic blood pressure was <90 mmHg steadily rose (Figure 6). In general, type 2 Diabetic patients whose diastolic blood pressure is <90 mmHg are 29.5% more likely to have good glycemic control as compared with those whose diastolic blood pressure is $\geq$ 90 mmHg (AOR=1.295,95%CI (1.101, 1.522))(Table 1).

The proportion of good glycemic control of T2DM patients whose systolic blood pressure was <140 mmHg and $\geq$ 140 mmHg fluctuated over time. The proportion of good glycemic control of T2DM patients whose systolic blood pressure was <140 mmHg steadily rose (Figure 7). On the whole, type 2 Diabetic patients whose systolic blood pressure is <140 mmHg are 29.5% more likely to have good glycemic control as compared with those whose systolic blood pressure is $\geq$ 140 mmHg(AOR=1.601, 95%CI(1.352, 1.895))(Table 1).

Type 2 Diabetic patients whose creatinine increased by one mg/dl are about 47.7% less likely to have good glycemic control (AOR=0.523, 95%CI (0.415, 0.660))(Table 1).

Discussion

In this study, generalized linear mixed model analysis was used to identify the determinant factors that affect glycemic control among type 2 diabetes mellitus patients. In bivariate analysis residence, age of the patient, treatment, weight, duration of T2DM since diagnosis, duration of T2DM per visit since diagnosis, follow up time, proteinuria, diastolic blood pressure, systolic blood pressure and creatinine were significantly associated with glycemic control among T2DM patients. In the generalized linear mixed model the variable residence, age of the patient, weight, duration of T2DM since diagnosis, duration of type 2DM per visit, follow up time, proteinuria, diastolic blood pressure, systolic blood pressure and creatinine were significantly associated with glycemic control among type 2 diabetic patients.

The result of this study showed that the level of glycemic control among type 2 diabetic patients is 58.4%, which is consistent with the study done in Zambia (61.3%), Limmu Genet Hospital (63.8%), Suhul Hospital (63.5%), Nigeria (55%), Ayider Specialized hospital (48.7%) and Shonen Gibe Hospital (59.2%) (15, 32-36). Whereas it is below than the study conducted at a Tikur Anbessa hospital (80%), Debre Tabor General Hospital (71.4%), South Africa (83.8%), Kenya (81.6%), India (91.8%), Palestine (80.5%), Dessie Referral hospital (70.8%), Jimma University teaching Hospital (70.9%), Turkey (67.5%), Myanmar (72.1%), and Saudi Arabia (74.9%) (12, 13, 15, 19-26). The possible justification for the discrepancy might be the difference in the quality of care given to the patients in different hospitals and the method used to assess the glycemic level.

This showed that residents had a significant association with glycemic control of type 2 diabetes patients. Type 2 Diabetic patients who reside in rural are 47.2% less likely to have good glycemic control as compared with those who reside in urban. The higher rate of poor glycemic control observed among rural residents was consistent with the findings of a previous study conducted at Dessie Referral Hospital, and the University of Gondar Referral Hospital (14, 17). This might be due to the lower awareness, treatment and control of diabetes among persons living in rural areas (27).

Our study showed that the duration of diabetes since diagnosis and duration per visit had a significant association with glycemic control of type 2 diabetes patients. Type 2 diabetic patients with longer duration since diagnosis and duration per visit are about 0.8 % and 5.1% less likely to have good glycemic control, respectively. This is in line with studies done at Tikur Anbessa Hospital, Dessie Referral Hospital, South Africa, Limmu Genet Hospital, Malaysia, Ayider Referral Hospital, Palestine, Jordan, and Saudi Arabia (15, 17, 19, 23, 24, 26, 28-30). The possible justification may be the duration increases the ability to secrete insulin will decrease in type 2 diabetes mellitus.

The current showed that increasing weight had significant predictors of glycemic control of type 2 diabetes patients. This is in line with studies done at Suez Canal University Hospital Egypt and southwest Ethiopia (10, 18).

The main limitation of the study is the limited information on important predictors such as family history and the type of interventions, including the type of exercises and nutritional status of a patient that may have influenced the outcome variables. Due to a lack of data on these potential predictors for most of the patients involved in the study, we were unable to include them in the analyses. Therefore, more public health and epidemiology researches are needed to examine the impact of these variables on population health in general and in particular, people living with T2DM to control glycemic over time and to identify new risk factors for T2DM.

Conclusion and recommendations

The level of glycemic control among type 2 diabetes patients was poor. 23.25% of the variation was explained in the fitted model due to adding the random effects in the generalized linear mixed model. Type 2 diabetes mellitus patients having higher age of the patient, higher weight, reside in rural, longer duration of T2DM since diagnosis, longer duration of type 2DM per visit, increase creatinine, positive protein urea, diastolic blood pressure $\geq$ 90, and systolic blood pressure $\geq$ 140 were significant predictors of poor glycemic control among type 2 DM patients. During diabetes patient follow up, clinicians should give appropriate attention to these significant variables for glycemic control since it is the main goal of diabetes management. Special attention should be given to DM patients with longer duration. Health professionals shall put their effort into evidence generation, health promotion and awareness creation about diabetes mellitus and its control.

Methods

Study design and period

Institutional based retrospective follow-up study design was used. Records of newly diagnosed type 2 DM patients who were enrolled between December 2011 and December 2012 were selected and followed continuously until January 2017.

Study Area and Population

This study was done on type 2 DM patients at the Felege Hiwot and Debre Markos Referral Hospitals. Which are located in the capital city of Amhara Regional State, Bahir Dar city, and capital of east Gojjam zone, Debre Markos town respectively.

The study population was all type 2 diabetic patients aged 18 years or older who were coming to the aforementioned referral hospitals for diagnosis and follow from December 2011 to December 2012. These patients were followed until January 2017. Patients with at least two observations were included in the analysis leading to a total of 191 patients and 5220 observations.

Data collection procedures and data quality control

Type 2 diabetic patients on anti-diabetic medication(s) for at least three months and at least two consecutive blood glucose measurements within three months were included in the study. The longitudinal data were extracted from the patients' card using checklists. The primary outcome was glycemic control. For this study, we categorized the study participants into two groups based on the American Diabetes Association (ADA) recommendation (24): Good glycemic control: fasting blood glucose of 70–130 mg/dl (24) and poor glycemic control: fasting blood glucose of $<70\text{mg/dl}$ and $>130\text{mg/dl}$ (24).

Both baseline and time-dependent characteristics were assessed from the patients' registration card. The first characteristic assessed was the demographic variables such as age, sex and residence. The second characteristic assessed was the clinical variables such as hypertension comorbidity, which was defined as a history of antihypertensive drug use or $\text{SBP} \geq 140 \text{ mmHg}$ or $\text{DBP} \geq 90 \text{ mmHg}$ (25), type of treatment of DM, weight, duration of the disease, duration of treatment and vascular complications such as retinopathy, nephropathy, neuropathy, stroke, peripheral arterial disease and coronary heart disease. These complications were determined

based on the clinical decision of the physician. Diabetic retinopathy was defined by both direct and indirect ophthalmoscope assessments done by retinal specialists confirmed by fundus photography. Neuropathy was defined by a history of numbness, paraesthesia, tingling sensation confirmed by touch sensation by 10 g monofilament, vibration sense by biothesiometer and ankle reflex. Nephropathy was defined as worsening of blood pressure control, swelling of the foot ankle, hands or eyes, increased need to urinate, protein in the urine with a confirmation by tests like blood test, urine test, renal function test and imaging test. Stroke is defined as patients with sudden difficulty in speech and comprehension, sudden paralysis or numbness of the face, arm or leg, sudden trouble with walking and confirmation imaging with computerized tomography (CT) scan or magnetic resonance imaging (MRI). Peripheral arterial disease (PAD) was defined by a history of intermittent claudication, coldness in the lower extremities (especially when compared with the other side), and weak or absent peripheral pulses in the lower extremities and confirmation via Doppler ultrasound. Coronary heart disease (CHD) was diagnosed by symptoms of angina, shortness of breath, a crushing sensation in the chest, pain in the shoulder or arm and sweating. Additionally, CHD was confirmed by electrocardiogram (ECG) or echocardiogram (26, 27). The third characteristics assessed were physiological characteristics such as creatinine, fasting blood sugar, systolic blood pressure (SBP), diastolic blood pressure (DBP) and proteinuria.

These data were collected by two nurses who had experience on-diabetic follow-up. To control the data quality, training was given to the data collectors and their supervisor. The data extraction checklist was pre-tested for consistency of understanding the review tools and completeness of data items. The necessary adjustments were made on the final data extraction format and the filled formats were checked daily by the supervisor.

Ethics approval and consent to participate

Ethical approval to conduct the study and human subject research approval for this study was received from Debre Markos University, Natural and Computational Science College, Research Ethics Committee and the medical director of the Hospital. We confirm that all methods were carried out by relevant guidelines and regulations. As the study was retrospective, informed consent was not obtained from the study participants, but data were anonymous and kept confidential. Due to the retrospective nature of the study, the need for informed consent was

waived by the Research Ethics Committee of Natural and Computational Science College (Debre Markous University) University.

Data Analysis

Descriptive statistics were used to describe the percentage and frequency of the patients about all covariates. In addition, a line graph was used to see the progression of glycemic control proportion with time for each variable. A generalized linear mixed model with a logit link was used to identify the predictors of glycemic control among type 2 diabetic patients by analyzing the repeated measure of data of the glycemic status of the patients. The odds ratio was used to assess the association between glycemic control and risk factors.

Generalized Linear Mixed Model

GLMMs are generally defined such that, conditioned on the random effects u , the dependent variable Y (glycemic control for the i^{th} type 2 diabetes patient's), is distributed according to the exponential family with its expectation related to the linear predictor $X\beta + Zu$ via a logit link function g :

$$g(E[y|u]) = X\beta + Zu.$$

Here X and β are the fixed effects design matrix, and fixed effects; Z and u are the random effects design matrix and random effects. Generalized linear mixed models are special cases of hierarchical generalized linear models in which the random effects are normally distributed.

Parameter Estimation for Generalized linear mixed models

The marginal quasi-likelihood method was used to estimate the model parameters. The complete likelihood for all the observed data is formulated as (31)

$$\ln p(y, u) = \ln \int p(y|u)p(u)du$$

The likelihood function has no general closed-form, and integrating over the random effects is usually extremely computationally intensive. In addition to numerically approximating this integral, methods motivated by Laplace approximation have been proposed(32).

Model Building Strategies for Generalized linear mixed models

To build generalized linear mixed model analysis the procedure we followed is first we fit a univariable model for each of the explanatory variables and based on statistical significance identifies variables to be candidates for the multivariable analysis. As naturally different factors/variables do not operate separately, multivariable analysis helps to control for confounders and analyze the effects of a factor in the presence of other factors in the model.

We used Akaike and Bayesian information criteria to select the appropriate generalized linear mixed model, and the model with the smallest AIC or BIC was considered the best fit (30, 31).

List of Abbreviations

ADA: America Diabetes Association, AIC: Akaike information criteria, AOR: Adjusted odds ratio, BIC: Bayesian information criteria, CHD: coronary heart disease, CL: Confidence interval, COR: Crude odd ratio, DBP: Diastolic Blood pressure, DM: diabetes Mellitus, DMR: Debre Markos Referral Hospital, FHRH: Felege Hiwot Referral Hospital, IDF: International Diabetes Federation, PAD: Peripheral arterial disease, SBP: Systolic Blood pressure, T2DM: Type 2 Diabetes Mellitus, UKPDS: United Kingdom Prospective Diabetes Study.

Declarations

Ethics approval and consent to participate

Ethical approval to conduct the study and human subject research approval for this study was received from Debre Markos University, Natural and Computational Science College, Research Ethics Committee and the medical director of the Hospital. We confirm that all methods were carried out by relevant guidelines and regulations. As the study was retrospective, informed consent was not obtained from the study participants, but data were anonymous and kept confidential. Due to the retrospective nature of the study, the need for informed consent was waived by the Research Ethics Committee of Natural and Computational Science College (Debre Markous University) University.

Consent for publication

Not applicable

Availability of Data and Materials

The data sets analyzed in this study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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The source of funding for this research is Debre Markous University. The funding body has no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Author's contribution

NG conceived the study, formulated the design, drafted the manuscript, analyzed and interpreted the data. AS participated in the conception of the study and revised the manuscript critically for important intellectual content. All the authors have read the manuscript and approved the manuscript for submission.

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Figures

Figure 1

Fluctuation in glycemic control over time, among type 2 diabetes patients at Felege Hiwot and Debre Markos Referral Hospital, December, 2011-December,2017

Figure 2

Fluctuation in Good glycemic control over time by Gender among type 2 diabetes patients at Felege Hiwot and Debre Markos Referral Hospital, Decemper, 2011-, December, 2017

Figure 3

Fluctuation in Good glycemic control over time by residence among type 2 diabetes patients at Felege Hiwot and Debre Markos Referral Hospital, Decemper, 2011-, December, 2017

Figure 4

Fluctuation in Good glycemic control over time by Treatment among type 2 diabetes patients at Felege Hiwot and Debre Markos Referral Hospital, Decemper, 2011-, December, 2017

Figure 5

Fluctuation in Good glycemic control over time by Proteinurea among type 2 diabetes patients at Felege Hiwot and Debre Markos Referral Hospital, Decemper, 2011-, December, 2017

Figure 6

Fluctuation in Good glycemic control over time by diastolic blood pressure among type 2 diabetes patients at Felege Hiwot and Debre Markos Referral Hospital, Decemper, 2011-, December, 2017

Figure 7

Fluctuation in Good glycemic control over time of systolic blood pressure among type 2 diabetes patients at Felege Hiwot and Debre Markos Referral Hospital, Decemper, 2011-, December, 2017

Figure 8

Fluctuation in Good glycemic control over time by age group among type 2 diabetes patients at Felege Hiwot and Debre Markos Referral Hospital, Decemper, 2011-, December, 2017