BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-065250
Article Type:	Original research
Date Submitted by the Author:	03-Jun-2022
Complete List of Authors:	Sendekie, Ashenafi; University of Gondar College of Medicine and Health Sciences, Clinical pharmacy Belachew, Eyayaw; University of Gondar College of Medicine and Health Sciences, clinical pharmacy Dagnew, Ephrem Mebratu; Debre Markos University College of Health Science, Clinical pharmacy Netere, Adeladlew; University of Gondar College of Medicine and Health Sciences, clinical pharmacy
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, General endocrinology < DIABETES & ENDOCRINOLOGY, Diabetes & endocrinology < INTERNAL MEDICINE

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Rate of glycemic control and associated factors in type 2 diabetes mellitus patients treated with insulin-based therapy at the selected hospitals of Northwest Ethiopia

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

Author's affiliations

[1]Department of Clinical Pharmacy, School of Pharmacy, College of Medicine and Health Sciences, University of Gondar; Gondar, Ethiopia

[2]Department of Clinical Pharmacy, College of Health Science, Debre Markos University, Debre Markos, Ethiopia

*Corresponding Author

Ashenafi Kibret Sendekie

Email: ashukib02@yahoo.com / Ashenafi.kibret@uog.edu.et

Po Box: 196

Abstract

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

Designs: Institutional-based multicenter cross-sectional study design was employed.

Settings: The diabetes follow-ups clinics of Northwest Ethiopia hospitals.

Participants: All adult T2DM patients treated with insulin-based therapy at the selected hospitals.

Main Outcome measures: Good glycemic control; fasting blood glucose (FBG) levels ranges from 70 to 130 mg/dl, and poor glycemic control was FBG < 70 and > 130 mg/dl. A logistic regression model was used to identify determinants of poor glycemic control. A P-value < 0.05 with 95% confidence interval in the multivariable analysis model was taken significant.

Results: Of 403 study participants, 54.8% were males with a mean of age 55.03(±10.8) years. Though insulin was initiated, the majority of the participants (72.5%) did not achieve target fasting blood glucose (FBG). The overall mean FBG was far higher from the target level. Patients who did not practice self-monitoring of blood glucose (SMBG) were found more likely to have poor glycemic control than those who were practiced self-monitoring (P < 0.001). Whereas patients who had a normal body mass index (P=0.011) and being treated with premixed insulin-based therapy (P=0.04) were associated with lower likelihood of poor glycemic control than patients with obesity and being treated with NPH insulin based-regimen, respectively.

Conclusion: The current study demonstrated that significant numbers of the study samples did not achieve glycemic targets and the mean FBG level was far higher than the expected clinical goals. Poor glycemic control was more likely presented in patients who were not practiced self-monitoring of blood glucose, patients with obesity and in patients treated with NPH insulin-based therapy than their counterparts.

Strengths and limitations of this study

- This study examined the rate of glycemic control using FBG based on ADA recommendations in these resource limited settings where HbA1c could not use routinely to monitor blood glucose level.
- It has also highlighted the determinants of poor glycemic control.
- It used as a benchmark for clinicians and future researchers to examine glycemic control and predictors in patients with T2DM who are treated in insulin-based therapy.
- Glycosylated hemoglobin (HbA1c), which indicates the average blood glucose level of the past three months, was not used to determine glycemic level because of the study settings could not use routinely and FBG, which shows a short-term glycemic index, was used.

Introduction

Diabetes mellitus (DM) is one of the most common chronic diseases characterized by elevated blood glucose levels (1, 2). Though DM has several types, Type 2 Diabetes Mellitus (T2DM) is the most commonest and characterized as progressive, gradual deterioration in pancreatic beta-cell function, decreasing insulin levels and increasing its resistance, eventually leads to chronic hyperglycemia (3-5). Uncontrolled hyperglycemia is an immediate cause for developing macro vascular and micro vascular 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 country having the largest diabetes population. An estimated prevalence of this disorder had dramatically been increased from 3.8% to 5.2% (8).

The primary goal of treating patients with diabetes is to achieve and maintain the therapeutic targets of serum glucose levels. The American diabetes association (ADA) recommends serum glucose target levels such as the glycosylated hemoglobin (HbA1c) less than 7% and the fasting blood glucose (FBG) levels ranges from 70 to 130 mg/dl (9), which could satisfactorily prevent complications and therapeutic related costs accompanying with diabetes. Thus, patients with T2DM can be treated with various regimen types, for example, they could initially treat with

non-pharmacologic means followed by oral antidiabetics (OADs). At the beginning of the therapy, many patients could potentially attain the desired goals; however, through time multidrug regimens including insulin become important (10). The inclusion of insulin in the regimen is very crucial to decrease the long-term risks of diabetic complications (11). In the meantime, when the HbA1c is more than 10% and/or FBG >250mg/dl, the initial management options either alone or in combined form are less likely to achieve the target glycemic goal; therefore, initiating insulin might be compulsory at this stage(12).

Broadly speaking, several literatures were demonstrated in developed countries, and disclosed that insulin-based therapy in patients with T2DM has positive clinical impacts (13-15). Moreover, factors determining the poor glycemic control levels have been investigated. In contradiction with the former evidences, in developing countries, the rate of glycemic control and factors for poor glycemic status in patients with T2DM who have been treated with insulin-based therapy is not supported with sufficient literatures and data is scarce. To the best of authors' search, there is only a single study in Ethiopia that determined the level of glycemic control in newly insulin-initiated patients with T2DM (16). However, the current study is different from the previous study in terms of the study design and settings which the current study is a multicenter prospective cross-sectional study with incorporation of important clinical and socio-demographic variables which can affect glycemic control such as; body mass index (BMI), Self-blood glucose monitoring 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 glycemic control and determines the level of blood glucose is an important issue in order to apply appropriate intervention to improve glycemic control, and prevent long-term complications results from diabetes. Therefore, this study was aimed to assess rate of glycemic control and determinants in T2DM patients treated with insulin-based therapy in Northwest Ethiopian selected hospitals. The study will help to understand the extent of glycemic control and the impact of predictor variables towards glycemic control in type 2 diabetes patients in these resources limited and among one of the highest diabetes population in sub-Saharan Africa countries.

Materials and Methods

Study design and setting

Institutional-based multicenter cross-sectional was employed in the Northwest Ethiopian hospitals from October to December, 2021. The study hospitals were selected randomly among several public and university hospitals found in the region, and University of Gondar Comprehensive specialized hospital (UoGCSH), Felege-Hiwot Comprehensive specialized hospital (FHCSH), Tibebe-Ghion Comprehensive Specialized hospital (TGCSH) and Debre-Tabor comprehensive specialized hospital (DTCSH)) were among the included hospitals. These hospitals are found in Gondar, Bahir-Dar and Debre-Tabor cities and have been serving for more than about 25 million people.

Study population and selection criteria

This institutional based cross-sectional study was done on T2DM patients with which capable of being interviewed and had completed medical records. These patients have been attended in chronic medical ambulatory clinics of the hospitals. The patients were eligible in the study if they met the following inclusion criteria: (1) Patients diagnosed with T2DM and ≥18 years; (2) Had been treated with insulin-based regimen; (3) Had been followed for a minimum of three months. Whereas pregnancy, patients who refused to participate, patients couldn't communicate or 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 with 50% prevalence rate of poor glycemic control levels in patients with T2DM who have been treated with insulin-based therapy because of absence of previous similar study in the study areas. We also assumed that 5% for the two-tailed type-I error ($Z\alpha$=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 by using consecutive sampling technique those all T2DM patients have been treated with insulin-based therapy who fulfilled the inclusion criteria and coming for follow up during the data collection periods were approached until the required sample is maintained.

Operational definitions

Body mass index (BMI): It was measured in terms of patient's weight in kilogram (kg) divided by the square of patient's height in meters (kg/m^2). Based on the world health organization BMI classification, BMI classified and interpreted as < 18.5 kg/m2 (underweight), 18.5-24.9 kg/m2 (normal weight), 25- 29.5 kg/m2 (overweight) and ≥ 30 kg/m2 (obesity).

Self-monitoring blood glucose (SMBG): Indicates whether a patient has had an experience to measure the serum blood glucose levels at home.

Macrovascular complications: Complications such as; stroke, ischemic heart disease, heart failure, coronary artery disease, peripheral vascular disease.

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

Data collection instruments and procedures, and quality control management

Data was collected on direct patient interviews and extracting the patients' medical records using structured questionnaires. The data abstraction format was prepared after reviewed different related clinical literatures on similar topics and some modifications were made considering the local clinical settings. Then pre-test 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: (I) socio-demographic characteristics and patients' self-care practices such as Self-monitoring of blood glucose (SMBG) status, smoking status, alcohol drinking status, physical activity status; (II) clinical history and characteristics; and (III) medications history and characteristics. Clinical

characteristics include durations since diagnosis and initiation of treatments, blood pressure (BP), FBG levels, lipid profiles, Serum creatinine (SCr), 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 by digital weight scale and stadiometer as physical examination part. Treatment intensification was made according to ADA recommendations and glibenclamide and/or metformin were used in combination with insulin (NPH or premixed). The average FBG level was computed from the average of three different records, at least one month apart, was used to determine the level of glycemic control. The data was collected by experienced nurses after getting of training for two 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 was extracted, and the patients were interviewed.

Glycemic control outcome measure

Glycemic control: In this study, good glycemic control refers to FBG levels ranges from 70 to 130 mg/dl and FBG < 70 and > 130 mg/dl categorized under poor glycemic level.

Data entry processing and analysis

Data entrance, quality, completeness, consistency and clarity were checked before any further analysis was performed. Then it was entered in to Epi Info version 8, and transported and analyzed with the SPSS version 22. Normality of the data was determined by Q-Q plot and histograms. Descriptive statistics were used to present the sample characteristics. Means with standard divisions (SD) were also used to display results for continuous 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 glycemic control status. P-value < 0.05 was considered as statistically significant.

Patient and public involvement

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

Results

Socio-demographic 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/m2). Higher proportions of the surveyed (37.2%) had completed the secondary school educational level and almost 60% of them were ever non-smoker (58.8%). About less than one-thirds (31%) were practiced the SMBG at home (Table 1).

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

Variables	Category	Frequency	Percent	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	
T2DM duration (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 and 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 Moderate Vigorous	181 138 84	44.9 34.3 20.8	
Family history of DM	Yes No	263 140	65.3 34.7	

Clinical characteristics and Medication patterns of the participants

About three-fourths (72%) of the study participants had diagnosed with hypertension. Likewise, almost sixty percent were with dyslipidemia and macro vascular complications accounts 16.9% on top of T2DM. The majority of the participants, 65.5% and 56.3% were with systolic BP <140 mmHg and diastolic BP < 90 mmHg, respectively (Figure 1). Almost sixty percent of the patients with T2DM (59.8%) had been treated with 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).

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

Medications	Category	Frequency	Percent
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
Others class of medications	Aspirin (ASA)	240	59.6
	Amitriptyline	23	5.7
	Gastrointestinal	14	3.5
	ART medication (TDF/3TC/DTG)	11	2.7

	Antibiotics	10	2.5
	Anti-asthmatic drugs	5	1.2
	Antithyroid drugs	5	1.2

Rate of glycemic control in type 2 diabetes patients treated with insulin-based therapy

The overall glycemic control level was computed for the study participants. The mean FBG level of the study participants (measured in mg/dl) was 177.1 (± 54.3) (ranges: 62 to 406 mg/dl). A higher proportion of the study individuals (72.5%) were found to have poor level of glycemic control with only 27.5% of the study participants achieved target fasting glucose level. From the insulin types, more than half (52.2%) patients who were treated with the premixed insulin-based regimen achieved target FBG level (Figure 2). But frequent episode of hypoglycemia was also high (38.9%) in those patients treated with the premixed insulin-based regimens than patients who were treated with the NPH insulin-based therapy.

Determinants of the poor glycemic control levels in the study samples

Logistic regression analysis was performed to examine the relationship between the primary outcome and the number of predictor variables. Following this, the multivariable logistics regression had revealed that there have been independent factors with which determined the FBG levels on patient with T2DM treated with insulin-based regimen. Consequently, there had been found that, holding all other predictor variables constant, the odds of poor glycemic control in patients who did not practice the SMBG levels at home coefficient is about 7.6 with [95% CI (3.117- 18.394); P<0.001]. On the other hand, patients who had normal BMI were significantly associated with lower likelihood of poor glucose status by 55% with AOR of 0.450 (95% CI [0.062-3.226]: P=0.011) compared with obese patients. Further, individuals who were treated by premixed insulin-based regimen were also significantly associate with lower likelihood of poor glycemic control than who were treated by NPH insulin-based therapy (AOR=0.356, 95%CI [0.127-0.959]; P =0.04) (Table 3).

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

Variables		Glycemic control		COR (95% CI)	P-value	AOR (95% CI)	P-value
		Poor	Good				
Residency:	Urban	165	72	0.704(0.447-1.107)	0.129	0.934(0.377 2.311)	0.882
	Rural	127	39	1		1	
SMBG practice:	No	236	42	6.923(4.277-11.208)	0.000	7.572(3.117-18.394)	0.000*
	Yes	56	69	1		1	
BMI (kg/m^2):	Underweight	27	7	0.321(0.099-1.0403)	0.034	0.196(0.024-1.566)	0.124
	Normal	152	83	0.153(0.064-0.366)	0.000	0.119(0.023-0.611)	0.011*
	Overweight	41	15	0.228(0.082-0.633)	0.005	0.450(0.062-3.226)	0.430
	Obesity	72	6	1		1	
Smoking status:	Currently smoker	42	27	0.613(0.350-1.073)	0.010	0.315(0.101-1.087)	0.055
	Previously smoker	80	17	1.855(1.023-3.362)	0.087	1.588(0.555-4.530)	0.047
	Nonsmoker	170	67	1	0.042	1	0.389
Physical activity:	Sedentary	132	49	0.634(0.336-1.197)	0.160	0.686(0.219-2.148)	0.518
	Moderate	92	46	0.471(0.246-0.901)	0.023	0.445(0.132-1.498)	0.191
	Vigorous	68	16	1		1	
Insulin Type:	Premixed	43	47	0.235(0.143-0.386)	0.000	0.356(0.127-0.959)	0.040*
	NPH	249	64	1		1	
Amlodipine:	Yes	54	12	1.872(0.960-3.651)	0.066	1.579(0.430-5.793)	0.491
	No	238	99	1		1	
Atenolol:	Yes	10	9	0.402(0.159-1.017)	0.054	0.323(0.091-1.148)	0.081
	No	282	102	1		1	
Lipid lowering agent:	Atorvastatin	109	34	1.924(0.955-3.873)	0.067	2.241(0.889-5.583)	0.083
	Simvastatin	30	18	1		1	
Frequent clinical hypoglycemic							
	Yes	24	28	0.265(0.146-0.483)	0.000	0.779(0.230-2.635)	0.688
	No	268	83	1		1	
SBP (mmHg):	≥140	110	29	1.709(1.052-2.776)	0.03	0.860(0.356-2.078)	0.737
	< 140	182	82	1		1	

Note: COR, crude odds ratio; AOR, adjusted odds ratio; CI, confidence interval; SMBG, self-monitoring blood glucose *indicates the statistically significant at $P < 0.05$

Discussion

This institutional based multi-center cross-sectional study has gone some way towards highlighting the characteristics of glycemic control by using FBG and associated factors in patients with T2DM who were on insulin-based regimen therapy in the resource limited settings where glycemic control could not monitor routinely with HbA1C. In this study, we have obtained comprehensive results proving that most of the T2DM patients had not achieved the desired serum glycemic levels and for this there have been several factors which potentially determined the target goals. The current study demonstrated that significant numbers of the study samples could not achieve glycemic targets and the mean FBG level was far higher than the expected clinical goals. Moreover, not practicing the SMBG at home was significantly associated with poor glycemic control. On the other hand, patients with normal weight and who were treated with the premixed insulin-based therapy were found to have significant reduction of poor glycemic levels than obese individuals and participants who were treated with NPH insulin-based regimen, respectively.

The evidence from this study suggested that though patients with T2DM had been treated with insulin-based regimen, only around one-fourth of the patients took part the survey achieved the target serum glucose levels. The finding is consistent with the previous findings (13, 14, 16-18). Insulin is often used as an adjuvant to oral glucose lowering agent in T2DM patient who could not attain the recommended glucose levels. 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 (19), insufficient dose titration of insulin could result these effects. Similarly, our results shared a number of similarities with earlier findings. Furthermore, non-adherence to the recommended insulin titration might be due to insufficient communication between clinicians and patients (20). Thus, to attain the maximum clinical benefits, insulin could be titrated to a daily recommended dose with a close monitoring follow-up to prevent the lower serum glucose levels below the target. However, the current finding significantly differs from previous results reported in the literatures (15, 21, 22). The source of the discrepancies might be due to difference in the titration of the recommended daily dose of 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 variation in target glycemic level achievement of insulin treated patients with diabetes.

We have demonstrated that patients who did not practice SMBG at home were more likely to have poor glucose control compared with those who did, and this is corroborated with various preceding studies (23, 24). This might be because of insufficient access for self-monitoring of blood glucose in these resources limed settings. The finding suggests that enhancing the self-monitoring blood glucose practice could be encouraged in order to increase adherence of SMBG which used to control blood glucose levels in patients with diabetes mellitus. The current study also revealed that patients who had normal level of BMI (P=0.011) were significantly associated with lower likelihood of poor glycemic control than those patients with obesity. Consistently previous studies revealed that patients with greater BMI were resulted in poor glycemic control (25-27). This relation might justify those patients with higher BMI or obesity caused for insulin resistance and in turn it result in poor glycemic 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 taking premixed insulin-based regimen were found to have lower likelihood of poor glycemic control than those were treated with NPH insulin-based regimen. This might be because of the premixed insulin preparation has two types of insulin which could potentially cover both the pre-prandial and post-prandial glucose release, and it was matched with previous studies (16, 28). However, consistently with the previous study (29), patients who were treated with premixed insulin-based regimen had developed frequent clinical hypoglycemia. Therefore, when premixed insulin is recommended to patients, hypoglycemic episodes could be watched carefully.

Generally, poor glycemic control in patients with diabetes is a result of multifactorial contributing factors including the progressive nature of disease its self, the patients' adherence level of their medications and adherence to lifestyle modifications of the patients. Therefore, both healthcare providers and patients them self could be vigilant to delay the progress of the disease by achieving target glucose levels. Besides, insulin-initiation as well as titration would be individualized on the basis of contributing factors for poor glycemic control in individual patients.

Conclusion

This multicenter institutional-based survey showed that significant numbers of T2DM patients had not achieved the desired serum glucose level with the mean FBG level was far higher than the expected glycemic level goals. Moreover, not practicing the SMBG at home was significantly associated with poor glycemic control. On the other hand, patients with normal BMI and who were treated with the premixed insulin-based therapy were associated with lower likelihood of poor glycemic levels than their counterparts. Therefore, insulin initiation and titration in patients with T2DM could be individualized and consider the potential factors of glycemic control.

Author's contributions

AKS contributed to the conception, project administration, formal analysis, investigation, methodology, data curation, resources, writing of the original draft of the manuscript, reviewing and editing. **EAB** & **EMD** contributed to the formal analysis, methodology, data curation, review and editing of the final manuscript. **AKN** contributed to the supervisions, formal analysis, methodology, data curation, validation, review and editing of the final manuscript. All authors of this manuscript read and approved the final version of this manuscript.

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.

Funding

The study was not funded and granted by any institution.

Declaration of conflict of interests

The authors state that they have no conflict of interest.

Availability of supporting data

All necessary documents are present in the manuscript if others like datasets are available from the correspondent author on reasonable request.

Ethical approval and consent to participate

The study was ethically approved by ethical review committee of the University of Gondar with a reference number of Sop/037/2021. Participants were informed with both written and verbal consent forms after the objectives of the study were briefed. Confidentiality was kept and sufficiently anonymized, and publication consent was not required.

List of abbreviations

ADA, American diabetes association; BMI, body mass index; FBG, Fasting blood glucose; HbA1c, Glycosylated hemoglobin; NPH, Neutral Protamine Hagedorn; OADs, Oral Antidiabetics; T2DM, Type 2 Diabetes Mellitus

ORCID iDs

Ashenafi Kibret Sendekie https://orcid.org/0000-0001-5982-853X

Eyayaw Ashete Belachew https://orcid.org/0000-0002-0421-4327

Ephrem Mebratu Dagnew https://orcid.org/0000-0003-1117-2636

Adeladlew Kassie Netere https://orcid.org/0000-0003-0519-509X

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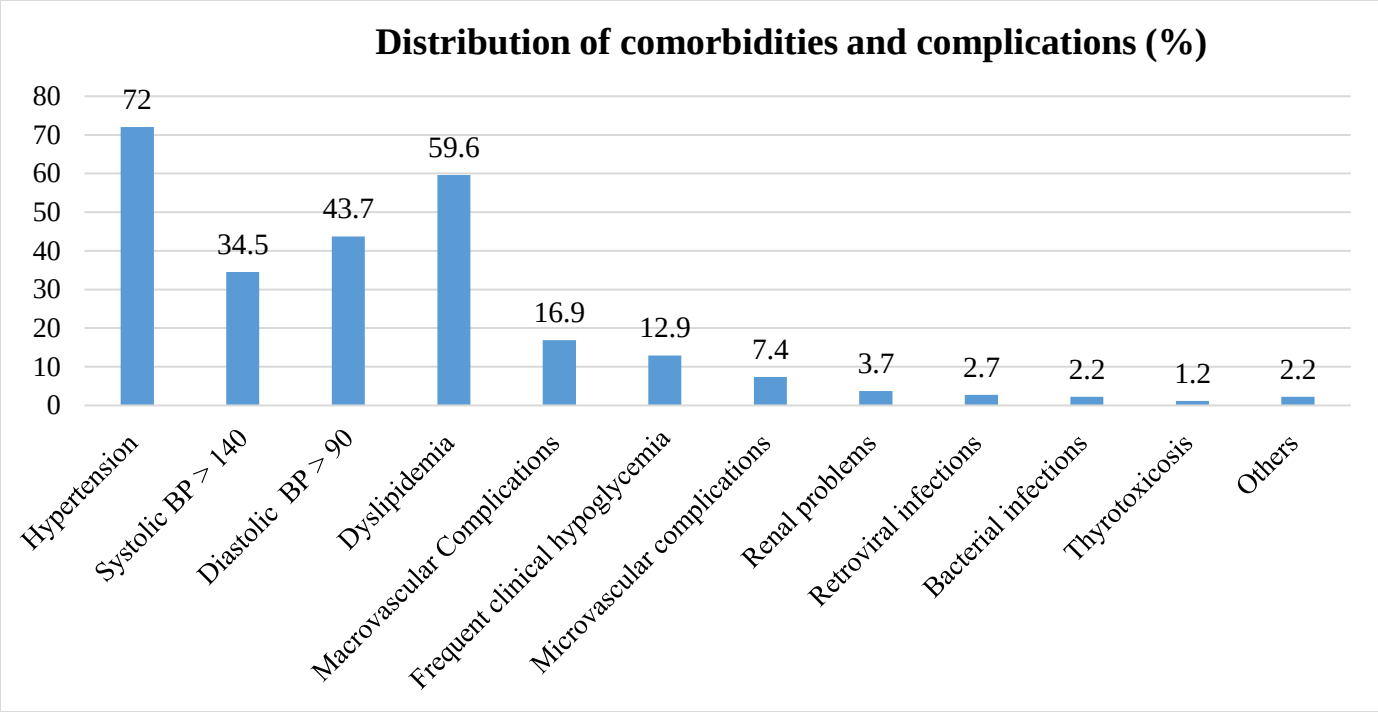
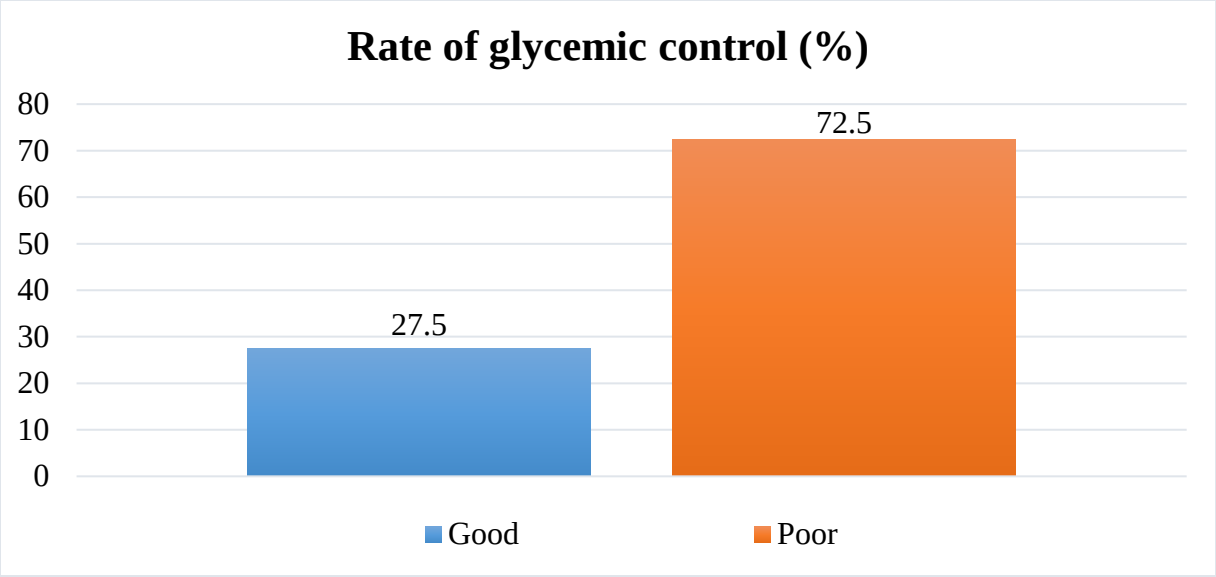
Figure legends

Figure 1 Distributions of comorbidities and complications in T2DM patients treated with insulin-based therapy attending hospitals of Northwest Ethiopian, 2021 (N=403)

Figure 2 Rate of glycemic control in T2DM patients treated with insulin-based therapy (N=403)



Note: Others; bronchial asthma, diabetic ketoacidosis, malaria, skin disorders, anemia, malnutrition



BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-065250.R1
Article Type:	Original research
Date Submitted by the Author:	18-Jul-2022
Complete List of Authors:	Sendekie, Ashenafi; University of Gondar College of Medicine and Health Sciences, Clinical pharmacy Belachew, Eyayaw; University of Gondar College of Medicine and Health Sciences, clinical pharmacy Dagnew, Ephrem Mebratu; Debre Markos University College of Health Science, Clinical pharmacy Netere, Adeladlew; University of Gondar College of Medicine and Health Sciences, clinical pharmacy
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Diabetes and endocrinology, Global health
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, General endocrinology < DIABETES & ENDOCRINOLOGY, Diabetes & endocrinology < INTERNAL MEDICINE

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

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

[1]Department of Clinical Pharmacy, School of Pharmacy, College of Medicine and Health Sciences, University of Gondar; Gondar, Ethiopia

[2]Department of Clinical Pharmacy, College of Health Science, Debre Markos University, Debre Markos, Ethiopia

*Corresponding Author

Ashenafi Kibret Sendekie

Email: ashukib02@yahoo.com / Ashenafi.kibret@uog.edu.et

Po Box: 196

Abstract

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

Designs: Institutional-based multicenter cross-sectional study design was employed.

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

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

Main Outcome measures: Good glycemic control; when fasting blood glucose (FBG) level ranges from 70 to 130 mg/dl, and FBG < 70 and > 130 mg/dl was considered poor glycemic control. A logistic regression model was used to identify determinants of poor glycemic control. $P < 0.05$ at 95% confidence interval (CI) was statistically significant.

Results: Of 403 study participants, 54.8% were males with a mean of age 55.03±10.8 years. Though T2DM patients were treated with insulin-based therapy, the majority 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 practice self-monitoring of blood glucose (SMBG) were found more likely to have poor glycemic control compared to those who practiced 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 glycemic control compared to patients with obesity and who received NPH insulin based-regimens, respectively.

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

Strengths and limitations of this study

- This finding may suggest the level of glycemic control and its predictors among insulin treated patients with T2DM in the resource limited settings, which needs intervention and further investigation.
- Determining glycemic control using Glycosylated hemoglobin (HbA1c) might be valuable over FBG because it estimates the glycemic level of the past months.
- But HbA1c was not used to determine glycemic level since it was not available in the study settings and included subjects.
- FBG, which shows a short-term glycemic index was used to determine glycemic control, may have its own limitation but it may be worthy than putting aside in the resource limited settings.
- Some variables like macro and micro complications which 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 characterized by elevated blood glucose levels (1, 2). Though DM has several types, Type 2 Diabetes Mellitus (T2DM) is the commonest type of diabetes, and characterized 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 hyperglycemia (3-5). Uncontrolled hyperglycemia 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 country having the largest diabetes population. An estimated prevalence of this disorder had dramatically been 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/m2, 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 hemoglobin (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 initially treat with non-pharmacologic 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). In the meantime, when the HbA1c is more than 10% and/or FBG >250mg/dl, the initial management options either alone or in combined form are less likely to achieve the target glycemic goal; therefore, initiating insulin would be compulsory at this stage(13).

Broadly speaking, several literatures were 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 glycemic control levels have been investigated. In contradiction with the former evidences, in developing countries, the rate of glycemic control and factors for poor glycemic status in patients with T2DM who have been treated with insulin-based therapy is not supported with sufficient literatures and data is scarce. To the best of authors' search, there is only a single study in Ethiopia that determined the level of glycemic control in newly insulin-initiated patients with T2DM (17). However, the current study is different from the previous study in terms of the study design and settings which the current study is a multicenter prospective cross-sectional study with incorporation of important clinical and socio-demographic variables which can affect glycemic control. Such variables include body mass index (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 glycemic control and determines the level of blood glucose is an

important issue in order to apply appropriate intervention to improve glycemic control, and prevent long-term complications results from diabetes. Therefore, this study was aimed to assess level of glycemic control and determinants in T2DM patients treated with insulin-based therapy at the selected hospitals in Northwest Ethiopia. The study will help to understand the extent of glycemic control and the impact of predictor variables towards glycemic 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 multicenter cross-sectional study was employed at the selected hospitals in the 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 Specialized hospital (UoGCSH), Felege-Hiwot Comprehensive Specialized hospital (FHCSH), Tibebe-Ghion Comprehensive Specialized hospital (TGCSH) and Debre-Tabor comprehensive specialized hospital (DTCSH)) were settings where the study sample was collected. These hospitals are found 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 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; (3) Had been on treatment for a minimum of three months. Whereas pregnancy, patients who refused to participate, patients couldn't communicate or 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 glycemic 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 by using consecutive sampling technique those all T2DM patients have been treated with insulin-based therapy who fulfilled the inclusion criteria and coming for follow up during the data collection periods were approached until the required sample is maintained.

Glycemic control outcome

Glycemic control: In this study, good glycemic control refers to FBG levels ranges from 70 to 130 mg/dl and FBG < 70 and > 130 mg/dl categorized under poor glycemic level.

Operational definitions

Body mass index (BMI): It was measured in terms of patient's weight in kilogram (kg) divided by the square of patient's height in meters (kg/m^2). Based on the world health organization BMI classification, BMI classified and interpreted as < 18.5 kg/m2 (underweight), 18.5-24.9 kg/m2 (normal weight), 25- 29.5 kg/m2 (overweight) and ≥ 30 kg/m2 (obesity).

Self-monitoring blood glucose (SMBG): Indicates whether a patient has had an experience to measure the serum blood glucose levels at home.

Macrovascular complications: Complications such as; stroke, ischemic heart disease, heart failure, coronary artery disease, peripheral vascular disease.

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

Hypoglycemia: A clinical episodes of hypoglycemia and/or FBG of < 70 mg/dl recorded on the patients' medical records was taken as hypoglycemia.

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) which targets employers from rural and informal sectors through the Federal Ministry of Health (FMOH) 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 (EHIA) is working through improving risk pooling among different groups of the population; such as between rich and poor, healthy and sick (20, 21). Community-based health insurance 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 was collected on direct patient interviews and extracting the patients' medical records using structured questionnaires. The data abstraction format was prepared after reviewed different related clinical literatures on similar topics and some modifications were made considering the local clinical settings. Then pre-test 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 (**Supplementary file**): (I) socio-demographic characteristics and patients' self-care practices such as SMBG status, smoking status, alcohol drinking status, physical activity status; (II) clinical history and characteristics; and (III) medications history and characteristics. Clinical characteristics include durations since diagnosis and initiation of treatments, blood pressure

(BP), FBG levels, lipid profiles, Serum creatinine (SCr), 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 by digital weight scale and stadiometer as physical examination part. Treatment intensification was made according to ADA recommendations and glibenclamide and/or metformin were used in combination with insulin (NPH or premixed). The average FBG level was computed from the average of three different records, at least one month apart, was used to determine the level of glycemic control. The data was collected by experienced nurses after getting of training for two 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 was 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 performed. Then it was entered in to Epi Info version 8, and transported and analyzed with the SPSS version 22. Normality of the data was determined by Q-Q plot and histograms. Descriptive statistics were used to present the sample characteristics. Means with standard divisions (±SD) were also used to display results for continuous variables. One-way ANOVA with Post hoc test was used to examine mean glucose level difference between antidiabetic treatement groups. Logistic regression was used to assess association of glycemic 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 glycemic control status. $P < 0.05$ at 95% CI was statistically significant.

Patient and public involvement

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

Results

Socio-demographic 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/m2). Higher proportions of the surveyed (37.2%) had completed the secondary school educational level and almost 60% of them were ever non-smoker (58.8%). About less than one-thirds (31%) were practiced the SMBG at home (**Table 1**).

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

Variables	Category	Frequency	Percent	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 and 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 Moderate Vigorous	181 138 84	44.9 34.3 20.8	
Family history of DM	Yes No	263 140	65.3 34.7	

Clinical characteristics and Medication patterns of the participants

About three-fourths (72%) of the study participants had diagnosed with hypertension. Likewise, almost sixty percent were with dyslipidemia and macro vascular complications accounts 16.9% on top of T2DM. The majority of the participants, 65.5% and 56.3% were with systolic BP <140 mmHg and diastolic BP < 90 mmHg, respectively (**Figure 1**). Almost sixty percent of the patients with T2DM (59.8%) had been treated with 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**).

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

Medications	Category	Frequency	Percent	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	
Others 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	
	Anti-asthmatic 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)

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

The overall glycemic 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 to 406 mg/dl). But the patients who were treated with triple antidiabetics medications of insulin plus metformin plus glibenclamide had worse FBG level (Mn =189.7) than patients who were treated by insulin plus metformin (Mn =170.1) and insulin (Mn =174.3). A one-way ANOVA also proved that the difference in FBG level between the treatment group 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 level between insulin plus metformin plus glibenclamide (Mn =189.7) and insulin plus metformin (Mn = 170.1) treatment groups (P = 0.002). But the rate of hypoglycemia was higher in the triple therapy (15.8%) compared to dual (11.2%) and insulin (13%). The overall rate of hypoglycemia was reported to be 12.9%.

A higher proportion of the study individuals (72.5%) were found to have poor level of glycemic control with only 27.5% of the study participants achieved target fasting glucose level (**Figure 2**). From the insulin types, more than half (52.2%) patients who were treated with the premixed insulin-based regimens achieved target FBG level. But frequent episode of hypoglycemia was also high (38.9%) in those patients treated with the premixed insulin-based regimens compared to patients who were treated by NPH insulin-based therapy (5.4%); P < 0.001.

Determinants of the poor glycemic 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 had revealed that there had been independent factors with which determined the level of glycemic control on insulin treated patient with T2DM. Consequently, holding all other predictor variables constant, patients who did not practice the SMBG at home were found more like to have poor glycemic control compared to patients who did practice SMBG [AOR = 7.572, 95% CI (3.117-

18.394); P < 0.001]. In contrast, patients who had normal BMI were found less likely to have poor glycemic control compared to patients with obesity [AOR = 0.450, 95% CI [0.062-3.226]: P = 0.011). Further, patients who were treated by premixed insulin-based regimens were also found less likely to have poor glycemic control to compared to patients who were treated by NPH insulin-based regimes [AOR = 0.356, 95%CI (0.127-0.959); P = 0.04) (**Table 3**).

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

Variables		Glycemic control		COR (95% CI)	P-value	AOR (95% CI)	P-value
		Poor	Good				
Residency:	Urban	165	72	0.704(0.447-1.107)	0.129	0.934(0.377 2.311)	0.882
	Rural	127	39	1		1	
SMBG practice:	No	236	42	6.923(4.277-11.208)	0.000	7.572(3.117-18.394)	0.000*
	Yes	56	69	1		1	
BMI (kg/m^2):	Underweight	27	7	0.321(0.099-1.0403)	0.034	0.196(0.024-1.566)	0.124
	Normal	152	83	0.153(0.064-0.366)	0.000	0.119(0.023-0.611)	0.011*
	Overweight	41	15	0.228(0.082-0.633)	0.005	0.450(0.062-3.226)	0.430
	Obesity	72	6	1		1	
Smoking status:	Currently smoker	42	27	0.613(0.350-1.073)	0.010	0.315(0.101-1.087)	0.055
	Previously smoker	80	17	1.855(1.023-3.362)	0.087	1.588(0.555-4.530)	0.047
	Nonsmoker	170	67	1	0.042	1	0.389
Physical activity:	Sedentary	132	49	0.634(0.336-1.197)	0.160	0.686(0.219-2.148)	0.518
	Moderate	92	46	0.471(0.246-0.901)	0.023	0.445(0.132-1.498)	0.191
	Vigorous	68	16	1		1	
Insulin Type:	Premixed	43	47	0.235(0.143-0.386)	0.000	0.356(0.127-0.959)	0.040*
	NPH	249	64	1		1	
Amlodipine:	Yes	54	12	1.872(0.960-3.651)	0.066	1.579(0.430-5.793)	0.491
	No	238	99	1		1	
Atenolol:	Yes	10	9	0.402(0.159-1.017)	0.054	0.323(0.091-1.148)	0.081
	No	282	102	1		1	
Lipid lowering agent:	Atorvastatin	109	34	1.924(0.955-3.873)	0.067	2.241(0.889-5.583)	0.083
	Simvastatin	30	18	1		1	
Frequent clinical hypoglycemia							
	Yes	24	28	0.265(0.146-0.483)	0.000	0.779(0.230-2.635)	0.688
	No	268	83	1		1	
SBP (mmHg):	≥140	110	29	1.709(1.052-2.776)	0.03	0.860(0.356-2.078)	0.737
	< 140	182	82	1		1	

Note: COR, crude odds ratio; AOR, adjusted odds ratio; CI, confidence interval; SMBG, self-monitoring blood glucose *indicates the statistically significant at P < 0.05

Discussion

This institutional based multi-center cross-sectional study has gone through highlighting the level of glycemic control and associated factors in patients with T2DM who were treated with insulin-based regimens by using FBG in the resource limited settings where glycemic control could not monitor routinely with HbA1C. The clinical characteristics of the participants in the current 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). Which the current study may reflect the characteristics and management practice of T2DM patients in the country.

Indeed, this study revealed those most of patients with the T2DM could not achieve the desired serum glycemic levels even though they were treated with insulin-regimes. This study also identified important factors which potentially determined the level of glycemic control. The current study demonstrated that the mean blood glucose level was far higher than the recommended target glycemic level. Moreover, not practicing the SMBG was significantly associated with poor glycemic 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 glycemic control than obese patients and participants who were 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 T2DM patient who could not attain the recommended glucose levels with initial preferred treatment of oral antidiabetic 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 these effects. For instance, in the current study, the average daily dose of insulin was 16.9 mg (ranges: 6 to 40 mg) and even though premixed insulin has good effect on glycemic control through controlling of post-prandial glucose, still majority of patients were treated with NPH insulin-based regimens. Thus, the

findings suggest that need of insulin titration in terms of the dose and the regimens types could be recommendable. Non-adherence to the recommended insulin titration might be due to insufficient communication between clinicians and patients (25) regarding to post-prandial glucose level of home measurement, fear of adverse effects like hypoglycemia 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 difference in the titration of the recommended daily dose of 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 variation in target glycemic level achievement of insulin treated patients with diabetes.

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

This study demonstrated those patients who did not practice SMBG at home were more likely to have poor glycemic control compared to 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 in order to increase adherence of SMBG which used to control blood glucose levels in patients with diabetes mellitus. The current study also indicated those patients who had normal level of BMI (P=0.011) were found less likely to have poor glycemic control than those patients

with obesity. Consistently, previous studies revealed that patients with higher BMI were resulted in poor glycemic control (30-32). This relation might justify those patients with higher BMI or obesity caused for insulin resistance and in turn it results in poor glycemic 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 by premixed insulin-based regimens were found less likely to have poor glycemic control compared to patients who were received NPH insulin-based regimens. This might be because of the premixed insulin regimens has two types of insulin preparations (short acting and intermediate acting) which could potentially cover both the pre-prandial and post-prandial glucose release, and it was matched with previous studies (17, 33). In addition, the post-prandial 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 hypoglycemia. Hypoglycemic 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, hypoglycemic episodes could be watched carefully and patients need to be aware and self-manager of the symptoms.

Indeed, poor glycemic control in patients with diabetes may be affected not only by the factors discussed in this study but also it might be a result of 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 them self could be vigilant to delay the progress of the disease by achieving target glucose levels. Besides, insulin-initiation as well as titration would be individualized on the basis of contributing factors for poor glycemic control in individual patients. Generally, this study examined the rate of glycemic control using FBG based on ADA recommendations in these resource limited settings where HbA1c could not use routinely to monitor blood glucose level. It used as a benchmark for clinicians and future researchers to examine glycemic control and predictors in patients with T2DM who are treated in insulin-based therapy.

Conclusion

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

Author's contributions

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** & **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 read and approved the final version of this manuscript.

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.

Funding

The study was not funded and granted by any institution.

Declaration of conflict of interests

The authors state that they have no conflict of interest.

Availability of supporting data

All necessary documents are present in the manuscript if others like datasets are available from the correspondent author on reasonable request.

Ethical approval and consent to participate

The study was ethically approved by ethical review committee of the University of Gondar with a reference number of Sop/037/2021. Participants were informed with both written and verbal consent forms after the objectives of the study were briefed. Confidentiality was kept and sufficiently anonymized, and publication consent was not required.

List of abbreviations

ADA, American diabetes association; BMI, body mass index; FBG, Fasting blood glucose; HbA1c, Glycosylated hemoglobin; NPH, Neutral Protamine Hagedorn; OADs, Oral Antidiabetics; T2DM, Type 2 Diabetes Mellitus

ORCID iDs

Ashenafi Kibret Sendekie https://orcid.org/0000-0001-5982-853X

Eyayaw Ashete Belachew https://orcid.org/0000-0002-0421-4327

Ephrem Mebratu Dagnew https://orcid.org/0000-0003-1117-2636

Adeladlew Kassie Netere https://orcid.org/0000-0003-0519-509X

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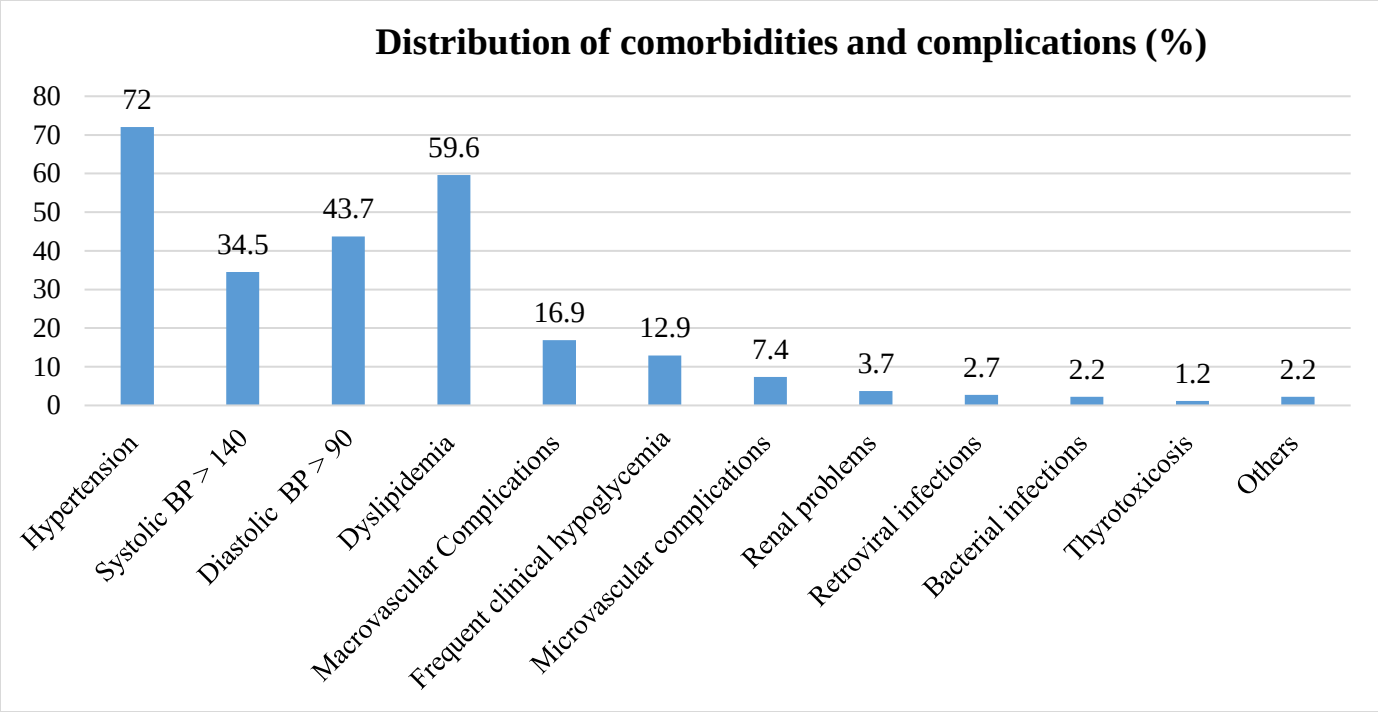
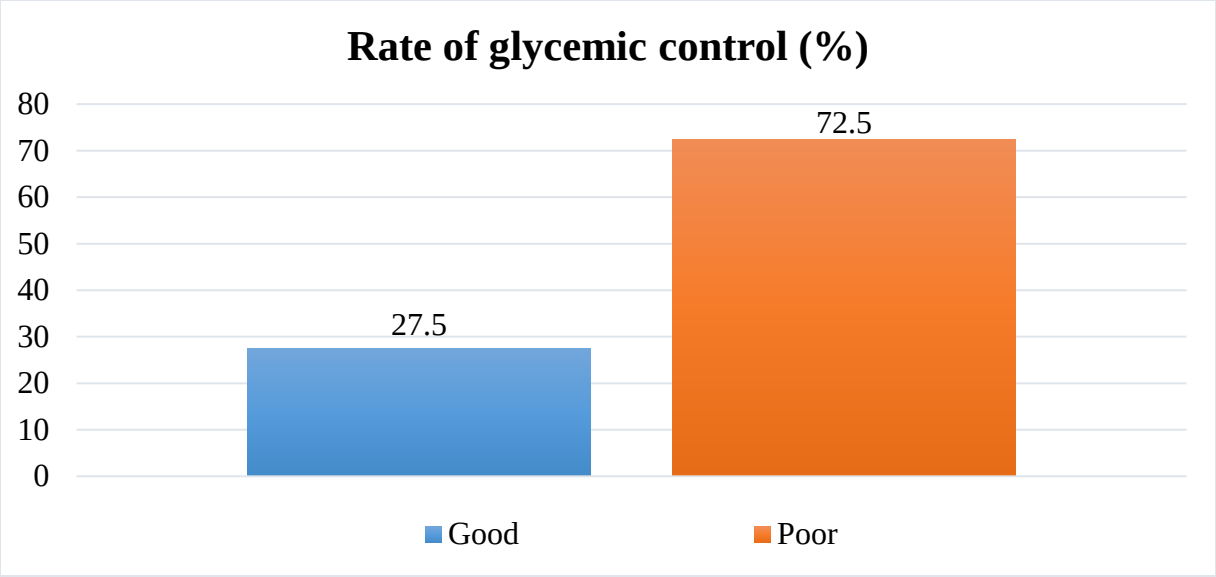
Figure legends

Figure 1 Distributions of comorbidities and complications in T2DM patients treated with insulin-based therapy attending hospitals of Northwest Ethiopian, 2021 (N=403)

Figure 2 Rate of glycemic control in T2DM patients treated with insulin-based therapy (N=403)



Note: Others; bronchial asthma, diabetic ketoacidosis, malaria, skin disorders, anemia, malnutrition



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.

STROBE Checklist

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

	Item No	Recommendation	Reported on page No & lines
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page, line 3 & page 2 line 4.
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2, lines 8-20.
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4, lines 16-30.
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 5, line 2-7.
Methods			
Study design	4	Present key elements of study design early in the paper	Page 5, line 10
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5, lines 10-17.
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Page 5, lines 18-25.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 6, lines 16-27 & page 7 lines 1-6.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*N/A*
Bias	9	Describe any efforts to address potential sources of bias	Page 6, lines 12-15.
Study size	10	Explain how the study size was arrived at	Page 6, lines 1-11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 7, lines 25-29 & Page 8, lines 1-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 8, lines 14-22.
		(*b*) Describe any methods used to examine subgroups and interactions	Page 8, lines 17-18.
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	N/A
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	N/A
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 12, Table 3.
		(*b*) Report category boundaries when continuous variables were categorized	Page 9, Tabe 1 & Page 12 Table 3.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Page 11
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 16, lines 2-8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 3, lines 1-13.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 15, lines 18-25.
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 15, 25-29.
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 16, lines 20-21

*Give information separately for exposed and unexposed groups.