BMJ Open

Rate of glycaemic control and associated factors in patients with type 2 diabetes mellitus treated with insulin-based therapy at selected hospitals in Northwest Ethiopia: a multicentre cross-sectional study

Ashenafi Kibret Sendekie ,[1] Eyayaw Ashete Belachew ,[1] Ephrem Mebratu Dagnew,[2] Adeladlew Kassie Netere [1]

To cite: Sendekie AK, Belachew EA, Dagnew EM, *et al*. Rate of glycaemic control and associated factors in patients with type 2 diabetes mellitus treated with insulin-based therapy at selected hospitals in Northwest Ethiopia: a multicentre cross-sectional study. *BMJ Open* 2022;**12**:e065250. doi:10.1136/bmjopen-2022-065250

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-065250).

Received 03 June 2022
Accepted 16 August 2022

[1]Clinical Pharmacy, University of Gondar College of Medicine and Health Sciences, Gondar, Ethiopia
[2]Clinical Pharmacy, Debre Markos University College of Health Science, Debre Markos, Amhara, Ethiopia

Correspondence to
Ashenafi Kibret Sendekie; ashukib02@yahoo.com

ABSTRACT

Objectives This study was aimed to determine the level of glycaemic control and associated factors in patients with type 2 diabetes mellitus (T2DM) treated with insulin-based therapy.

Designs Institutional-based multicentre cross-sectional study design was employed to conduct this study.

Settings The diabetes follow-up clinics of selected hospitals in Northwest Ethiopia.

Participants Adult patients with T2DM treated with insulin-based therapy at the selected hospitals who met the eligibility criteria were the study participants.

Main outcome measures Good glycaemic control; when fasting blood glucose (FBG) level ranged from 70 to 130 mg/dL, and FBG <70 and >130 mg/dL was considered poor glycaemic control. A logistic regression model was used to identify determinants of poor glycaemic control. A p<0.05 at 95% CI was statistically significant.

Results Of 403 study participants, 54.8% were males with a mean age of 55.03±10.8 years. Though patients with T2DM were treated with insulin-based therapy, most of the participants (72.5%) could not achieve the target FBG. The overall mean FBG was 177.1±54.3, and far from the target glucose level. Patients who could not practise self-monitoring of blood glucose were found more likely to have poor glycaemic control compared with those who practised self-monitoring (p<0.001). Whereas patients who had a normal body mass index (p=0.011) and who were treated with premixed insulin-based therapy (p=0.04) were found less likely to have poor glycaemic control compared with patients with obesity and who received NPH insulin based-regimens, respectively.

Conclusion This study demonstrated that a significant proportion of the study samples could not achieve glycaemic targets and the average blood glucose was far higher than the recommended glycaemic target level. Insulin initiation and titration, considering the determinants of glycaemic control, could be recommended to achieve target glycaemic levels.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This finding indicated that the level of glycaemic control and its predictors among patients with T2DM treated with insulin-based therapy in the resource-limited settings needs intervention and further investigation.
⇒ Determining glycaemic control using glycosylated haemoglobin (HbA1c) might be valuable over fasting blood glucose (FBG) because it estimates the glycaemic level over the past months.
⇒ But HbA1c was not used to determine glycaemic level since it was not available in the study settings and included subjects.
⇒ FBG, which shows a short-term glycaemic index was used to determine glycaemic control, may have its own limitations but it may be worthy than putting aside in the resource-limited settings.
⇒ Some variables such as macrocomplications and microcomplications that were extracted from the patients' medical records may not be consistent throughout the records.

INTRODUCTION

Diabetes mellitus (DM) is one of the most common chronic diseases characterised by elevated blood glucose levels.[1 2] Though DM has several types, type 2 DM (T2DM) is the most common type of diabetes, and characterised by progressive and gradual deterioration in pancreatic beta-cell function, which results in decreasing insulin levels and increasing its resistance and eventually leads to chronic hyperglycaemic.[3–5] Uncontrolled hyperglycaemic is an immediate cause for developing macrovascular and microvascular complications, and premature death.[2] Diabetes had been reported as the major public health threats in Africa, and it was 24 million in the

year 2021 and estimated to be 55 million in 2045, which accounts more than 5%.[6] In Ethiopia, about more than two and half million adults have been living with diabetes[7] and it makes Ethiopia as one of the sub-Saharan Africa countries with the largest diabetes population. An estimated prevalence of this disorder had been dramatically increased from 3.8% to 5.2%.[8] While T2DM estimated to be higher than this figure with a pooled prevalence of 8% in the facility-based studies.[9] Older age commonly higher than 40 years old, family history, body mass index (BMI) ≥25 kg/m^2, having hypertension, physical inactivity, alcohol drinking and cigarette smoking are among the most reported significant risks of T2DM in Ethiopian population.[9]

The primary goal of treating patients with diabetes is to achieve and maintain the therapeutic targets of serum glucose levels. The American Diabetes Association recommends serum glucose target levels such as the glycosylated haemoglobin (HbA1c) less than 7% and the fasting blood glucose (FBG) levels ranges from 70 to 130 mg/dL,[10] which could satisfactorily prevent complications and therapeutic-related costs accompanying with diabetes. Thus, patients with T2DM can be treated with various regimens types, for example, they could be initially treated with non-pharmacological means, followed by oral antidiabetics (OADs). At the beginning of the therapy, many patients might potentially attain the desired goals; however, through time multidrug regimens including insulin become important.[11] The inclusion of insulin in the regimens is very crucial to decrease the long-term risks of diabetic complications.[12] Meanwhile, when the HbA1c is more than 10% and/or FBG >250 mg/dL, the initial management options either alone or in combined form are less likely to achieve the target glycaemic goal; therefore, initiating insulin would be compulsory at this stage.[13]

Broadly speaking, several studies have demonstrated in developed countries, and disclosed that insulin-based therapy in patients with T2DM has positive clinical impacts.[14–16] Moreover, factors determining the poor glycaemic control levels have been investigated. In contradiction with the former evidences, in low-income and middle-income countries, the rate of glycaemic control and factors to poor glycaemic status in patients with T2DM who have been treated with insulin-based therapy are not supported with sufficient literatures and data is scarce. To the best of authors' search, there is only a single study in Ethiopia that has determined the level of glycaemic control in newly insulin-initiated patients with T2DM.[17] However, this study is different from the previous study in terms of the study design and settings which the current study is a multicentre prospective cross-sectional study with incorporation of important clinical and sociodemographic variables which can affect glycaemic control. Such variables include BMI, Self-monitoring of blood glucose (SMBG) practice of the patients and other dietary, work and physical exercise-related factors which are not considered in the earlier study because of its retrospective nature of the study. Identification of such different patient-related and clinical factors associated with glycaemic control and determining the level of blood glucose is an important issue to apply appropriate intervention to improve glycaemic control and prevent long-term complications results from diabetes. Therefore, this study was aimed to assess level of glycaemic control and determinants in patients with T2DM treated with insulin-based therapy at the selected hospitals in Northwest Ethiopia. The study will help to understand the extent of glycaemic control and the impact of predictor variables towards glycaemic control in insulin-treated patients with T2DM in the resources-limited settings and among one of the largest diabetes populations in the sub-Saharan Africa.

MATERIALS AND METHODS

Study design and settings

Institutional-based multicentre cross-sectional study was conducted at the selected hospitals in Northwest Ethiopia from October to December 2021. The study hospitals were selected randomly among several public and University hospitals found in the region. University of Gondar Comprehensive Specialised hospital (UoGCSH), Felege-Hiwot Comprehensive Specialised hospital (FHCSH), Tibebe-Ghion Comprehensive Specialised hospital (TGCSH) and Debre-Tabor comprehensive specialised hospital (DTCSH)) were settings where the study sample was collected. These hospitals are located in Gondar, Bahir-Dar and Debre-Tabor cities and have been serving for more than 25 million people in their catchment areas.

Study population and selection criteria

This study was applied on patients with T2DM who were capable of being interviewed and who had completed medical records. These patients had been attended in the chronic medical ambulatory clinics of the hospitals. The patients were included in the study if they met the following criteria: (1) Patients diagnosed with T2DM and age ≥18 years; (2) Had been treated with insulin-based regimens and (3) Had been on treatment for a minimum of 3 months. While pregnant pteints, patients who refused to participate, patients who couldn't communicate or were severely ill, and had incomplete medical records to relevant data were excluded from the study.

Sample size determination and sampling technique

The sample size calculation was prepared in compliance with a single population proportion formula. Considering 50% prevalence rate of poor glycaemic control levels in patients with T2DM who have been treated with insulin-based therapy, to obtain a maximum representative sample size. We also assumed that 5% for the two-tailed type-I error (Zα=1.96); two-sided 95% confidence level and resulted about 385 samples. Finally, a total of 424 patients were considered in the study after assuming 10% potential nonresponse to the interview or/and missed

and lost data. The final sample size was proportionally allocated to the selected hospitals based on previously estimated number of patients with T2DM in the settings. Consequently; 175, 125, 68 and 56 eligible participants were approached in UoGCSH, FHCSH, DTCSH and TGCSH hospitals, respectively.

Study participants from the selected hospitals were included using consecutive sampling techniques; all patients with T2DM who had been treated with insulin-based therapy and who fulfilled the inclusion criteria and coming for follow-up during the data collection periods were approached until the required sample is maintained.

Outcome measures

Glycaemic control

In this study, good glycaemic control refers to FBG levels ranging from 70 to 130 mg/dL and FBG <70 and >130 mg/dL categorised under poor glycaemic level.

Operational definitions

Body mass index

It was measured in terms of patient's weight in kilogram (kg) divided by the square of patient's height in metres (kg/m^2). Based on the WHO BMI classification, BMI classified and interpreted as <18.5 kg/m^2 (underweight), 18.5–24.9 kg/m^2 (normal weight), 25–29.5 kg/m^2 (overweight) and ≥30 kg/m2 (obesity).

Self-monitoring blood glucose

Indicates whether a patient had an experience in measuring the serum blood glucose levels at home.

Macrovascular complications

Complications such as; stroke, ischaemic heart disease, heart failure, coronary artery disease, peripheral vascular disease.

Microvascular complications

Complications such as; diabetic nephropathy, peripheral neuropathy and diabetic retinopathy.

Hypoglycaemia

A clinical episodes of hypoglycaemia and/or FBG of <70 mg/dL recorded on the patients' medical records was taken as hypoglycaemia.

Health insurance

It is a prepayment system where individuals or households pay small and their contributions are pooled together to get healthcare services at the time of illness and protect them from catastrophic health expenditures. In Ethiopian, the government have been worked on the implementation of two types of health insurance systems.[18] The first is Community-based Health Insurance (CBHI) that targets employers from rural and informal sectors through the Federal Ministry of Health of Ethiopia,[19] and it brings some improvements in the population's health and in the financing structure of healthcare. The second type of health insurance system is Social Health Insurance (SHI), which comprises the population engaged in the formal sectors of the economy. In recent times, the Ethiopian health insurance agency is working to improvie risk pooling among different groups of the population; such as between rich and poor, healthy and sick.[20 21] CBHI packages in Ethiopia include all necessary family health services and curative care of disease conditions, which are part of the primary health packages excludes dental implementations, optic services and out of country referrals.[18 20]

Data collection instruments and procedures, and quality control management

Data were collected on direct patient interviews and extracting the patients' medical records using structured questionnaires. The data abstraction format was prepared after reviewing different related clinical literatures on similar topics and some modifications were made considering the local clinical settings. Then, pretest was done on 5% of the subjects in one of the study areas to ensure completeness of abstraction format and were excluded from the final analyses. Then, an appropriate amendment was employed. The data collection tool had three sections (online supplemental file 1): (1) sociodemographic characteristics and patients' self-care practices such as SMBG status, smoking status, alcohol drinking status, physical activity status; (2) clinical history and characteristics; and (3) medication history and characteristics. Clinical characteristics include durations since diagnosis and initiation of treatment, blood pressure (BP), FBG levels, lipid profiles, serum creatinine, comorbidities and complications, and medication history section contained medications used for treating both T2DM and other comorbidities and complications. The weight and height of the participants were measured using digital weight scale and stadiometer as physical examination part. Treatment intensification was made according to ADA (American Diabetes Association) recommendations and glibenclamide and/or metformin were used in combination with insulin (NPH (neutral protamine hagedorn) or premixed). The average FBG level was computed from the average of three different records, at least 1 month apart, was used to determine the level of glycaemic control. The data were collected by experienced nurses after getting of training for 2 days. The supervisor explicitly clarified the purpose of the study and data abstraction tool; and was monitoring the collection procedure closely. Once the medical record identification numbers were entered to the Microsoft excel 2013 and checked for repetition, the data were extracted and the patients were interviewed.

Data entry processing and analysis

Data entrance, quality, completeness, consistency and clarity were checked before any further analysis was

Table 1 Sociodemographic characteristics of patients with T2DM treated with insulin-based therapy attending hospitals in Northwest Ethiopian, 2021 (N=403)

Variables	Category	Frequency	Percentage (%)	Mean±SD
Sex	Male	221	54.8	
	Female	182	45.2	
Age (years)				55.0 (±10.8)
Residency	Urban	237	58.8	
	Rural	166	41.2	
Duration of T2DM since diagnosis (years)	1–5	30	7.4	13.6 (± 3.8)
	6–10	141	35	
	11–20	187	46.4	
	> 20	45	11.2	
Body weight (kg)	–	–	–	65.6 (±8.3)
BMI (kg/m^2)	Underweight	34	8.4	
	Normal	235	58.3	
	Overweight	56	13.9	
	Obesity	78	19.4	
Educational status	Unable to read or write	55	13.6	
	Primary school	133	33	
	Secondary school	150	37.2	
	College and above	65	16.1	
Health insurance	Yes	306	75.9	
	No	97	24.1	
SMBG practice at home	Yes	125	31	
	No	278	69	
Smoking status	Currently smoking	69	17.1	
	Previously smoker	97	24.1	
	Nonsmoker at all	237	58.8	
Work-related physical activity	Sedentary	181	44.9	
	Moderate	138	34.3	
	Vigorous	84	20.8	
Family history of DM	Yes	263	65.3	
	No	140	34.7	

BMI, body mass index; DM, diabetes mellitus; SMBG, self-monitoring of blood glucose; T2DM, type 2 diabetes mellitus.

performed. Then, it was entered in to Epi Info V.8, and transported and analysed with the SPSS V.22. Normality of the data was determined by Q-Q plot and histograms. Descriptive statistics were used to present the sample characteristics. Means with ±SDs were also used to display results for continuous variables. One-way analysis of variance (ANOVA) with post hoc test was used to compare mean glucose level difference between antidiabetic treatement groups. Logistic regression was used to assess the association of glycaemic control with predictor variables. Variables with p value of ≤0.2 in the bivariable analysis were considered for further multivariable analysis to identify the factors potential linked with poor glycaemic control status. A p<0.05 at 95% CI was statistically significant.

Patient and public involvement

There was no patient and public involvement in the study design and methodology.

RESULTS

Sociodemographic characteristics of the study participants

Initially 424 patients were approached, and 403 completed the questionnaire with a response rate of 95%. Male respondents were over represented (54.8%) and the mean (±SD) age of the samples was 55.0±10.8. Just fewer than sixty percent of the participants were with normal BMI range (18.5–24.5 kg/m^2). Ahigher proportions of the surveyed (37.2%) had completed the secondary school educational level and almost 60% of them were ever non-smoker (58.8%). Less than one-thirds (31%) practised the SMBG at home (table 1).

Clinical characteristics and medication patterns of the participants

About three-fourths (72%) of the study participants had diagnosed with hypertension. Likewise, almost 60% were with dyslipidaemia and macrovascular complications accounts 16.9% on top of T2DM. Most of the participants,

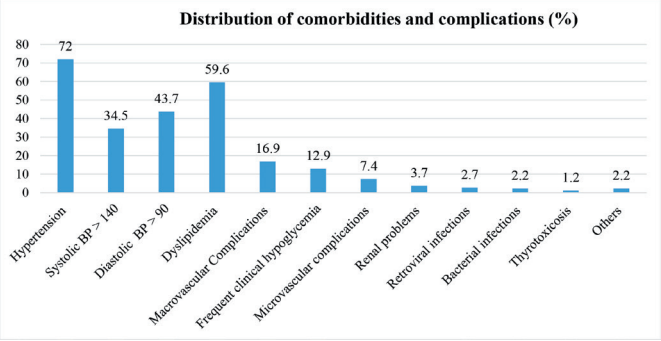

Figure 1 Distributions of comorbidities and complications in patients with T2DM treated with insulin-based therapy attending hospitals of Northwest Ethiopian, 2021 (N=403). Others; bronchial asthma, diabetic ketoacidosis, malaria, skin disorders, anaemia, malnutrition. BP, blood pressure; T2DM, type 2 diabetes mellitus.

65.5% and 56.3% were with systolic BP <140 mm Hg and diastolic BP <90 mm Hg, respectively (figure 1). Almost 60% of the patients with T2DM (59.8%) had been treated with a dual combination of insulin plus metformin followed by triple combinations of Insulin plus metformin plus glibenclamide (34.5%). Of the insulin types NPH took higher proportions (77.7%). Enalapril (70%) and atorvastatin (35.5%) were the most prescribed antihypertensive and lipid-lowering agents, respectively (table 2).

Level of glycaemic control in patients with type 2 diabetes treated with insulin-based therapy

The overall glycaemic level of the study participants was computed, and it was estimated to be FBG level (measured in mg/dL) of 177.1 (± 54.3) (ranges: 62–406 mg/dL). But the patients who were treated with triple antidiabetic medications of insulin plus metformin plus glibenclamide had worse FBG levels (Mn=189.7) than patients who were treated using insulin plus metformin (Mn=170.1) and insulin (Mn=174.3). A one-way ANOVA also proved that the difference in FBG levels between the treatment groups was statistically significant, $F^2 = 5.94$, p=0.003. The post hoc test using Tukey HSD revealed that there is a statistically significant difference in FBG levels between insulin plus metformin plus glibenclamide (Mn=189.7) and insulin plus metformin (Mn=170.1) treatment groups

Table 2 Proportions of medications in patients with T2DM treated with insulin-based therapy

Medications	Category	Frequency	Percentage (%)	Mean (±SD)
T2DM medications	Insulin alone	23	5.7	
	Insulin+metformin	241	59.8	
	Insulin+metformin+glibenclamide	139	34.5	
Type of insulin used	NPH	313	77.7	
	Premixed	90	22.3	
Antihypertensive medications	Enalapril	282	70	
	Amlodipine	66	16.4	
	Hydrochlorothiazide	55	13.6	
	Atenolol	19	4.7	
	Metoprolol	15	3.7	
	Nifedipine	12	3%	
	Furosemide	7	1.7	
Lipid-lowering agents	Atorvastatin	143	35.5	
	Simvastatin	48	11.9	
Other class of medications	Aspirin	240	59.6	
	Amitriptyline	23	5.7	
	Gastrointestinal	14	3.5	
	ART medication (TDF/3TC/DTG)	11	2.7	
	Antibiotics	10	2.5	
	Antiasthmatic drugs	5	1.2	
	Antithyroid drugs	5	1.2	
Average daily dose of insulin (unit)				16.9 (±5.7)
Average daily dose of metformin (mg)				1356.8 (±428.9)
Average daily dose of glibenclamide (mg)				13.2 (±5.1)

ART, anti retroviral therapy; NPH, neutral protamine hagedorn; T2DM, type 2 diabetes mellitus.

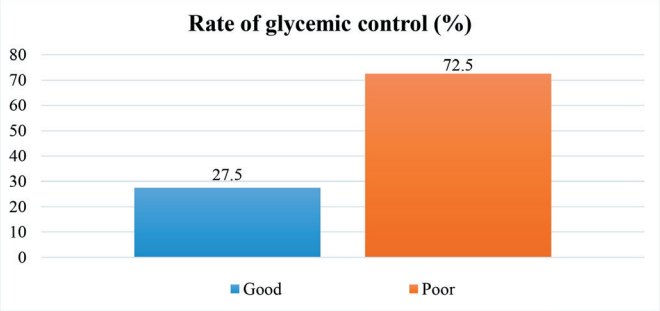

Figure 2 Rate of glycaemic control in patients with T2DM treated with insulin-based therapy (N=403). T2DM, type 2 diabetes mellitus.

(p=0.002). But the rate of hypoglycaemia was higher in the triple therapy (15.8%) compared with dual (11.2%) and insulin (13%). The overall rate of hypoglycaemia was reported to be 12.9%.

A higher proportion of the study individuals (72.5%) were found to have poor level of glycaemic control with only 27.5% of the study participants achieved target fasting glucose level (figure 2). Of the insulin types, more than half (52.2%) patients who were treated with the premixed insulin-based regimens achieved the target FBG level. But frequent episodes of hypoglycaemia were also higher (38.9%) in those patients treated with the premixed insulin-based regimens compared with patients who were treated by NPH insulin-based therapy (5.4%); p<0.001.

Determinants of the poor glycaemic control levels in the study samples

Logistic regression analysis was performed to examine the relationship between the primary outcome and the predictor variables. Following this, the multivariable logistics regression revealed that there had been independent factors with which determined the level of glycaemic control in insulin-treated patient with T2DM. Consequently, holding all other predictor variables constant, patients who did not practise the SMBG at home were found more like to have poor glycaemic control compared with patients who did practise SMBG (adjusted OR, AOR=7.572, 95% CI (3.117 to 18.394); p<0.001). In contrast, patients who had normal BMI were found less likely to have poor glycaemic control compared with patients with obesity (AOR=0.450, 95% CI (0.062 to 3.226): p=0.011). Further, patients who were treated by premixed insulin-based regimens were also found less likely to have poor glycaemic control to compared with patients who were treated by NPH insulin-based regimes (AOR=0.356, 95% CI (0.127 to 0.959); p=0.04) (table 3).

DISCUSSION

This institutional based multicentre cross-sectional study has gone through highlighting the level of glycaemic control and associated factors in patients with T2DM who were treated with insulin-based regimens by using FBG in the resource-limited settings where glycaemic control couldn't be monitored routinely with HbA1C. The clinical characteristics of the participants in this study were comparable with the previous studies conducted in the country, which most of the participants had cardiovascular disorders like hypertension and diabetes-related macrovascular complications, and most of the participants received metformin plus insulin combination regimens.[17] This study may reflect the characteristics and management practice of patients with T2DM in the country.

Indeed, this study revealed those most of patients with the T2DM could not achieve the desired serum glycaemic levels even though they were treated with insulin regimens. This study also identified important factors which potentially determine the level of glycaemic control. This study demonstrated that the mean blood glucose level was far higher than the recommended target glycaemic level. Moreover, not practising the SMBG was significantly associated with poor glycaemic control. On the other hand, patients with normal BMI and who were treated by the premixed insulin-based regimens were found less likely to have poor glycaemic control than obese patients and participants who received NPH insulin-based regimens, respectively.

The evidence from this study indicated that though patients with T2DM have been treated with insulin-based regimens, in consistent with the previous studies,[14 15 17 22 23] only around one-fourth of the patients achieved the target glucose levels. Insulin is often used as an adjuvant to oral glucose lowering agent in patient with T2DM who could not attain the recommended glucose levels with initial preferred treatment of OAD agents. But it is very likely that participants may have erroneously taking insufficient daily dose and incorrect titration of insulin and this may have brought about poor changes in glucose levels. As put forward by the previous study,[24] insufficient dose titration of insulin could result in these effects. For instance, in this study, the average daily dose of insulin was 16.9 mg (ranges: 6–40 mg) and even though premixed insulin has a good effect on glycaemic control by controlling postprandial glucose, still majority of patients were treated with NPH insulin-based regimens. Thus, the findings indicate that need for insulin titration in terms of the dose and the regimen types could be recommendable. Non-adherence to the recommended insulin titration might be due to insufficient communication between clinicians and patients[25] regarding postprandial glucose level of home measurement, fear of adverse effects like hypoglycaemia and healthcare providers might be reluctant to close follow-up. Thus, to attain the maximum clinical benefits, insulin could be titrated to a daily recommended dose and regimens with a close monitoring follow-up to prevent the lower serum glucose levels below the target. In the contrary, the current finding significantly differs from previous results reported in the literatures.[16 26 27] The source of the discrepancies might be due to differences in the titration of the recommended daily dose of

Table 3 Bivariable and multivariable logistics regression analysis of variables associated with glycaemic levels of patients with T2DM

Variables	Glycaemic control					
	Poor	Good	COR (95% CI)	P value	AOR (95% CI)	P value
Residency						
Urban	165	72	0.704 (0.447 to 1.107)	0.129	0.934 (0.377 to 2.311)	0.882
Rural	127	39	1		1	
SMBG practice						
No	236	42	6.923 (4.277 to 11.208)	0	7.572 (3.117 to 18.394)	0.000*
Yes	56	69	1		1	
BMI (kg/m^2)						
Underweight	27	7	0.321 (0.099 to 1.0403)	0.034	0.196 (0.024 to 1.566)	0.124
Normal	152	83	0.153 (0.064 to 0.366)	0	0.119 (0.023 to 0.611)	0.011*
Overweight	41	15	0.228 (0.082 to 0.633)	0.005	0.450 (0.062 to 3.226)	0.43
Obesity	72	6	1		1	
Smoking status						
Currently smoker	42	27	0.613 (0.350 to 1.073)	0.01	0.315 (0.101 to 1.087)	0.055
Previously smoker	80	17	1.855 (1.023 to 3.362)	0.087	1.588 (0.555 to 4.530)	0.047
Nonsmoker	170	67	1	0.042	1	0.389
Physical activity						
Sedentary	132	49	0.634 (0.336 to 1.197)	0.16	0.686 (0.219 to 2.148)	0.518
Moderate	92	46	0.471 (0.246 to 0.901)	0.023	0.445 (0.132 to 1.498)	0.191
Vigorous	68	16	1		1	
Insulin type						
Premixed	43	47	0.235 (0.143 to 0.386)	0	0.356 (0.127 to 0.959)	0.040*
NPH	249	64	1		1	
Amlodipine						
Yes	54	12	1.872 (0.960 to 3.651)	0.066	1.579 (0.430 to 5.793)	0.491
No	238	99	1		1	
Atenolol						
Yes	10	9	0.402 (0.159 to 1.017)	0.054	0.323 (0.091 to 1.148)	0.081
No	282	102	1		1	
Lipid lowering agent						
Atorvastatin	109	34	1.924 (0.955 to 3.873)	0.067	2.241 (0.889 to 5.583)	0.083
Simvastatin	30	18	1		1	
Frequent clinical hypoglycaemia						
Yes	24	28	0.265 (0.146 to 0.483)	0	0.779 (0.230 to 2.635)	0.688
No	268	83	1		1	
SBP (mm Hg)						
≥140	110	29	1.709 (1.052 to 2.776)	0.03	0.860 (0.356 to 2.078)	0.737
<140	182	82	1		1	

*Indicates the statistically significant at p<0.05.
AOR, adjusted OR; BMI, body mass index; COR, crude OR; NPH, neutral protamine hagedorn; SBP, systolic blood pressure; SMBG, self-monitoring blood glucose; T2DM, type 2 diabetes mellitus.

insulin. Moreover, variations in medical care and socio-demographic, nutritional habits, living standards and knowledge on prevention and treatment strategies across the study countries might be the reasons for variations in target glycaemic level achievement of insulin-treated patients with diabetes.

This study also examined differences in glucose levels among treatment groups. The finding revealed those patients who were treated with triple therapy of insulin plus metformin plus glibenclamide had significantly worse glucose levels compared with patients treated by dual combination of insulin plus metformin and insulin alone (p=0.002). The finding may imply those patients with poor glucose levels could need additional antidiabetic agents on the top of insulin. But hypoglycaemia episodes were higher in patients treated with the triple treatment groups compared with patients treated with insulin plus metformin and insulin alone. This could be potentially could be because of the dual hypoglycaemic burden of insulin and glibenclamide. Therefore, patients treated with insulin plus glibenclamide should be highly vigilant and motivated to aware and manage hypoglycaemic risks.

This study demonstrated those patients who did not practise SMBG at home were more likely to have poor glycaemic control compared with those who did, and this is corroborated with the previous studies.[28 29] This might be because of lack of access of apparatus for SMBG at home. The finding suggests that enhancing the self-monitoring blood glucose practice could be encouraged to increase the adherence of SMBG that used to control blood glucose levels in patients with DM. The current study also showed that patients who had a normal level of BMI (p=0.011) were found to be less likely to have poor glycaemic control than those patients with obesity. Consistently, previous studies have revealed that patients with higher BMI result in poor glycaemic control.[30–32] This relation might justify those patients with higher BMI or obesity caused to insulin resistance and in turn it results in poor glycaemic target achievement in the long term. Thus, patients with diabetes could be recommended to reduce their overweight to a normal level by different recommended daily physical activities and modification of diets.

Moreover, this finding revealed that patients who were treated with premixed insulin-based regimens were found less likely to have poor glycaemic control compared with patients who were received NPH insulin-based regimens. This might be because the premixed insulin regimen has two types of insulin preparations (short acting and intermediate acting), which could potentially cover both the preprandial and postprandial glucose release, and it was matched with previous studies.[17 33] In addition, the postprandial glucose level was at the comfortable level in patients treated with premixed insulin regimens. However, consistently with the previous study,[34] patients who were treated with premixed insulin-based regimens had developed frequent clinical hypoglycaemia. Hypoglycaemic episodes have been more frequent while soon after administration and sometimes they existed in patients participated in physical activity. Therefore, when premixed insulin is recommended to patients, hypoglycaemic episodes could be watched carefully and patients need to be aware and self-manager of the symptoms.

Indeed, poor glycaemic control in patients with diabetes may be affected not only by the factors discussed in this study but also might result from multifactorial contributing factors including, the progressive nature of disease its self, the type of medication regimens preferred and combined, the patients' adherence level of their medications and adherence to lifestyle modifications of the patients. Therefore, both healthcare providers and patients themselves could be vigilant to delay the progress of the disease by achieving target glucose levels. In addition, insulin initiation as well as titration would be individualised on the basis of contributing factors for poor glycaemic control in individual patients. Generally, this study examined the rate of glycaemic control using FBG based on ADA recommendations in these resource-limited settings where HbA1c could not be used routinely to monitor blood glucose level. It was used as a benchmark for clinicians and future researchers to examine glycaemic control and predictors in patients with T2DM who are treated with insulin-based therapy.

CONCLUSION

This multicentre institutional-based study showed that a significant proportion of patients with T2DM could not achieve the target glucose level with the mean FBG level was far higher than the recommended glycaemic level. Not practising SMBG was found to be significantly associated with poor glycaemic control. Patients with normal BMI and patients treated with premixed insulin-based regimens were found less likely to have poor glycaemic control compared with their counterparts. Therefore, insulin initiation and titration in patients with T2DM could be individualised and consider potential factors of glycaemic control.

Acknowledgements The authors would like to thank the University of Gondar to provide ethical approval to the study and the selected hospitals to for their positive cooperation during the study. We would also like to forward our gratitude to the data collectors and study participants.

Contributors AKS contributed to the conception, data curation, formal analysis, investigation, methodology, project administration, resources, writing of the original draft of the manuscript, reviewing and editing. EAB and EMD contributed to the data curation, formal analysis, methodology, review and editing of the final manuscript. AKN contributed to data curation, formal analysis, methodology, supervision, validation, review and editing of the final manuscript. All authors of this manuscript have read and approved the final version of this manuscript. AKS is responsible for the overall content as the guarantor of this paper.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The study was ethically approved by ethical review committee of the University of Gondar with a reference number of Sop/037/2021. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

ORCID iDs
Ashenafi Kibret Sendekie http://orcid.org/0000-0001-5982-853X
Eyayaw Ashete Belachew http://orcid.org/0000-0002-0421-4327
Adeladlew Kassie Netere http://orcid.org/0000-0003-0519-509X

REFERENCES

1 World Health Organization. *Global report on diabetes*. Geneva: World Health Organization, 2016.
2 World Health Organization. World health statistics 2018: monitoring health for the SDGs, sustainable development goals. Geneva World Health Organization; 2018.
3 Mudaliar S. Choice of early treatment regimen and impact on β-cell preservation in type 2 diabetes. *Int J Clin Pract* 2013;67:876–87.
4 Kahn SE, Cooper ME, Del Prato S. Pathophysiology and treatment of type 2 diabetes: perspectives on the past, present, and future. *Lancet* 2014;383:1068–83.
5 Gentile S, Strollo F, Viazzi F, *et al*. Five-year predictors of insulin initiation in people with type 2 diabetes under real-life conditions. *J Diabetes Res* 2018;2018:1–10.
6 Sun H, Saeedi P, Karuranga S, *et al*. IDF diabetes atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract* 2022;183:109119.
7 International Diabetes Federation. IDF diabetes atlas. In: *Brussels*. 8th ed. International Diabetes Federation, 2017: 147.
8 Bishu KG, Jenkins C, Yebyo HG, *et al*. Diabetes in Ethiopia: a systematic review of prevalence, risk factors, complications, and cost. *Obes Med* 2019;15:100132.
9 Zeru MA, Tesfa E, Mitiku AA, *et al*. Prevalence and risk factors of type-2 diabetes mellitus in Ethiopia: systematic review and meta-analysis. *Sci Rep* 2021;11:21733.
10 American Diabetes Association. 6. Glycemic Targets: *Standards of Medical Care in Diabetes—2020*. *Diabetes Care* 2020;43:S66–76.
11 Cappon G, Vettoretti M, Sparacino G, *et al*. Continuous glucose monitoring sensors for diabetes management: a review of technologies and applications. *Diabetes Metab J* 2019;43:383–97.
12 Nathan DM, DCCT/EDIC Research Group. The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: overview. *Diabetes Care* 2014;37:9–16.
13 Kuritzky L. Addition of basal insulin to oral antidiabetic agents: a goal-directed approach to type 2 diabetes therapy. *MedGenMed* 2006;8:34.
14 Blonde L, Meneghini L, Peng XV, *et al*. Probability of achieving glycemic control with basal insulin in patients with type 2 diabetes in real-world practice in the USA. *Diabetes Ther* 2018;9:1347–58.
15 Mata-Cases M, Mauricio D, Franch-Nadal J. Clinical characteristics of type 2 diabetic patients on basal insulin therapy with adequate fasting glucose control who do not achieve HbA1c targets. *J Diabetes* 2017;9:34–44.
16 Brož J, Janíčková Ždárská D, Štěpánová R, *et al*. Addition of basal insulin to oral antidiabetic agents in patients with inadequately controlled type 2 diabetes leads to improved HbA1c levels: metabolic control, frequency of hypoglycemia, and insulin titration analysis as results of a prospective observational study (Bali study). *Diabetes Ther* 2019;10:663–72.
17 Sendekie AK, Teshale AB, Tefera YG. Glycemic control in newly insulin-initiated patients with type 2 diabetes mellitus: a retrospective follow-up study at a university hospital in Ethiopia. *PLoS One* 2022;17:e0268639.
18 Insurance EH. Ministry of health- Ethiopia. Available: https://www.moh.gov.et/site/Ethiopian_Health_Insurance [Accessed 15 July 2022].
19 Agency EHI. *Evaluation of community-based health insurance pilot schemes in Ethiopia*, 2015.
20 Haile M, Ololo S, Megersa B. Willingness to join community-based health insurance among rural households of Debub bench district, bench Maji zone, Southwest Ethiopia. *BMC Public Health* 2014;14:591.
21 Wang H, Ramana GNV. *Universal Health Coverage for Inclusive and Sustainable Development : Country Summary Report for Ethiopia*. Washington, DC: World Bank, 2014.
22 Brož J, Janíčková Žďárská D, Urbanová J, *et al*. Current level of glycemic control and clinical inertia in subjects using insulin for the treatment of type 1 and type 2 diabetes in the Czech Republic and the Slovak Republic: results of a multinational, multicenter, observational survey (DIAINFORM). *Diabetes Ther* 2018;9:1897–906.
23 Kostev K, Dippel FW, Rathmann W. Glycemic control after initiating basal insulin therapy in patients with type 2 diabetes: a primary care database analysis. *Diabetes Metab Syndr Obes* 2015;8:45–8.
24 Nathan DM, Buse JB, Davidson MB, *et al*. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American diabetes association and the European association for the study of diabetes. *Diabetes Care* 2009;32:193–203.
25 Berard L, Bonnemaire M, Mical M, *et al*. Insights into optimal basal insulin titration in type 2 diabetes: results of a quantitative survey. *Diabetes Obes Metab* 2018;20:301–8.
26 Chien M-N, Chen Y-L, Hung Y-J, *et al*. Glycemic control and adherence to basal insulin therapy in Taiwanese patients with type 2 diabetes mellitus. *J Diabetes Investig* 2016;7:881–8.
27 Blak BT, Smith HT, Hards M, *et al*. A retrospective database study of insulin initiation in patients with type 2 diabetes in UK primary care. *Diabet Med* 2012;29:e191–8.
28 Ji L, Su Q, Feng B, *et al*. Glycemic control and self-monitoring of blood glucose in Chinese patients with type 2 diabetes on insulin: baseline results from the COMPASS study. *Diabetes Res Clin Pract* 2016;112:82–7.
29 Oluma A, Abadiga M, Mosisa G, *et al*. Magnitude and predictors of poor glycemic control among patients with diabetes attending public hospitals of Western Ethiopia. *PLoS One* 2021;16:e0247634–e.
30 Demoz GT, Gebremariam A, Yifter H, *et al*. Predictors of poor glycemic control among patients with type 2 diabetes on follow-up care at a tertiary healthcare setting in Ethiopia. *BMC Res Notes* 2019;12:207.
31 Chan WB*et al*. Glycaemic control in type 2 diabetes: the impact of body weight, beta-cell function and patient education. *QJM* 2000;93:183–90.
32 Wagai GA, Romshoo GJ. Adiposity contributes to poor glycemic control in people with diabetes mellitus, a randomized case study, in South Kashmir, India. *J Family Med Prim Care* 2020;9:4623–6.
33 Liu G, Dou J, Pan Y, *et al*. Comparison of the effect of glycemic control in type 2 diabetes outpatients treated with premixed and basal insulin monotherapy in China. *Front Endocrinol* 2018;9:639.
34 Bellido V, Suarez L, Rodriguez MG, *et al*. Comparison of Basal-Bolus and premixed insulin regimens in hospitalized patients with type 2 diabetes. *Diabetes Care* 2015;38:2211–6.

Sendekie AK et al.

Informed consent and Data collection tools

1. **Informed Consent form**

Dear participant,

We are from University of Gondar and Debre Markos university research teams, and we would like to kindly request your consent to participate on the study. The aim of this study is to assess "Rate of glycemic control and associated factors in type 2 diabetes mellitus patients treated with insulin-based therapy at the selected hospitals of Northwest Ethiopian". This is a cross-sectional study; the questioner comprises of questions regarding your socio-demographics information, clinical charachterstics, medications that used to treat your problems. This questionnaire will hardly take your 5-6 minutes and all the information we obtain will remain strictly confidential and your answer and name will never be revealed. We assure you that it is totally a voluntary participation and feel free to refuse or to withdraw at any point in the study.

Do you agree to participate in this study? 1. Yes ---- 2. No ----

If yes, please ready for interview for the following socio-demographic and some clinical charachterstics questions, the rest will take from your medical records.

II. Data collection tools

I. Patients' socio-demographic characteristics

Variables	**Category**
Sex	1. Male 2. Female
Age (in years)	---
Wight	---
Height	---
Body mass index (BMI)	---
Duration of diabetes mellitus since diagnosis (years)	----
Residence	1. Urban 2. Rural
Education status	1. Unable to write and read 2. Primary school

Sendekie AK et al.

	3. Secondary school 4. College and University
Use health insurance	1. Yes 2. No
Self-monitoring of blood glucose (SMBG)	1.Yes 2. No
Smoking status	1. Currently smoker 2. Previously smoker 3. Nonsmoker at all
Work related/physical activity/day	1. Sedentary 2. Moderate 3. Vigorous
Family history of T2DM	1. Yes 2. No

II. Clinical characteristics of insulin treated patients type 2 diabetes mellitus

Characteristics		
Blood pressure records		Systolic blood pressure (SBP) ---- Diastolic blood pressure (DBP ----
Laboratory values		
Blood glucose level	HbA1c (%) (three records)	HbA1C1_____ HbA1C 2_____ HbA1C3_____ **Average HbA1C _____**
	FBG (mg/dl)	FBG1_____ FBG2_____ FBG3_____ Average FBG_____
Lipid profiles	LDL-Cholesterol	
	HDL-Cholesterol	
	Total triglyceride	
	Total-Cholesterol	
Renal function test	Creatinine(mg/dl)	
Electrolytes	Na+	
	K+	

Sendekie AK et al.

Complications and comorbidities	
Hypertension	
Dyslipidemia	
Renal problems (CKD, AKI)	
Macrovascular complications	
Microvascular complications	
Bacterial infections	
Diabetic ketoacidosis	
Hypoglycemia	
Other complications	

III. Medications with daily doses of insulin treated patients with type 2 diabetes mellitus

Medications		Average daily doses (if necessary, particularly for antidiabetic and lipid-lowering agents is a must)
Antidiabetic medications	Metformin	
	Glibenclamide	
	Insulin (NPH or Premixed)	
Type of insulin regimens	NPH	
	Premixed	
Antihypertensive agents	Angiotensin converting enzyme inhibitors (ACEIs)	
	Calcium channel blockers (CCBs)	
	Beta-blockers	
	Angiotensin converting enzyme inhibitors (ACEIs)	
Lipid lowering agents	Simvastatin	
	Atorvastatin	
	Lovastatin	
Others	Aspirin	
	Amitriptyline	

Note: => HbA1C1 and/or FBG should be taken the records of three consecutive samples at least one month apart, and the average of the three records could be taken as current glycemic level.

Sendekie AK et al.

⇨ Doses of medications could be taken from the average doses of respective follow-up times.

Sendekie AK, *et al. BMJ Open* 2022; 12:e065250. doi: 10.1136/bmjopen-2022-065250