Impact of metformin dose titration and self care practices on glycemic control of type 2 diabetes mellitus patients at Felege Hiwot Referral Hospital, Northwest Ethiopia

By

Misgan Ararsie, B.Pharm

A research thesis submitted to the department of pharmacy, college of public health and medical sciences, Jimma University in partial fulfillment for the requirements of Master of Science in clinical pharmacy

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Advisors

1. **Tewodros Eyob, B.Pharm, MSc in Clinical Pharmacy**
2. **Mirkuzie Woldie MD, MPH**

Abstract

Background: *Recent targets for glycemic management in patients with type 2 diabetes mellitus (T2DM) require optimization of dosing strategies for oral antidiabetics. Metformin is the first choice in the absence of contraindications with dose-related antihyperglycemic efficacy that extends to daily doses of 2000 mg/day. So metformin dose titration with appropriate self care practice is the cornerstone to see the intended antihyperglycemic efficacy of metformin in T2DM.*

Objective: *To assess the impact of metformin dose titration and self care practices on glycemic control of T2DM patients at Felege Hiwot Referral Hospital (FRH).*

Methods and Participants: *A retrospective-general cohort study was conducted. All T2DM patients who had started metformin from March 01, 2010 to March 31, 2012, and came for follow up at the diabetes mellitus (DM) clinic during the study period were included. Data were collected by face-to-face interview and medical chart review. Data were analyzed by SPSS version 20.0. Logistic regression, Repeated Measures ANOVA, and Kaplan Meier survival analysis were used.*

Results: *Nineteen (23.7%) of patients were on the metformin dose of 1500 mg and above, whereas 61 (76.3%) of patients were on metformin dose of less than 1500 mg. Twenty four (30.0%), and twenty three (28.7 %) of the patients had attained the desired fasting plasma glucose (FPG) level of below 130 mg/dl in the first two, and six months of metformin therapy respectively. The mean FPG in the first two, and six months of therapy was 190 mg/dl (standard deviation (SD) = 70.9), and 179.9 mg/dl (SD=57.7) respectively. Titrated form of metformin in the first two months of therapy had a 70.2%, 66.1% and 70.2% control of FPG than the untitrated metformin at the two, six and twelve month period respectively.*

Conclusion: *More than two-third of the participants had suboptimal dose titration where less than one-third of them had FPG level below130 mg/dl. So practitioners should practice the titration of metformin during the first two months of therapy depending on the FPG level of the patients.*

Key Words: *metformin, T2DM, dose titration, retrospective, cohort, self-care, Ethiopia*

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Abbreviations

AACE	American Association of Clinical Endocrinologists
ADA	American Diabetes Association
ARR	Absolute Risk Reduction
BSc	Bachelor of Science
DM	Diabetes Mellitus
EASD	European Association for the Study of Diabetes
FPG	Fasting Plasma Glucose
FRH	Felege Hiwot Referral Hospital
GI	Gastro Intestinal
HbA1C	Glycated Hemoglobin
JUSH	Jimma University Specialized Hospital
NIDDM	Non-insulin dependent diabetes mellitus
NNT	Number needed to Treat
OGLA	Oral glucose lowering agents
RCTs	Randomized Controlled Trials
RR	Risk Ratio
SCr	Serum Creatinine
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
T2DM	Type 2 Diabetes Mellitus
UK	United Kingdom
UKPDS	United Kingdom Prospective Diabetes Study

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1. Introduction

1.1 Background

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (1). Africa will experience the greatest rise in the prevalence of DM in the next ten years. The prevalence is expected to rise from 12.1 million (3.8%) to 23.9 million (4.7%) from 2010 to 2030 of the adult population, a 98.1 % rise (2). Type 2 diabetes accounts for more than 90% of diabetes in Sub-Saharan Africa, and prevalence ranged from 1% in rural Uganda to 12% in urban Kenya (3)**.** The prevalence of DM in Ethiopia is also rising and it is expected to increase from 826,000 (2.0%) in 2010 to 2,030,500 (2.8%) in 2030 (2). Sixty two percent of patients at Jimma University Specialized Hospital (JUSH) have T2DM and 96.1% are with hypertension (4). Type 2 diabetes results from impaired insulin secretion and reduced peripheral insulin sensitivity. It frequently coexists with obesity, dyslipidemia, atherosclerotic vascular disease, and hypertension (1).

Diabetes is a chronic illness that requires continuing medical care and ongoing patient self-management. Self- management is a crucial element of good diabetes care. Self-management of diabetes can significantly decrease the development and/or progression of diabetic complications, and it has been found to be cost-effective in primary practice settings (5). Several large-scale trials have demonstrated that comprehensive interventions that include self-management can prevent complications from T2DM (6-7).

Currently available oral antidiabetic drugs of T2DM are categorized as agents that stimulate insulin secretion (sulphonylureas, meglitinides, glucagon-like peptide 1 (GLP-1) analogues and dipeptidyl peptidase-4 (DPP-4) inhibitors), reduce hepatic glucose production (biguanides), delay digestion and absorption of intestinal carbohydrate (α-glucosidase inhibitors), improve insulin action (thiazolidinediones) (8-10). Biguanides (metformin) and thiazolidinediones are the only classes that directly improve insulin action. Metformin is effective only in the presence of insulin, and its major effect is to decrease endogenous glucose production by the liver. In addition, it increases glucose utilization in peripheral tissues such as muscle and liver (11-13). The American Diabetes Association

(ADA) and the European Association for the Study of Diabetes (EASD) proposed metformin therapy initiation in the absence of contraindications with lifestyle intervention, at the time of diagnosis (14-17)

Metformin has little effect on blood glucose in normoglycemic states, so termed as 'antihyperglycemic' rather than 'hypoglycemic'. The efficacy of metformin in T2DM is dose-related across most of its dosage range, up to 2,500–3,000 mg/day. About 2,000 mg/day represent the optimal dose (18-20). On the other hand meta-analysis of RCTs uncovers that metformin at dose of 850 mg twice daily and 250 mg twice or three times daily decreases the rate of conversion from prediabetes to diabetes serving as prevention method (21).

The majorities of adverse events with metformin therapy are gastro intestinal (GI), and usually appear after initiation, and subside over several months of continued therapy. The impact of GI adverse events during initiation may be minimized by titrating from an initial dose of 500 mg, and by taking metformin with or immediately after food (22-24). Although most of the GI complains occur at high dose, meta-analysis comparing the efficacy of the different doses of metformin on seven trials, with either metformin monotherapy or as an add-on therapy shows the lack of dose-response relation for GI side-effects (25).

In situations where metformin high dose is unlikely to achieve the glycemic target, it may not be practical to use the full dose range. On these occasions, the dosage should revert to the lowest dose to achieve the maximum effect and consideration given to combination therapy (26-27). Metformin-based combination therapy significantly improves glycemic control beyond that achieved with either agent alone; as a result it is considered as a rational and effective strategy for enhancing glycemic control in T2DM patients (26).

A high incidence of lactic acidosis led to the withdrawal of the biguanide phenformin. The incidence of lactic acidosis with metformin is very rare between 3–9 cases and 2–4 deaths/100,000 patient-years and is up to 20 times lower than the incidence with phenformin (28). Metformin is contraindicated in renal impairment (SCr > 1.5 mg/dl in men and >1.4 mg/dl in women), systemic illnesses like septicemia, acute myocardial infarction, alcohol abuse, shock, and congested heart failure (29).

1.2 Statement of the Problem

The incidence of clinical complications of T2DM was significantly associated with the level of glycemia. According to the United Kingdom Prospective Diabetes Study (UKPDS) 35 if glycemic control is not optimal in patients with T2DM the risk of diabetic complications increases with the increase in level of glycemia (30)**.** As a result, challenging new targets for FPG and HbA1C in patients with diabetes have been agreed for clinical practice(31)**.** Additionally evidences from different studies showed that, unless glycemia is managed intensively, the development and/or progression of micro and macrovascular complications will increase with the correspondent increase of glycemic level (7, 32-33).

Maximum dosage of oral antidiabetic therapy in individual patients is frequently limited by the risk-benefit profiles of individual therapies, for example weight gain and hypoglycemia associated with insulinotropic agents (9, 34). Metformin is as effective as sulphonylureas in controlling FPG (35)**,** but its risk-benefit profile across the full therapeutic dose range of 500–3000 mg/day is less well described.

In the UKPDS 34, significant improvements in macrovascular outcomes leading to fewer deaths are observed for overweight patients receiving metformin therapy for a median period of 10 years than those patients treated with sulphonylureas and insulin despite with no overall difference in glycemic control (32)**.** The benefits observed in the UKPDS 34 are achieved at a relatively high dose of metformin. In contrast, evidence from the literature (36-37) suggests that many patients may not achieve the expected benefit of metformin if it is not titrated to sufficient dosage.

Diabetes is a predominately self-managed disease, so effective self-management requires patients to understand and use multiple technologies, medications, and complex treatment strategies (38). However, evidences from diabetes knowledge, attitude and practice studies showed that diabetic patients had poor self-management and practice (39-40).

Comorbidity type affects diabetes care. Concordant illnesses are associated with either similar or better care, probably because their management is congruent with that for diabetes (41). Discordant illnesses are associated with a decrease in diabetes care, possibly as a result of competition for time, attention, or other limited resources. Dominant illnesses result in significant decrease in diabetes care that may be appropriate given their poor prognoses (41-43).

A study done at different health institutions of Addis Ababa showed that the diabetic care was below the acceptable standard and diabetes complications are common. In one of the studies (44), 70 (36%) of the patients develop diabetic foot ulcer on follow up and 7 (4%) patients are diagnosed with diabetes after they developed diabetic foot ulcer where ill-fitting or new shoes are the cause for their foot disease in 48 (24.0%) of the patients (44-45).

Health facility based study at the diabetic follow-up clinic of JUSH, showed that the mean metformin dose is not optimal (mean ± SD) 882.0 ± 406.1 mg for T2DM patients. The mean FPG level among these patients is with mean ± SD of 171.7 ± 63.6 mg/dl; and over two-third, 73.1%, have a mean FPG above the target level of 130 mg/dl; Eventually about 33% become insulin requiring during the course of their diabetes(46). Other studies of this same hospital showed glycemic control is below normal and diabetes complications are common (4, 47-48).

Metformin-based combination therapy significantly improves glycemic control beyond that achieved with either agent alone; but on a health facility based study at the diabetic follow-up clinic of JUSH, patients taking a single oral glucose lowering agent (OGLA) alone had a better glucose levels than those taking combination of OGLAs; and also patients taking lower doses of OGLA had better blood sugar control than those taking higher doses. Among patients taking combination OGLA, 56.6% were taking glibenclamide ≥20 mg/d and metformin≥1000 mg/d. Despite having FPG above target level, no modification was done for glycemic management for 69.3% of these patients (46).

Despite this, according to the available data, no study has assessed the optimal dose of metformin and its impact on glycemic control in the first two months of metformin titration in the study area. Hence this study aims to assess the impact of first two months metformin dose titration on glycemic control of T2DM patients and the influence of self care practices on glycemic level at Felege Hiwot Referral Hospital Northwest Ethiopia.

2. Literature Review

A consensus recommendations from the Global Partnership for Effective Diabetes Management statement on 2005 shows that patients with HbA1c of > 9% should be started with a combination of metformin-glibenclimide in parallel with diet/exercise. Glycated hemoglobin level of < 6.5% or FPG of <110 mg/dl should serve as a goal to achieve and maintain, whereas > 6.5 % serve as a goal to titrate medication doses of combination therapies with the goal of HbA1c < 6.5% by 6 months. The same sequence of titration starting from the lowest dose of the combination as the individual drug titration is followed during treatment (49-50).

Inadequate glycemic control is a common problem for most of the diabetic patients. A national survey done in Brazil conducted from February 2006 to March 2007, revealed that 73% of T2DM patients had poor glycemic control with the overall prevalence being 76% (51). A similar study from Venezuela showed that the prevalence of inadequate glycemic control was 76% (52).

Comorbid illnesses are common among patients with diabetes. In 2004, 88.6% of patients with diabetes who responded to the Medical Expenditure Panel Survey reported having at least one additional chronic illness, while close to 15% reported having four or more (53). On another retrospective cohort study conducted in the United States between the years 2001 to 2004 on 42,826 new-onset diabetic patients only 20% of patients had no comorbidities (41).

A consensus statement from the ADA and the EASD on 2009 shows that HbA1C levels of <7% should serve as a goal to achieve and maintain, whereas > 7% serve as a goal to titrate medication doses, and change interventions at as rapid a pace as when not being achieved. A low-dose metformin, 500 mg, taken once or twice per day with meals (breakfast and/or dinner) or 850 mg once per day should serve as a starting dose in metformin use for T2DM treatment after failure of life style intervention. After 5–7 days, if GI side effects have not occurred, dose should advance to 850, or two 500 mg tablets, twice per day taken before breakfast and/or dinner. If GI side effects appear as doses advanced, dose should be decreased to previous lower dose and should be tried to advance the dose at a later time (15).

Metformin treatment should be titrated to its maximally effective dose over 1–2 months, as tolerated; if life-style intervention and maximal tolerated dose of metformin fail to achieve or sustain glycemic goals, another medication should be

added within 2–3 months of the initiation of therapy or at any time when HbA1C goal is not achieved. The maximum effective dose can be up to 1,000 mg twice per day; modestly greater effectiveness has been observed with doses up to about 2,500 mg/day (14-15).

A parallel-group dose-response study conducted in Texas, United States of America (USA), randomized 451 patients with FPG of at least 180 mg/dl despite prior treatment with diet or sulphonylurea to therapy with metformin at daily doses of 500 mg, 1000 mg, 1500 mg, 2000 mg or 2500 mg for 11 weeks. Statistically significant reductions in FPG compared with placebo, occurred at doses of 1000 mg and above, with the greatest effects occurring at 2000 mg and 2500 mg/day. Glycated hemoglobin is improved at all dosages. There is a decrease in HbA1C of more than 1.5% at doses of 1500 mg/day and above. Reductions in FPG and HbA1c increased with the dose of metformin up to a dose of 2000 mg which corresponded with reductions of 79.2 mg/dl and 2% respectively. At the highest dose, 2500 mg, the net reduction in FPG and HbA1C are not significantly different from 2000 mg(18).

A 52-week double-blind study conducted in 70 centers in USA evaluated metformin-glibenclamide combination tablets (Glucovance) in 477 patients with hyperglycemia. Patients are allocated according to HbA1C and patients with HbA1C< 9.0% or HbA1C> 9.0% received initial treatment with metformin/glibenclamide 500 mg/2.5 mg bid or 500 mg/5 mg bid, respectively. Treatments are titrated upwards by one tablet per day at weeks 2 and 4 if FPG is >126 mg/dl. Daily dosages are increased further by one tablet/day at weeks 13, 26 and 39. Reductions in HbA1C are maintained with a mean reduction of 1.7% after 52 weeks. Mean changes in FPG from the baseline in patients treated with metformin/glibenclamide 500 mg/2.5 mg, 500 mg/5 mg, and in all patients, were 35 mg/dl, 74 mg/dl and 55 mg/dl, respectively (54).

A double-blind study done at Leeds, United Kingdom (UK), investigating the effects of metformin in 75 patients with established T2DM and FPG ≥108 mg/dl are randomized to receive placebo or metformin at doses of 1500 mg or 3000 mg for six months. Fasting plasma glucose and HbA1C are increased in placebo-treated patients over the six-month study period. In contrast, metformin significantly reduced both parameters. The 3000 mg dose of metformin is

significantly more effective in reducing FPG when compared with the 1500 mg dose. The mean fall in plasma glucose with 3000 mg dose is 36 mg/dl after 3 weeks and 64.8 mg/dl at 6 months. Comparable figures for 1500 mg dose are 14.4 and 9 mg/dl (19).

A 16-week, multicenter, randomized, double-blind, parallel clinical trial on 76 T2DM patients in China had evaluated the efficacy and safety of glibenclamide/metformin combined tablet compared to glibenclamide or metformin alone. Doses of glibenclamide 5 mg bid; metformin 500 mg bid; glibenclamide /metformin 2.5 mg/500 mg bid; or glibenclamide /metformin 5.0 mg/500 mg bid were used and the doses were titrated every 2 weeks to a maximum of 4 tablets per day if the patient's FPG still exceeded 140 mg/dl. Efficacy was evaluated by the changes from baseline in HbA1c and FPG at week 16, and was found that patients who received glibenclamide /metformin combination tablets had greater reductions in FPG and HbA1c compared with glibenclamide or metformin monotherapy (55). A similar result was obtained from a study that assessed patients with T2DM in a multicenter, randomized, parallel group, double-blind trial in USA (56).

A retrospective study conducted in Hawaii during 2006-2009 on patients of HbA1c >9% examines the factors related to sustained poor glycemic control where 68.5% of patients are with poor glycemic control. Longer duration of diabetes (10 or more years are more than 9 times likely to have poor control than patients who had diabetes for 3 years or less), being under age 35, and patients taking 15 or more medications are significantly associated with sustained poor glycemic control compared with patients taking fewer than 5 medications. In contrast, patients with insurance coverage for their medications, sex, and history of coronary artery disease and congestive heart failure are not significantly associated with poor glycemic control (57).

On the other hand, a study done in Malaysia showed that good adherence and monotherapy were predictors of better glycemic control for T2DM patients (58). On another cross sectional study done in Malaysia between 2001- 2002 on T2DM patients, the variables with significant effects on glycemic control are ethnicity, age and duration of DM where patients with less than 5 years are with better glycemic control (59).

A study in Australia comparing the effects of escalating doses of metformin on glycemia in nine patients with T2DM; the metformin daily dose is commenced at 500 mg and then increased in a stepwise manner at two-weekly intervals to 1500 mg and then 3000 mg. Fasting blood sugar and 24-hour glucose profiles are evaluated at the end of each two week treatment period. The twenty-four hour glucose profile demonstrates a clear dose-response relationship, with reduced plasma glucose concentrations with each increase in the dose of metformin. Both parameters are significantly reduced at all metformin doses, compared with baseline. Whilst the 1500 mg and 3000 mg doses of metformin are significantly more effective than the 500 mg dose in reducing both fasting and 24-hour plasma glucose concentrations, the benefits observed with 3000 mg/day are not statistically significantly greater than with 1500 mg/day (60).

A cross sectional study conducted in Malaysia showed that only 17.4% of the patients achieved the recommended glycemic target of A1C less than 6.5% despite all of respondents were on medication (61). In a Kenyan study at routine diabetes care clinic over a period of six months, January 1998 to June 1998, about 60% of diabetic patients did not achieve the target glycemic level mid morning random blood sugar and HbA1c (62).

On a study done at Jimma university Specialized Hospital diabetic clinic, level of glycemic control is not significantly affected by sociodemographic characteristics of the patient, duration of diabetes, health education, and frequency of visits (46).

2.1 Conceptual Frame Work

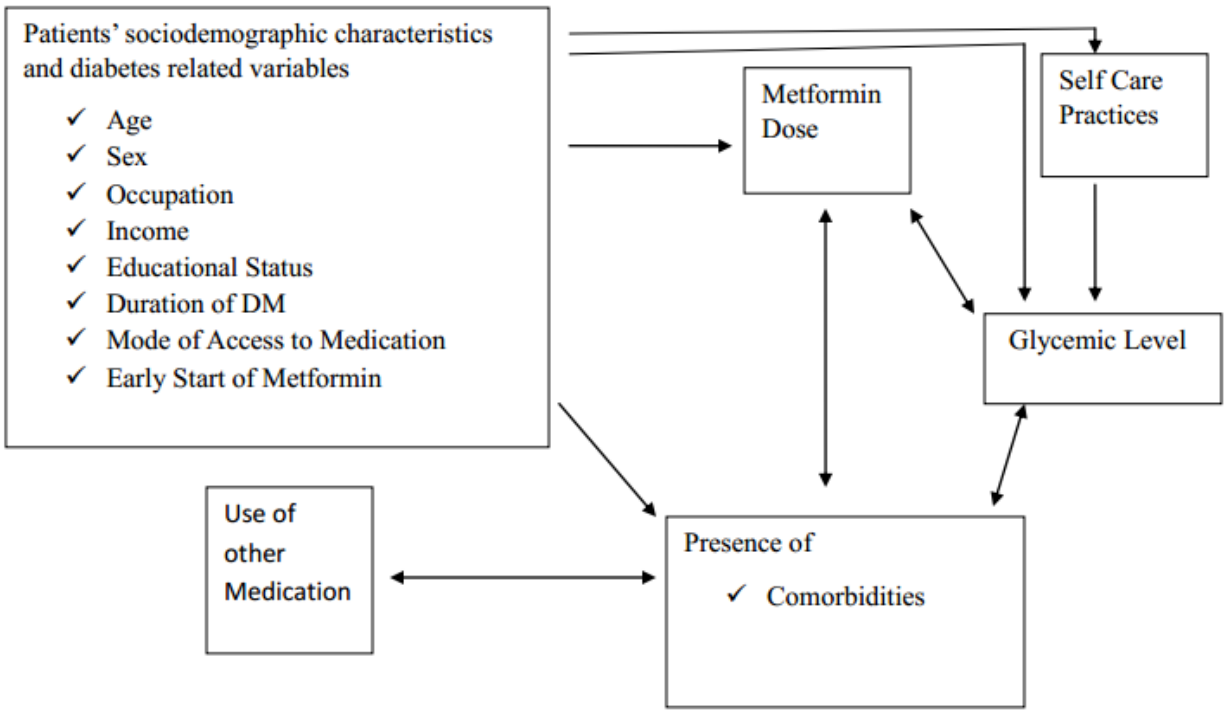

Figure 1: The possible interrelationship between different variables that influence the glycemic level

3. Significance of the Study

The present study had examined the practice of metformin dose titration and its impact on treatment outcome (i.e. glycemic control) in T2DM patients. It had identified the influence of self care practices that may affect glycemic control thereby metformin dose titration at Felege Hiwot Referral Hospital. It also determined the percentage of diabetic patients for whom metformin dose titration is not done properly as per the recommendations from literatures. In addition the study had explored the association between poor metformin dose titration and glycemic control in T2DM patients.

Knowledge on effect of self care practices and pattern of metformin dose titration is of great relevance for clinicians and patients to improve the level of self care and to use the optimal doses of metformin without significantly increasing toxicities of the medication. Therefore results from this study serves to inform practitioners on the impact of metformin dose titration and self care practice on glycemic control which ultimately reduces the burden of illness in diabetic patients at the Hospital.

It also informs practitioners about the status of care and initiates their motivation to improve the level of care. Eventually it serves as a base line for intervention.

4. Objectives of the Study

4.1 General Objective

- ✓ To assess the impact of metformin dose titration and self care practices on glycemic control of T2DM patients at Bahir Dar Felege Hiwot Referral Hospital, Northwest Ethiopia.

4.2 Specific Objectives

- ✓ To assess the proportion of patients who are on the recommended dose of metformin at the 2^{nd}, 6^{th} month, and at the end of one year.
- ✓ To measure the glycemic level at each increment and to estimate the time taken to attain optimal glycemic level
- ✓ To measure the average increment interval of metformin dose, and to estimate the time taken to reach the dose for the second week and the maximum recommended dose
- ✓ To assess self-care activities of diabetic patients at Bahir Dar Felege Hiwot Referral Hospital

4.3 Research Question

What proportion of type 2 diabetes mellitus patients take the titrated form of metformin?

5. Methods and Participants

5.1 Study Area and Period

This study was conducted from March 01 to March 31, 2013 at the outpatient diabetic follow up clinic of Felege Hiwot Referral Hospital. Felege Hiwot Referral Hospital is previously a referral hospital which is currently shifted to a teaching and referral hospital located in Bahir Dar town, Northwest Ethiopia, 565 km far from Addis Ababa. The hospital has a total of 284 beds. It has 275 technical and 187 administrative staffs. The hospital serves the people of Bahir Dar town and its surroundings, East and West Gojjam, Awi zone, and south Gondar. Diabetes clinic is one of the many chronic follow-up clinics of the hospital delivered twice weekly on Mondays and Tuesdays. The service is rendered by general nurses, and general practitioners.

5.2 Study Design

Hospital based retrospective general cohort study design was used.

5.3 Population

5.3.1 Source Population

The source population included all T2DM patients who had been followed at the diabetic follow up clinic of Felege Hiwot Referral Hospital with metformin.

5.3.2 Study Population

The study populations were all T2DM patients who had been followed at the diabetic follow up clinic of Felege Hiwot Referral Hospital with metformin for at least the previous one year and who came to the diabetic follow up clinic of Felege Hiwot Referral Hospital during the data collection period.

5.3.3 Inclusion and Exclusion Criteria

5.3.3.1 Inclusion Criteria

Diabetic patients who met the following criteria were included in the study:

- Patients who had started metformin with in March 01, 2010 and March 31, 2012
- Patients who were on metformin (alone or in combination) for at least a year.
- Type 2 DM patients who were either newly diagnosed or who had been only on life style adjustment (who were not in any kind of OHGA or insulin) before they

started metformin (alone (**M**) and in combination (**MG**) were included. First patients were classified in to two main groups as those who were taking metformin alone and those who were taking metformin in combination with glibenclamide. These patients were then incorporated in to one of the groups (either titrated or suboptimal dose of metformin groups) based on the prescribed dose of metformin during their first two months of therapy. Patients who were prescribed with metformin dose of less than 1500 mg in the first two months of therapy were included in to the suboptimal metformin dose group, whereas patients who were prescribed with metformin dose of 1500 mg or above in the first two months of therapy were included in to the titrated metformin dose group. Twenty four patients were included in the metformin titrated group where as sixty six patients were included in the suboptimal metformin dose group. Finally, patients attainment of recommended FPG level below 130 mg/dl at two, six, and twelve month period were reviewed.

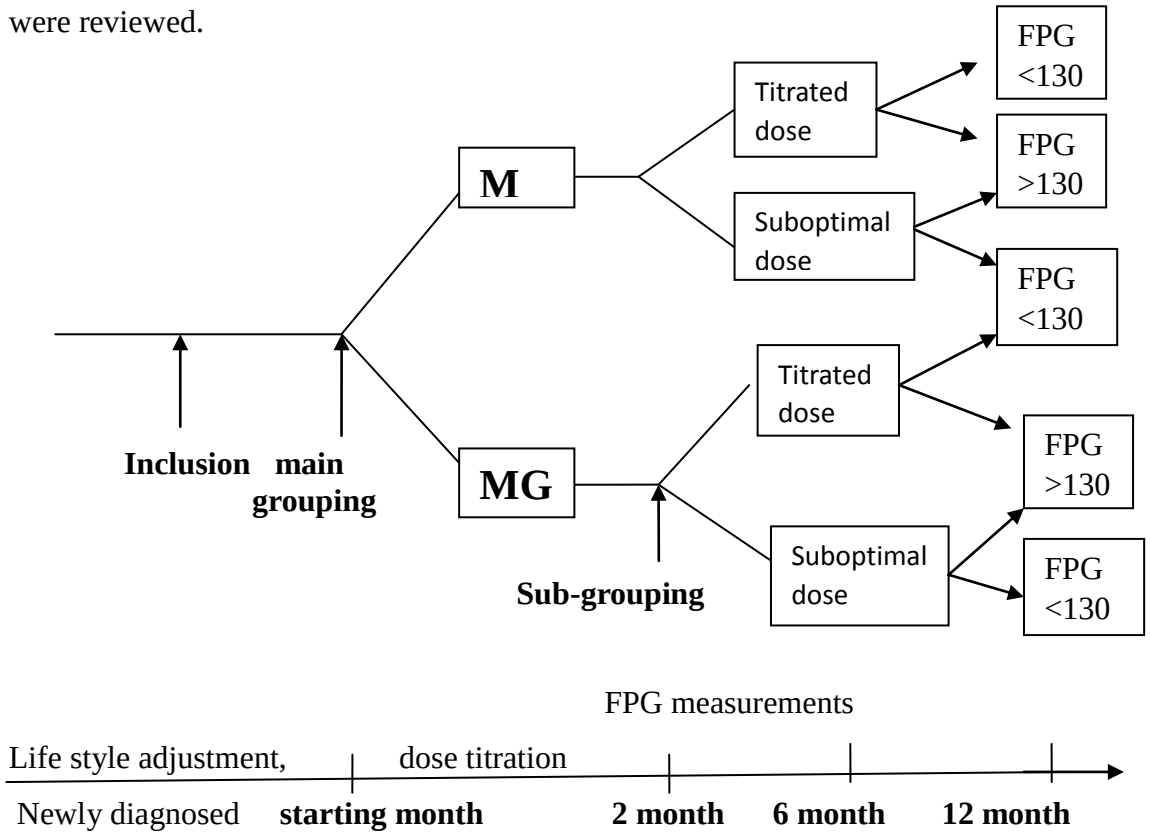

Figure 2: the sequential inclusion and grouping of participants in to the study

5.3.3.2 Exclusion Criteria

- Diabetic patients who are seriously ill to complete interview
- Patients who are started with a combination of insulin and metformin
- Patients with an appointment interval of two month period

5.4 Sample Size

The sample size for this study was calculated using the following formula that is used for calculating samples for cohort studies.

$$N = \frac{1}{[p(1-R)]^2}\left[Z_{1-\frac{\alpha}{2}}\sqrt{\left(1+\frac{1}{K}\right)U(1-U)} + Z_{1-\beta}\sqrt{pR(1-Rp)+\frac{p(1-p)}{K}}\right]^2$$

Where

$$U = \frac{K_p + pR}{K+1}$$

N is the final sample size that will be used

p is the expected incidence of FPG > 130 mg/dl in the metformin titrated patients, i.e. p = 0.05

R is the minimum relative risk to be detected, i.e. R = 2.5

α is the type I error rate which is acceptable, i.e. α = 0.05

β is the type II error rate which is acceptable, i.e. β = 0.20

$Z_{1-\alpha/2}$ and **$Z_{1-\beta}$** refers to the unit normal deviates corresponding to α and β, i.e. $Z_{1-\alpha/2} = 1.96$ and $Z_{1-\beta} = 0.84$

K is the ratio of number of patients treated with metformin by the recommended titration pattern to the number of patients treated with metformin not by the recommended titration pattern, i.e. K = 3; after a series of calculations **U** becomes 0.06875 and **N** becomes 80.

5.5 Sampling Technique

All ambulatory T2DM patients, who came to Felege Hiwot Referral Hospital for their routine diabetic follow up during the data collection period, were included consecutively till a total of 80 patients had been obtained provided that they met the inclusion criteria.

5.6 Variables and Measurement

5.6.1 Variables

5.6.1.1 Independent Variables

- ✓ Age
- ✓ Sex
- ✓ Occupation
- ✓ Income
- ✓ Educational Status
- ✓ Duration of DM
- ✓ Mode of Access to Medication
- ✓ Diet Modification
- ✓ Exercise
- ✓ Social Drug Use
- ✓ Use of Traditional Medicine
- ✓ Attending Diabetic Education
- ✓ Membership of Diabetic Association
- ✓ Metformin Dose
- ✓ Comorbid Conditions
- ✓ Use of Other Medications

5.6.2.2 Dependent Variables

- ✓ Glycemic Level

5.6.2 Data Collection Technique and Instrument

Data was collected by two different techniques. Patients' sociodemographic, diabetic related variables and self care practices were collected by face to face interview. Metformin dose, glycemic level at that given dose of metformin, and other additional medications that patients had taken were extracted from review of patient medical records. Participants were interviewed using the Amharic version of questionnaire. The first part of the questionnaire focused on patients' sociodemographic and diabetic related characteristics. The second part of the questionnaire had assessed the patients self care practices. Finally the last part of

the questionnaire dealt the first, second, six month, and one year pattern of metformin use and clinical parameters like comorbid conditions, and drugs for these comorbid conditions that were extracted from patients' medical record review.

5.7 Data Collection Procedures

Since the study is institution based, data was collected as patients came for their diabetic follow up by three BSc. clinical nurses and one senior clinical nurse as a supervisor. Data for this study was collected through face-to-face interview and review of the patients' card on patients who had visited the diabetic follow up clinic of Felege Hiwot Referral Hospital during the data collection period. As the patient was taking his/her turn at the waiting area, consent was asked after the data collector clearly explains the purpose of the study to the patient. A patient was interviewed in a separate class room using the Amharic version of a questionnaire. For patients who had repeated clinic visits during the study period, data was collected during their first visits and an identification mark was put on their medical cards to avoid double interviewing.

Data regarding the patient's demographic and diabetic characteristics was collected by individually interviewing patients using a questionnaire. General characteristics such as age, sex, occupation, educational status, and duration of diabetes were included. Metformin dose, comorbidities and other additional medications that the patients were taking for comorbid conditions were extracted from review of patient medical records.

5.8 Operational Definitions and Definition of Terms

Adherence: A patient was classified as if he/ she were adherent to his /her medication if he/she answered to all four adherence questions of the validated Morisky scale as no; otherwise he/she was non adherent.

Diet Modification: a patient is on diet modification if he/ she is following the dietary restriction pattern of eating injera, maize, potatoes, bread, Macaroni, fish and vegetables. On the contrary if he/ she is not eating factory products like packed juices, soft drinks, candies, cakes, cookies, margarine, biscuits, sugar, and natural products like butter, meat.

Dose Titration: dose is titrated if the dose of metformin is increased by a week interval by 500 mg per day if the FPG concentration of the patient is greater than 130 mg/dl at the end of the first week treatment, and Metformin is titrated to its maximally effective dose (1500-2000 mg) over 1–2 months (14-15).

Exercising: A person who reports regular aerobic exercise (walking, jogging) of at least 30 min or its equivalent for every 5 days of the week; or whose occupation requires physical exertion daily will be considered to be physically active(63).

Glycemic Control: glycemia is controlled if the fasting plasma glucose is less than 130 mg/dl at the given dose of metformin (46).

5.9 Data Processing, Analysis, Interpretation and Presentation

Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 20.0. First data was edited and checked for completeness and then entered in to SPSS for descriptive statistical analysis. For categorical variables, frequencies and percentages were done. Data also was presented by possible continuous measures of central tendency or variation or both. Association between variables was checked using risk ratio. Binary logistic regression was used to determine factors affecting glycemic level where the candidate variables in multivariate analysis were variables with p-value of less than 0.25. Absolute risk reduction (ARR) and number needed to treat (NNT) were used to show the difference between the titrated dose and the untitrated dose of metformin. Repeated Measures ANOVA and Kaplan Meier survival analysis were used to assess the dose titration practices and impact of metformin dose titration on glycemic control respectively.

5.10 Data Quality Management

The data collection instrument format was developed in English and translated to Amharic and later back translated to English by different individuals for its accuracy and desired results.

The principal investigator had trained data collectors for two days about the study. They were given an orientation on the protocol and specific details concerning participation in the study.

The principal investigator was also been closely supervising the activity on a daily basis. At the end of each data collection days the principal investigator had checked the completeness of filled questionnaires and whether recorded information makes sense to ensure the quality of the data collected. Besides this, the principal investigator had carefully entered and thoroughly cleared the data before the commencement of the analysis.

5.11 Ethical Consideration

Ethical clearance and approval of the study was obtained from Institutional Review Board of Jimma University, College of Public Health and Medical Sciences before starting the actual data collection. Subsequent permission was granted from the authorities of Felege Hiwot Referral Hospital**.**

Participation of patients in this study was entirely voluntary and confidential and private information was protected. Non participation did not affect participants' care at the clinic. Each participant was asked a written consent before data collection. The right of participants to withdraw from the interview or not to participate was respected. All interviews were carried out at a separate room to keep the patients privacy.

5.11 Dissemination and Utilization of Results

The finding of the study was submitted to the Department of Pharmacy, College of Public Health and Medical Science (Jimma University), Ethiopian Diabetic Association Bahir Dar Branch, Amhara Regional State Health Bureau. The finding was presented during thesis defence, as a partial fulfillment of Master degree in Clinical Pharmacy. Finally attempts will be made to present the finding on scientific conferences and to publish it on peer reviewed journals.

6. Results

6.1 Patients' demographic characteristics: During the study period a total of 80 patients were voluntarily willing to participate in the study, fulfilled the inclusion criteria and included in this study, making the response rate 100%.

Forty one patients were females (51.3%). Fifty eight (72.5%) of the participants were within the age group of 35 to 64 years. The mean age of patients was 48 years (SD ± 11.16) that ranged from 16 to 75 years. Twenty five (31.3%) of the patients had completed secondary education (grade 9 up to 12). Twenty four (30%) of participants were civil servants and forty four (55%) of the participants earn a monthly income of more than one thousand Ethiopian birr (Table 1).

Table 1: Sociodemographic characteristics of T2DM patients and their association with recommended FPG level attainment at two, six, and twelve months time of metformin therapy among diabetic patients at the outpatient diabetic clinic of FRH, Ethiopia, March 01, 2010 – March 31, 2012

Variables		**FBG < 130 mg/dl**		**CRR (95% CI)**	**P-value**
		Yes (%)	**No (%)**		
Two † Month Value	Sex				**0.884**
	Male	12 (30.8)	27 (69.2)	Reference	
	Female	12 (29.3)	29 (70.7)	1.07 (0.41, 2.79)	
	Highest educational level				**0.467**
	No formal education	3 (16.7)	15 (83.3)	3.07 (0.67, 14.07)	0.147
	Primary education (1-8th grade)	6 (37.5)	10 (62.5)	1.02 (0.26, 3.9)	0.97
	Secondary education (9-12th grade)	7 (28)	18 (72)	1.58 (0.45, 5.4)	0.468
	Tertiary education (diploma & above)	8 (38.1)	13 (61.9)	Reference	
	Current occupation				**0.810**
	Civil servant	8 (33.4)	16 (66.6)	1.07 (0.30, 3.76)	0.908
	Merchant	4 (30.8)	9 (69.2)	1.21 (0.27, 5.39)	0.801
	Farmer	2 (15.4)	11 (84.6)	2.96 (0.50, 17.29)	0.228
	House wife	3 (30)	7 (70)	1.25 (0.24, 6.44)	0.784
	Others***	7 (35)	13 (65)	Reference	
	Age				**0.090**
	15-34	8 (53.3)	7 (46.7)	Reference	
	35-64	15 (25.9)	43 (74.1)	3.27 (1.01, 10.58)	0.047
	≥ 65	1 (14.3)	6 (85.7)	6.85 (0.65, 71.72)	0.108

	Monthly income (Ethiopian Birr)				**0.288**
	< 500	4 (30.8)	9 (69.2)	1.28 (0.34, 4.85)	0.711
	500-1000	4 (17.4)	19 (82.6)	2.71 (0.78, 9.38)	0.115
	> 1000	16 (36.4)	28 (63.6)	Reference	
Six Month Value	Sex				**0.697**
	Male	12 (30.8)	27 (69.2)	Reference	
	Female	11 (26.9)	30 (73.1)	1.21 (0.46, 3.19)	
	Highest educational level				**0.198**
	No formal education	3 (16.7)	15 (83.3)	3.07 (0.67, 14.07)	0.147
	Primary education (1-8th grade)	7 (43.8)	9 (56.2)	0.79 (0.21, 2.97)	0.729
	Secondary education (9-12th grade)	5 (20)	20 (80.0)	2.46 (0.65, 9.19)	0.180
	Tertiary education (diploma & above)	8 (38.1)	13 (61.9)	Reference	
	Current occupation				**0.756**
	Civil servant	8 (33.4)	16 (66.6)	1.07 (0.30, 3.76)	0.908
	Merchant	3 (23.1)	10 (76.9)	1.79 (0.36, 8.74)	0.469
	Farmer	2 (15.4)	11 (84.6)	2.96 (0.50, 17.2)	0.228
	House wife	3 (30)	7 (70)	1.25 (0.24, 6.44)	0.784
	Others***	7 (25)	13 (65)	Reference	
	Monthly income (Ethiopian Birr)				**0.680**
	< 500	4 (30.8)	9 (69.2)	1.05 (0.27, 4.00)	0.943
	500-1000	5 (21.8)	18 (78.2)	1.68 (0.51, 5.44)	0.387
	> 1000	14 (31.8)	30 (68.2)	Reference	

***** Statistically significant at P-value < 0.05

*** Student (6), Daily laborer (7), Deacon (2), Carpenter (2) and Tailor (5)

† The two month value and the twelve month value are similar

6.2 Clinical profiles and other characteristics of patients: The majority of participants (57.5%) were with free access to medication. Thirty six (45%) of patients reported that they were adherent to their medication. Fifty six (70%) of patients were attending the diabetic education where fourteen (25%) were members of Ethiopian diabetic association. Nineteen (23.7%) of patients were prescribed with the recommended metformin dose (i.e. greater than 1500 mg) out of which fourteen (73.7%) of the patients had attained the desired FPG level of less than 130 mg/dl in the first two months of metformin therapy. Forty one (51.2%) of study participants were on metformin alone therapy. Fourteen (17.5%) patients were with comorbidities (Table 2).

Table 2: Association of recommended FPG level attainment at two, six and twelve months of metformin therapy with patients' clinical parameters and self-care activities among diabetic patients at the outpatient diabetic clinic of FRH, Ethiopia, March 01, 2010 – March 31, 2012

Variables		FBG < 130 mg/dl		CRR (95% CI)	P-value
		Yes (%)	No (%)		
Two † Month Value	Drug Access				**0.921**
	Free	14 (30.5)	32 (69.5)	Reference	
	Pay	10 (29.5)	24 (70.5)	1.05 (0.39, 2.76)	
	Metformin use				**0.408**
	alone	14 (34.2)	27 (65.8)	Reference	
	with glibenclimide	10 (25.7)	29 (74.3)	1.50 (0.57, 3.95)	
	Titration at two month				**< 0.001**
	Yes	19 (79.1)	5 (20.9)	Reference	
	No	5 (9)	51 (91)	38.7 (17.0, 61.0)	
	Daily dose of metformin				**< 0.001**
	500 mg	3 (13.7)	19 (86.3)	19 (3.18, 39.35)	0.001
	1000 mg	7 (18)	32 (82)	13.7 (2.93, 26.0)	0.001
	1500 mg	5 (71.4)	2 (28.6)	1.2 (0.147, 9.76)	0.865
	2000 mg	9 (75)	3 (25)	Reference	
	Presence of comorbidity				**0.352**
	Yes	5 (35.7)	9 (64.3)	Reference	
	No	19 (28.7)	47 (71.3)	1.74 (0.54, 5.59)	
	Dietary modification				**0.045**
	Yes	14 (42.5)	19 (57.5)	Reference	
	No	10 (21.3)	37 (78.7)	2.72 (1.02, 7.27)	
	Regular exercise				**0.922**
	Yes	13 (29.6)	31 (70.4)	1.04 (0.40, 2.7)	
	No	11 (30.6)	25 (69.4)	Reference	
	Regular Foot Inspection				**0.126**
	Yes	20 (65.1)	37 (64.9)	Reference	
	No	4 (17.4)	19 (82.6)	2.56 (0.76, 8.59)	
	Checking inside of the foot wear				**0.049**
	Yes	19 (38)	31 (62)	Reference	
	No	5 (16.7)	25 (83.3)	3.06 (1.10, 9.36)	
	Walking bare foot				**0.223**
	Yes	2 (15.4)	11 (84.6)	2.68 (0.54, 13.2)	
	No	22 (32.9)	45 (67.1)	Reference	
	Membership to diabetic association				**0.903**
	Yes	5 (31.3)	11 (68.7)	Reference	
	No	19 (29.7)	45 (70.3)	1.07 (0.33, 3.52)	
	Attending diabetic Education				**0.246**
	Yes	19 (34)	37 (66)	Reference	
	No	5 (20.9)	19 (79.1)	1.95 (0.63, 6.04)	
	Medication adherence				**0.12**
	Yes	14 (38.9)	22 (61.1)	Reference	
	No	10 (22.8)	34 (77.2)	2.16 (0.81, 1.72)	

Six Month Value	Drug Access				**0.699**
	Free	14 (30.5)	32 (69.5)	Reference	
	Pay	9 (26.5)	25 (73.5)	1.21 (0.45, 3.26)	
	Metformin use				**0.116**
	alone	15 (36.6)	26 (63.4)	Reference	
	with glibenclimide	8 (20.6)	31 (79.4)	2.23 (0.81, 6.1)	
	Titration at two month				**< 0.001**
	Yes	18 (75)	6 (25)	Reference	
	No	5 (9)	51 (91)	30.6 (13.8, 59.1)	
	Daily dose of metformin				**< 0.001**
	500 mg	3 (13.7)	19 (86.3)	19 (3.18, 33.35)	0.001
	1000 mg	6 (15.4)	33 (84.6)	16.5 (3.43, 29.2)	< 0.001
	1500 mg	5 (71.4)	2 (28.6)	1.2 (0.147, 9.76)	0.865
	2000 mg	9 (75)	3 (25)	Reference	
	Presence of comorbidity				**0.29**
	Yes	5 (35.7)	9 (64.3)	Reference	
	No	18 (22.5)	48 (77.5)	1.88 (0.58, 6.07)	
	Dietary modification				**0.082**
	Yes	13 (39.4)	20 (60.6)	Reference	
	No	10 (21.3)	37 (78.7)	2.4 (0.89, 6.45)	
	Regular exercise				**0.862**
	Yes	13 (29.6)	31 (70.4)	Reference	
	No	10 (27.8)	26 (72.2)	1.09 (0.41, 2.89)	
	Regular Foot Inspection				**0.382**
	Yes	18 (31.6)	39 (68.4)	Reference	
	No	5 (21.8)	18 (78.2)	1.66 (0.53, 5.18)	
	Checking inside of the foot wear				**0.070**
	Yes	18 (36.0)	32 (64.0)	Reference	
	No	5 (16.7)	25 (83.3)	2.81 (0.91, 8.62)	
	Walking bare foot				**0.257**
	Yes	2 (15.4)	11 (84.6)	2.5 (0.51, 12.34)	
	No	21 (31.4)	46 (68.6)	Reference	
	Membership to diabetic association				**0.711**
	Yes	4 (25)	12 (75)	1.26 (0.36, 4.43)	
	No	19 (29.7)	45 (70.3)	Reference	
	Attending diabetic Education				**0.309**
	Yes	18 (32.2)	38 (67.8)	Reference	
	No	5 (20.9)	19 (79.1)	1.8 (0.579, 5.59)	
	Medication adherence				**0.414**
	Yes	12 (33.4)	24 (66.6)	Reference	
	No	11 (25)	33 (75)	1.5 (0.56, 3.96)	

***** Statistically significant at P-value < 0.05

† The two month value and the twelve month value are similar

Data were analyzed to determine whether there were any relationships between different variables and recommended fasting glycemic level attainment at two and six month time. Initial bivariate analysis showed that there was no relationship

between reducing risk of not attaining fasting glycemic goal and patients' sex, age, occupation, educational status, monthly income, drug access, metformin use (alone or in combination with glibenclimide), presence of comorbidity, regular exercise, regular foot inspection, walking bare foot, membership to diabetic association, attending diabetic education regularly, and self reported medication adherence. However, there was a statistically significant difference in reducing the risk of not attaining FPG level at two month and daily dose of metformin (P<0.001), the titration practice at two month (P <0.001), dietary modification (P=0.045) and checking the inside of the foot wear regularly (P=0.049) of patients. This was also true for patients' reduction of the risk of not attaining FPG level at six month and daily dose of metformin (P<0.001), and the titration practice during the first two months of therapy (P <0.001) (Table 1 and 2).

The previous bivariate analysis did not take into account the effect of confounding factors which may affect the relationship between these factors and reducing the risk of not attaining FPG level. Therefore, multivariable analysis was carried out and it showed that titration pattern at two month (p = 0.001) had significant relationship in reducing the risk of not attaining the recommended FPG level at both two and six months. Therefore titration pattern during the two month time was statistically significant predictor of reduction in the risk of not attaining recommended FPG level at two and six month period of metformin therapy. While dietary modification and checking the inside of the foot wear regularly were associated in reducing the risk of not attaining recommended FPG level in the bivariate analysis for the two month period but not in the final multivariate analysis. On the other hand daily dose of metformin and the titration practice at two month were variables with significant association in reducing the risk of not attaining recommended FPG level in the bivariate analysis for the two month as well as the six month period; but they are variables with significant correlation in an inverse pattern.

According to the multivariable analysis type 2 diabetic patients who were treated with metformin that was not titrated during the first two month period of therapy were 49.32 and 30.6 times more likely to be at risk of not attaining recommended fasting glycemic level compared to those who were treated with metformin that was titrated during the first two month period of therapy (ARR = 49.32; 95% CI:

32.84 – 66.74) and (ARR =30.6; 95% CI: 13.8 – 59.12) at the two and six month time respectively (Table 3).

Table 3: Predictors of failure to attain recommended two and six month FPG level of diabetic patients among diabetic patients at the outpatient diabetic clinic of FRH, Ethiopia, March 01, 2010 – March 31, 2012

FPG	Variable	CRR (95% CI)	P-value	ARR (95% CI)	P-value
Two † Month FPG	Titration at two month		<0.001		**0.001***
	Yes	Reference		Reference	
	No	38.7 (17.0, 61.0)		49.3 (32.84, 66.74)	
Six Month FPG	Titration at two month		<0.001		**0.001***
	Yes	Reference		Reference	
	No	30.6 (13.8, 59.12)		30.6 (13.8, 59.12)	

* Statistically significant at P-value <0.05

† The two month value and the twelve month value are similar

The absolute risk reduction (ARR) in controlling FPG at the end of 2, 6 and 12 month treatment periods between metformin titrated during the first two months of therapy and untitrated one were 0.702 (70.2%), 0.661 (66.1%) and 0.702 (70.2%) respectively. The number needed to treat (NNT) to control one additional FPG of the patients at the end of 2, 6 and 12 month treatment periods were 1.424, 1.51 and 1.424 respectively.

Only 24 (30 %), 23 (28.7%), and 24 (30%) patient's attained FBG goal recommended (70-130 mg/dL) at two, six, and twelve month of metformin therapy respectively. The average diabetic duration was 2.32 years (SD ± 1.11) and 77 (96.2%) of patients were with less than five years of duration. No patient is with duration of diabetes lasting above ten years. Fourteen (17.5%) patients were with medications for comorbidities. Two patients were using traditional herbs to manage their diabetes but no patient had had a habit of using social drugs (Table 4).

Table 4: Profiles of clinical characteristics of diabetic patients at the outpatient diabetic clinic of FRH, Ethiopia, March 01, 2010 – March 31, 2012

Characteristics	Frequency	Percent
Use of traditional medicines to manage DM		
Yes	2	2.5
No	78	97.5
Habit of using social drugs		
Yes	0	0
No	80	100
Diabetic duration (in years)		
<5	77	96.2
5-10	3	3.80
> 10	0	0
Two month FPG(mg/dl)		
< 130	24	30
≥ 130	56	70
Six month FPG(mg/dl)		
< 130	23	29
≥ 130	57	71
Twelve month FPG(mg/dl)		
< 130	24	30
≥ 130	56	70
Presence of medications for comorbidities		
Yes	14	17.5
No	66	82.5

Different comorbid diseases were recorded in the patients' medical chart of which hypertension was the most frequent occurring in 11 (78.7%) of the patients, while AIDS, urinary tract infection and gastric pain were encountered once in a patient (Table 5). Enalapril and nifedipine were the most commonly prescribed medications for the management of comorbidities at the study hospital (Table 6). But, medications like statins which are important for the prevention of thromboembolic complications of DM were not prescribed for any of the patients in this study.

Table 5: Comorbidities recorded on patients' chart among T2DM patients at the outpatient diabetic clinic of FRH, Ethiopia, March 01, 2010 – March 31, 2012

Types of diabetic comorbidities	Frequency	Percent
Hypertension	11	78.7
AIDS	1	7.1
Urinary tract infection	1	7.1
Gastric pain	1	7.1

Table 6: Drugs that were prescribed for diabetic patients for their comorbid conditions among diabetic patients at the outpatient diabetic clinic of FRH, Ethiopia, March 01, 2010 – March 31, 2012

Drugs	**Number of patients for whom the drug was prescribed**
Enalapril	4
Nifedipine	1
Enalapril + Nifedipine	4
Ciprofloxacin	1
Omeprazole	1
ASA + Enalapril	2
AZT + 3TC + NVP	1

Dose Titration Pattern of Metformin on Glycemic control

A. Dose Titration Pattern for Metformin

The mean dose of metformin in the first twelve months is 1056.25 mg (SD = 490.37). Doses of metformin on start, first to third visits and the fourth visit are 856.25mg, 1056.25 mg, and 1062.50 mg respectively (Table 7).

Table 7: Pattern of metformin dose titration during the first twelve months of metformin therapy among diabetic patients at the outpatient diabetic clinic of FRH, Ethiopia, March 01, 2010 – March 31, 2012

Dose titration pattern for metformin use in the first twelve months of therapy	**Month**	**Mean Dose (mg)**	**95% Confidence Interval**		**Test of within-subjects Effects**			
			Lower Bound	Upper Bound	Degree of freedom		F	p-value
					Month	Error		
	starting month	856.25	789.550	922.950	12	948	18.04	< 0.001*
	1^{st}-3^{rd} visits	1056.25	947.123	1165.377				
	4^{th} visit	1062.50	954.265	1170.735				
	5^{th} visit	1068.75	961.433	1176.067				
	6^{th} -7^{th} visits	1062.50	954.265	1170.735				
	8^{th}-12^{th} visits	1056.25	947.123	1165.377				

* = p – statistically significant value

The ANOVA analysis of the titration pattern among the first twelve months of metformin therapy showed a significant difference among the mean doses of the twelve months $F(12,948) = 18.04$, $p < 0.001$ from all sphericity assumed, greenhouse-geisser, huynh-feldt, and lower-bound tests of within-subjects effects; but the paired t-test of post-hoc analysis showed that, it is the titration from starting dose to other visiting doses that this significant variation occurred, $p < 0.001$ whereas titration variation among other visits themselves didn't show any significant statistical variation ($p > 0.05$) (Table 8).

Table 8: paired sample t-test p-values for comparison of mean doses of metformin at various monthly visits during the first twelve month of metformin therapy among diabetic patients at the outpatient diabetic clinic of FRH, Ethiopia, March 01, 2010 – March 31, 2012

Comparison Doses	**Paired differences**		**Minimum p-value observed**
	Max. mean dose difference (mg)	**Max. standard Deviation**	
Starting dose versus 1^{st} – 12^{th} visit doses	211.5	403.2	< 0.001* (max)
1^{st} visit Vs 4^{th} - 12^{th} visit doses	12.5	97.2	0.159
2^{nd} Vs 4^{rd} -12^{th} visit doses	12.5	97.2	0.159
3^{rd} Vs 4^{th} -12^{th} visit doses	12.5	97.2	0.159
4^{th} Vs 5^{th} -12^{th} visit doses	6.2	79.5	0.320
5^{th} Vs 6^{th} -12^{th} visit doses	12.5	78.5	0.159
6^{th} Vs 8^{th} -12^{th} visit doses	6.2	55.9	0.320
7^{th} Vs 8^{th} -12^{th} visit doses	6.2	55.9	0.320

* = p – statistically significant value

The titration pattern of metformin in the first twelve months of metformin therapy showed an increment from staring dose of 856.25 mg to first visit dose of 1056.25

mg, whereas the titration pattern from first visit dose of 1056.25 mg to the rest of the visits didn't show any numerical as well as statistically significant difference (Figure 3).

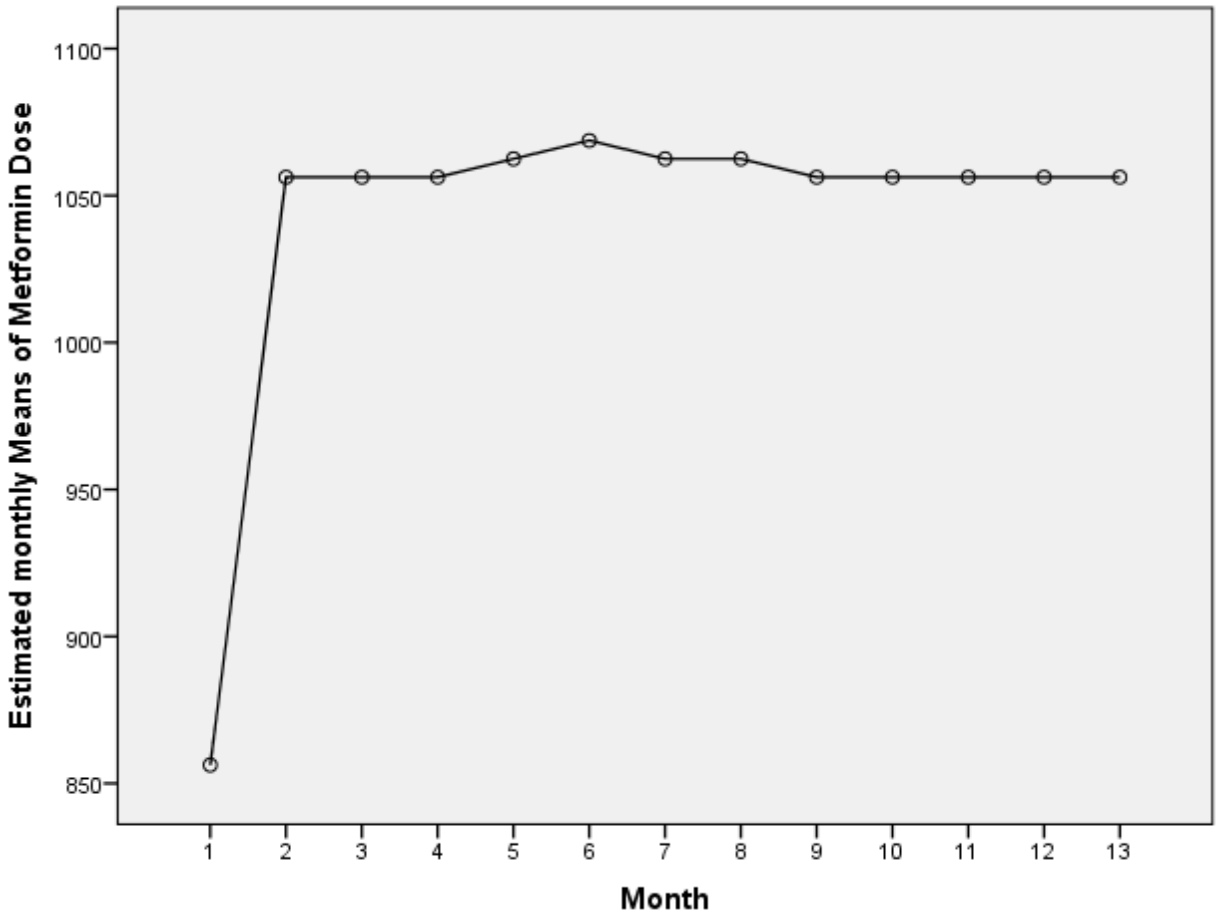

Figure 3: Pattern of metformin dose titration during the twelve month period of metformin therapy among diabetic patients at the outpatient diabetic clinic of FRH, Ethiopia, March 01, 2010 – March 31, 2012

B. Pattern of Glycemic Control by Metformin Use

The mean FPG in the first two, six, and twelve months was 190 mg/dl (SD = 70.9), 179.9 mg/dl (SD = 57.7), and 166.5 mg/dl (SD = 47.8) respectively. The mean fasting plasma glucose level at start of metformin, first, and second visits were 249.8 mg/dl, 195.7 mg/dl, and 183.8 mg/dl respectively (Table 9).

Table 9: Pattern of mean FPG level during the first twelve month period of metformin therapy among diabetic patients at the outpatient diabetic clinic of FRH, Ethiopia, March 01, 2010 – March 31, 2012

Pattern of FPG on metformin use in the first twelve months of therapy	**Month**	**Mean FPG (mg/dl)**	**95% Confidence Interval**	
			Lower Bound	Upper Bound
	starting month	249.8	230.044	269.556
	1st visit	195.7	178.869	212.706
	2nd visit	183.8	167.818	199.857
	3rd visit	190.4	171.548	209.327
	4th visit	181.5	166.402	196.648
	5th visit	169.8	156.247	183.478
	6th visit	165.5	152.818	178.182
	7th visit	163.6	151.538	175.837
	8th visits	159.5	147.298	171.777
	9th visit	160.9	146.186	175.614
	10th visit	147.6	137.884	157.366
	11th visit	144.1	133.686	154.664
	12th visit	145.2	135.348	155.202

The mean metformin dose increased in the first two months of the overall metformin therapy was 200 mg. The mean decrement in FPG level in the first two months (first six months for combination use) of the overall metformin therapy was 66 mg/dl. This titration pattern and the respective decrement in FPG unveils the average titration pattern of metformin was 25 mg/week with the least time to reach the two week and maximum dose of metformin being forty (40) weeks and sixty (60) weeks respectively. Similar to the titration pattern, the glycemic control was shocking by being 8.25 mg/dl/week decrement taking at least thirty one (31) weeks to control the FPG of patients.

Survival Analysis on Glycemic Control

Nineteen (23.7%) and sixty one (76.3%) of patients were using metformin titrated (> 1500 mg) and not titrated (<1500 mg) at the first two month of therapy during their twelve months of therapy respectively. Out of these patients fourteen (73.7%) and eight (13.1%) of patients achieved the desired FPG level during the first two months of therapy (for metformin alone) and six months of therapy (for combination use) in the titrated and non titrated metformin use respectively.

The mean FPG level in patients who were treated with metformin titrated at the first two month of therapy was 144.09 mg/dl (95% CI = 125.35, 162.84), whereas group of patients in whom metformin dose was not titrated during the first two month of therapy was 373.57 mg/dl (95% CI = 348.43, 398.72). The overall comparison of dose titration of metformin during the first two months of therapy showed a statistically significant value in attaining the desired FPG level at the end of the respective treatment periods (two month for metformin alone and six month for metformin combined with glibenclamide) with the log-rank value of $p < 0.001$ (Table 10 and Figure 4).

Table 10: Fasting Plasma Glucose level attainment characteristics of study participants on first two month titrated and non-titrated metformin dose at the outpatient diabetic clinic of FRH, Ethiopia, March 01, 2010 – March 31, 2012

First two month titration pattern of metformin	**Total number of cases/ participants**	**Number of events at two and/ or six month treatment period**	**Number censored**		**Mean FPG (mg/dl) [95% CI]**
			Number	percent	
Titrated at first two month time	19	14	5	26.3	144.1 (125.3, 162.8)
Not titrated at first two month time	61	8	53	86.9	373.5 (348.4, 398.7)

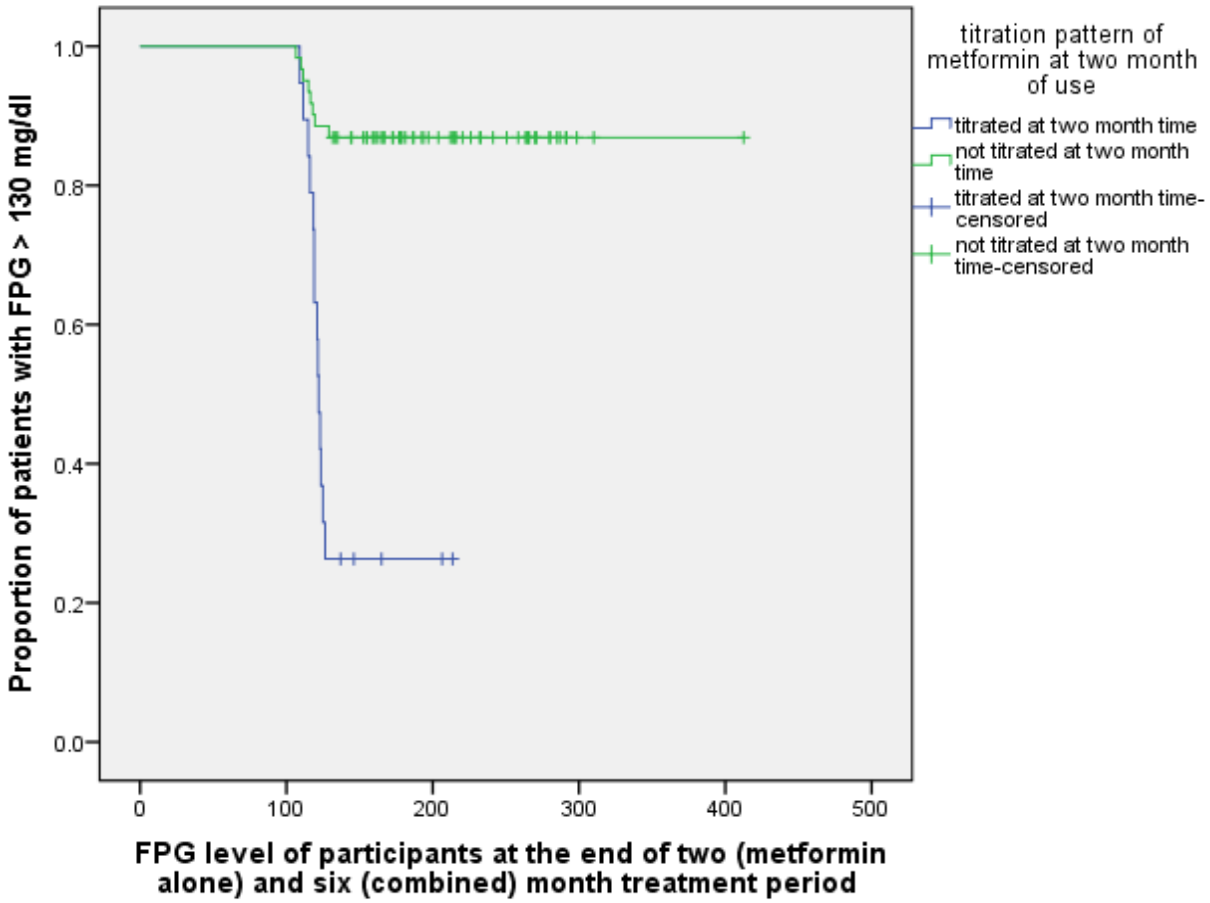

Figure 4: Level of recommended FPG attainment among group of patients where metformin is titrated at two month or not at the outpatient diabetic clinic of FRH, Ethiopia, March 01, 2010 – March 31, 2012

7. Discussion

It was found that metformin dose (either alone or in combination with glibenclamide) was optimally titrated only on less than one-third of the study population and the mean dose of metformin in the first twelve months of therapy was 1056.2 mg. An approximately similar result was obtained from a study in JUSH diabetic clinic where the mean dose of metformin was 882.0 mg (46). However, this finding is far from the recommendation at the consensus statement of the ADA and the EASD on 2009 for metformin alone and from the Global Partnership for Effective Diabetes Management statement on 2005 for combined use of metformin that every patient on metformin should be titrated to the highest 2000 mg level with in the first one or two months unless the glycemic level is controlled or decreased to non-diabetic range (14-15, 49-50). This diversion from the standard practice guidelines could be due to the practice that, only senior physicians could either increase dose or change regimen based on the FPG level of the patient during patient refill where in practice it is the follow up nurses that usually makes the refill whom doesn't have the mandate either to increase dose or change regimen accordingly. On the other hand, the practice that patients are appointed either in a monthly or a two monthly period makes the follow up very difficult to monitor the FPG level closely. In addition to the above reasons, it could be the GI side effects that halt the practice of metformin dose titration.

Patients who were taking metformin alone didn't show any statistically significant difference in controlling their FPG level than those who were using metformin combination. This is not in line with the finding from JUSH outpatient diabetic follow up clinic where patients taking a single oral hypoglycemics alone had a better glucose levels than those taking combination of oral hypoglycemics (46). Studies from abroad like china and USA, reveals that combination tablets had greater reductions in FPG and HbA1c compared with glibenclamide or metformin monotherapy (55-56). The observed gap could be due to differences on titration of doses of metformin to the highest effective dose in comparison to the metformin dose used in china and USA (alone or combination); despite having a FPG level of well above target level in the study hospital. The other possible reason of the two treatment arms not to bring a significant variation in controlling FPG level of the

patients could be the difference in baseline FPG level at the time treatment initition.

The titrated form of metformin (1500 mg and above), which is known to bring the required glycemic control as well as other beneficiary roles of metformin was used in only 19 (23.7%) of patients. Statistically significant reductions in FPG were observed in the titrated dose of metformin as compared to the 500 mg and 1000 mg dose; nevertheless, there was no any statistically significant variation in FPG control between the 2000 mg and 1500 mg dose. Similar finding was reported from dose-response study conducted in Texas, USA, on T2DM patients (18-19, 54, 60). However, a contradicting finding was reported on a study conducted in JUSH diabetic clinic where patients taking lower doses of oral hypoglycemic agents were with better glycemic control than those taking higher doses of oral hypoglycemic agents (46). This variation in glycemic control among the high versus low dose of oral hypoglycemics could be due to the variation in applying the self care practices along with the medications used. Besides the variation in self care practice, the dose that was demarked as a high dose was the 1000 mg low dose that doesn't bring significant change in comparison to the 500 mg metformin dose. In addition to the aforementioned reasons, this variation among high and low doses could be from doses of oral hypoglycemics studied other than metformin like glibenclamide. But, as far as this study is concerned, the correlation of high dose of metformin with better FPG control implies that there is much work to be done in creating awareness about the pattern of metformin dose titration and its importance for prescribers in the study hospital.

A small proportion of patients (30% of patients) on less than 130 mg/dl glycemic control demonstrated in this study might put large proportions of patients at risk of developing serious complications in the future. The benefits of good glycemic control are well documented and glycemic control is important predictor of many of the chronic complications of T2DM (7, 30, 32-33). These studies showed that attaining near normal glycemic level reduces and/or prevents the devastating complications of T2DM and/or early mortality and morbidity on the long run. Despite evidences supporting the importance of tight glycemic control and international guidelines such as ADA and AACE (64-65), several studies have shown that the correct management of glycemia is falling significantly short of

accepted treatment goals in Ethiopia (4, 44, 46-48) as well as in other countries (52, 57, 61-62).

Majority (72.5%) of the patients were in the age group between 35 and 64 years old. This is consistent with the findings of developing countries where most of the diabetic patients are between 40 and 60 years as compared to developed nations where the majority of patients are aged above 60 years (2). This indicates the great negative impact diabetes has on the economy of developing countries by provoking a significant loss of productive capacity.

Level of glycaemic control was not significantly affected by sociodemographic characteristics of the patient, duration of diabetes, number of medications, and health education. This is similar to the finding from JUSH diabetic clinic (46) but was dissimilar with other countries where ethnicity, age, number of medications, and duration of diabetes are significantly associated with level of glycemic control (57, 59); whereas insurance coverage for their medications, sex, and history of coronary artery disease and congestive heart failure are not significantly associated with poor glycemic control (57).

Although the presence of comorbid illnesses among patients with diabetes is a common phenomenon, the finding of this study reveals that comorbidities were present only on 17.5% of the patients. This finding is in opposite to studies of other countries where 88.6% of people with diabetes reported having at least one additional chronic illness, while close to 15% reported having four or more (53) and 80 % of new-onset diabetic patients had comorbidities (41). This exaggerated gap on prevalence of comorbidity could be due to variation in patients included in the study being very small, use of secondary data from patients' card for detecting presence of comorbidities, difference in qualification of expertise during diagnosis, or variation in pattern of diagnostic instruments or facilities like method of measuring adequate blood glucose control using FPG.

One of the self-care practice assessed in this study was diabetic foot care where 57 (71.2 %) patients reported that they regularly inspect their feet, 50 (62.5%) inspect the inside of their footwear and 13 (16.2%) regularly walk barefoot. Patients should be educated about their foot care because according to a previous study done on patients with diabetic foot ulcer at Tikur Anbessa Hospital (44) revealed that the cause of diabetic foot ulcer was ill-fittings or new shoes in 48(24%) of the

cases, which is easily preventable. Glycemic control was poor (mean FBG $\geq$ 140 mg/dl) before admission in 47 (81%) of the patients who developed diabetic foot ulcer indicating patients with poor glycemic control are at high risk for developing diabetic foot ulcer, the most feared and devastating complication of DM. Findings of the current study showed that none of the studied patients developed diabetic foot ulcer. However, the findings of this study is in parallel with a study conducted in Nigeria on diabetic foot care (39) where less than half (40.9% of patients) regularly inspect their feet, 47.7% inspect the inside of their footwear and 38.1% regularly walk barefoot. This could be explained by the short duration since patients developed diabetes, and only out patients were included in this study and poor record keeping. So attention should be given in terms of educating patients as poor glycemic control was common in the study hospital that increases the risk of developing diabetic foot ulcer.

Non-adherence to medications resulted in poor glycemic control and hence increased the risk of diabetic complications. In this study, 36 (45%) patients self reported that they adhered to their medication. This is approximate with the finding obtained from JUSH where 178 (51.3%) of the patients reported that they never missed their drugs (47) and Malaysia where 169 (41.7%) of the patients adhered to their antidiabetic medications (61). Despite studies from Malaysian (58, 61) T2DM patients, had revealed that patients who adhered to their medication had better glycemic control, adherence was not found to be statistically significant predictor of glycemic control ($P > 0.05$) in the current study. This might be due to the small sample size that is used for this study and this data was collected through self reporting method that may raise the possibility of social desirability bias and recall bias to draw a conclusion about the real relationship among the glycemic control and that of patients' medication adherence. The overall medication adherence was very poor and had implication that pharmacists should work in collaboration with other healthcare professionals to counsel patients on the use and importance of their medications and to promote better medication adherence.

8. Conclusion and Recommendations

8.1 Conclusion

It is evident from this study that more than two-third of T2DM patients were not on the sufficiently titrated dose of metformin at the first two months of therapy which had a significant negative impact on fasting glycemic control.

Despite the fact that international guidelines recommend tight glycemic control, poor glycemic control was more common and fasting glycemic control was below the standard at Felege Hiwot Referral Hospital.

Glycemic control was poor among patients who had poor metformin dose titration, did not do regular exercise and were non adherent to their medication.

Metformin dose titration during the first two months of therapy was the only independent predictors of recommended fasting glycemic level attainment at two month and six month time.

8.2 Recommendation

Taking into account the findings of this study the following recommendations are forwarded:

- Health care providers should practice the titration of metformin specifically during the first two months of therapy depending on the glycemic level of the patients
- Further studies should be carried out on glycemic control using A1C determination, lipid profile, urine albumin and patterns of diabetic complication in the study hospital as well as at the National level.

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Annex II. Data collection Instrument

I. Patient Information Sheet

Name of the principal investigator: Misgan Ararsie Kewoye

Name of study area: Felege Hiwot Referral Hospital, diabetic follow up clinic

Research budget covered by: Jimma University

Research objective: To assess the impact of metformin dose titration and self care practices on glycemic control at Felege Hiwot Referral Hospital

Significance of the study: The study will be used to inform the level of care and help practice metformin dose titration to the most effective dose at the diabetic follow up clinic basis. It will also have great relevance as a base line for interventions of healthcare programs targeting improved diabetes control at large.

Study procedure: The data collectors will interview patients using questions after obtaining consent from the patient. Then data will be extracted from medical records.

Risks: No risks except the time that patient spend during the interview.

Participant right: The patient has a right to stop the interview at any time, or to skip any question that he/she does not want to answer.

Beneficial: The study is beneficial for patient's quality service delivery for future encounters.

Incentives: You will not be provided any specific incentive for taking part in the research other than acknowledgment.

Confidentialities: The study result will not include patient's name and address.

Agreement: Patients are expected to be fully voluntary to participate in the study.

Whom to contact: If you have any kind of inconveniencies about the study, you can contact the following individuals:

1. Mr.Tewodros Eyob, Clinical Pharmacist, Jimma University (advisor of the study)
   - Tel: 0913243061 or +251471111256
   - email: teglight@gmail.com

2. Mr. Misgan Ararsie (principal investigator)
   - Tel: 0921283932
   - Email: mi.ar33@yahoo.com

II. Informed Consent

Name of principal investigator: Misgan Ararsie Kewoye **(Jimma University)**

Research title: To assess the impact of metformin dose titration and self care practices on glycemic control at Felege Hiwot Referral Hospital, Northwest Ethiopia

Card number_____

Code number_____

1. I confirm that I understand the information sheet for the above study and have had the opportunity to ask questions.
2. I understand that my participation is completely voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I understand that my medical notes will be looked at by data collectors of this study and necessary information will be extracted. I give permission for these individuals to have access to my records.
4. I agree to take part in the above study. I would like to confirm my agreement by signing.

Participant's name _____ Signature_____ date_____

Name of the data collector: _____ Signature: _____ date_____

Name of the principal investigator: _____ Signature: _____ date_____

Thank you for your participation and cooperation!

III. Questionnaire English Version

Jimma University

College of Public Health and Medical Sciences

Department of Pharmacy

Clinical Pharmacy Postgraduate Program

Hello! Good morning?

My name is Sr. / Ato ----------

I am data collector for master student Misgan Ararsie currently working his research work for graduation in Clinical Pharmacy in Jimma University, College of Public Health and Medical Sciences, Department of Pharmacy.

The objective of the research is to assess the impact of metformin dose titration and self care practices on glycemic control at Felege Hiwot Referral Hospital.

I would like to assure you that the study is confidential. I will not keep a record of your name and address. You have a right to stop the interview at any time, or to skip any question that you do not want to answer. Your correct answer to the questions can make the study achieve its goals. Therefore, you are kindly requested to respond genuinely and voluntary with patience. The interview may take few minutes. I would greatly appreciate your help in responding to this study.

Would you be willing to participate?

Yes_____go to the next page No_____ thank you and stop the interview

Result of the interview: 1. Completed 2. Partially completed

3. The interviewee refused 4. Others_____

Data collector's Name: _____ Signature _____

Supervisor's name: _____ Signature _____

A. Participants' Sociodemographic Characteristics and Diabetes Related Variables

No	Questions	Answer
101	Patient's sex	1.Male 2. Female
102	How old are you?	_____years
103	What is the highest education level you completed?	1. No formal education 2. Primary education (1-8 grade) 3. Secondary education (9-12 grade) 4. Tertiary education (diploma and above)
104	What is your current occupation?	1.Civil servant 2. Merchant 3. Farmer 4. House wife 5.Others (specify)_____
105	How much is your monthly income in Ethiopian Birr?	_____ Birr
106	How long it had been since you were diagnosed with diabetes mellitus?	1. _____weeks 2. _____ months 3. _____ years
107	How did you get your medicines?	1. Free 2. Paid

B. Participants' Self Care Practices

201	Do you follow a dietary modification to control your diabetes mellitus?	1.Yes 2. No
202	Do you perform regular exercises?	1. Yes 2. No
203	Do you inspect your feet regularly?	1. Yes 2. No
204	Do you inspect the inside of your footwear?	1. Yes 2. No
205	Do you regularly walk bare-foot?	1. Yes 2. No
206	Are you the member of Ethiopian Diabetic Association?	1. Yes 2. No
207	Do you usually attend a diabetic education?	1. Yes 2. No
208	Do you use Traditional Medicines for the management of your diabetes mellitus?	1. Yes 2. No
209	Do you have a habit of using social drugs?	1. Yes 2. No
210	Do you ever forget to take your medicine(s)?	1. Yes 2. No
211	Do you sometimes not being careful in taking your medicine(s)?	1. Yes 2. No
212	When you feel better, do you sometimes stop taking your medicine(s)?	1. Yes 2. No
213	Sometimes if you feel worse when you take your medicine(s), do you stop taking them?	1. Yes 2. No

IV. Patient Information Sheet Amharic Version

የህሙማን መረጃ ቅጽ

ዋና ተመራማሪ፡- ምሥጋን አራርሴ ከወየ (ጅማ ዩኒቨርሲቲ)

የጥናቱ ቦታ፡- ባህር ዳር ፈለገ ህይወትሪፈራል ሆስፒታል የስኳር በሽታ ክሊኒክ

የጥናቱን ወጭ የሚሸፍነዉ ድርጅት፡- ጅማ ዩኒቨርሲቲ

የጥናቱን አላማ፡- የዚህ ጥናት አላማ በባህር ዳር ፈለገ ህይወት ሆስፒታል የሁለተኛዉን አይነት የስኳር በሽታ ለማከም የሚያገለግለው የሜትፎርሚን መድኃኒት መጠን በትክክለኛው መንገድ ፣የሚፈለገውን ያህል ፣ እንዲሁም በተፈለገው ሰአት ለታካሚዎች መጠኑ እየተጨመረ መሆኑን እና የስኳር በሽታን በግል ለመቆጣጠር የሚያደርጉት ጥረት ምን ያህል ውጤታማ እንዳደረጋቸው ማወቅ፡፡

የጥናቱን ጥቅም፡- ይህ ጥናት ለስኳር በሽታ ህሙማን እንደ አካባቢዉ ተጨባጭ ሁኔታ ተገቢ የሆነ የማስተማርያ ፕሮግራም ለመቅረጽ እንዲሁም ለሃኪሞች ስለሚሰጠው አገልግሎት ተጨባጭ ሁኔታ ማሳወቅ እና ወደፊትም እየተሰጠ ያለው አገልግሎት በምን ያህል ደረጃ እንደተሻሻለ መነሻ በመሆን ለመገምገም ያገለግላል፡፡

የጥናቱ አካሄድ ዝርዝር፡- መረጃ ሰብሳቢዉ/ዋ የተሳታፊዉን/ዋን ፈቃደኛነት በመጠየቅ የስኳር በሽታን በግል ስለመቆጣጠር ቃለመጠይቅ ያደርጋል/ታደርጋለች፡፡ከዚህ በመቀጠለልም ስለ ሜትፎርሚን አጠቀቃም ሁኔታ ከታካሚው ካርድ ይወሰዳል፡፡

ጥናቱ ሊያስከትለዉ የሚችለዉ ጉዳት፡- ለቃለመጠይቁ ከሚባክነዉ ስአት ሌላ ይህ ጥናት የሚያስከትለዉ ጉዳት የለም፡፡

የተሳታፊ መብት፡- ተሳታፊዉ ቃለመጠይቁን የማቋረጥ ወይም መመለስ ያልፈለገዉን ጥያቄ የማለፍ መብቱ የተጠበቀ ነዉ፡፡

ማትጊያ፡- በዚህ ጥናት ላይ በመሳተፍዎ ከምስጋና ዉጭ የሚሰጥዎት የገንዘብ ክፍያ የለም፡፡

ምስጢራዊነት፡- የጥናቱ ዉጤት የጥናቱን ሳተፉዎች ስምና አድራሻ አያካትትም ፡፡

ስምምነት፡- ተሳታፊዎች በጥናቱ ለመሳተፍ ሙሉበሙሉ ፈቃደኛ መሆን ይጠበቅባቸዋል፡፡

ማንን ማነጋገር እነደሚገባዎ፡- ስለጥናቱ ለሚኖረዎት ማንኛዉም ቅሬታ የሚከተሉትን ግለሰቦች ማነጋገር ይችላሉ፡፡

- አቶ ቴዎድሮስ ኢዮብ፡- ክሊኒካል ፋርማሲስት፣ (የጥናቱ አማካሪ)
- ስልክ 0913243061 ወይም +251471111256
- ኢሜል teglight@gmail.com
- አቶ ምሥጋን አራርሴ ፡- በጅማ ዩኒቨርሲቲ የፋርማሲ ትምህርት ክፍል የክሊኒካል ፋርማሲ የድህረ ምረቃ ተማሪ (የጥናቱ ዋና ተመራማሪ)
- ስልክ 0921283932
- ኢሜል mi.ar33@yahoo.com

V. Informed Consent Amharic Version

የስምምነት ሰነድ

ዋና ተመራማሪ፡ ምሥጋን አራርሴ ከወየ (ጅማ ዩኒቨርሲቲ)

የጥናቱ ርዕስ፡- የሜትፎርሚን መድኃኒት መጠን በትክክለኛው መንገድ ፣የሚፈለገውን ያህል ፣ እንዲሁም በተፈለገው ሰአት ለታካሚዎች መጠኑ መጨመሩ እና የስኳር በሽታ በሽተኞች በሽታቸውን በግል ለመቆጣጠር የሚያደርጉት ጥረት በበሽታው ላይ የሚያሳድረው ተጽእኖ በባህር ዳር ፈለገ ህይወትሪፈራል ሆስፒታል

ካርድ ቁጥር _____

የምስጥር መለያ ቁጥር_____

1. ከዚህ በላይ ስለተጠቀሰዉ ጥናት በቂ መረጃ ተሰጥቶኛል፤ መረጃዉንም ተረድቻለሁ። እንሁም ግልጽ ያልሆነልኝን የመጠየቅ እድል ተስጥቶኛል::
2. በዚህ ጥናት ላይ ስሳተፍ ሙሉበሙሉ በራሴ ፍቃደኝነት መሆኑንና በማንኛዉም ጊዜ ማቆም እንደምችል፤ ይህም በማገኘዉ የህክምና አገልግሎት ወይም በህጋዊ መብቴ ላይ ምንም አይነት ተጽዕኖ እንደማኖረዉ ተገንዝቢያለሁ።
3. የህክምና መረጃዬ በጥናቱ መረጃ ስብሳቢዎች ለጥናቱ ሲባል እንደሚታይና አስፈላጊ መረጃ እንደሚወሰድ ተነግሮኝ ፈቅጃለሁ::
4. በዚህ መርምር ለመሳተፍ ፍቃደኛ ነኝ፤ ፈቃደኛነቴንም በፊርማዬ አረጋግጣለሁ።

የተሳታፊዉ ስም _____ፊርማ_____ ቀን_____

የመረጃ ሰብሳቢዉ _____ ፊርማ _____ ቀን_____

የዋናዉ ተመራማሪ_____ ፊርማ _____ቀን_____

ስለተሳትፎዎትና ትብብርዎት አመሰግናለሁ!

VI. Questionnaire Amharic Version

ጅማ ዩኒቨርሲቲ

የህብረተሰብ ጤናና የህክምና ሳይንሶች ኮልጅ

የፋርማሲ ትምህርት ክፍል

የክሊኒካል ፋርማሲ ድህረ ምረቃ ፕሮግራም

ቀን _____ የመጠይቅ መለያ ቁጥር_____

እንደምን አደሩ /ዋሉ?

ስሜ አቶ/ሲ/ር_____ይባላል፡፡

ምሥጋን አራርሴ በጅማ ዩኒቨርሲቲ የህብረተሰብ ጤናና የህክምና ሳይንሶች ኮሌጅ በፋርማሲ ትምህርት ክፍል የክሊኒካል ፋርማሲ የሁለተኛ ድግሪ ተማሪ ሲሆን በባህር ዳር ፈለገ ህይወትሪፈራል ሆስፒታል የሜትፎርሚን መድኃኒት መጠን በትክክለኛው መንገድ መጨመሩን እና የስኳር በሽታ ህሙማን በሽታቸውን በግል ለመቆጣጠር የሚያደርጉትን ጥረት በተመለከተ ለሚያካሂደዉ የመመረቂያ የምርምር ስራ መረጃ ሰብሳቢ ነኝ፡፡

የዚህ ጥናት አላማም በባህር ዳር ፈለገ ህይወትሪፈራል ሆስፒታል የሜትፎርሚን መድኃኒት መጠን በትክክለኛው መንገድ ፣የሚፈለገውን ያህል ፣ እንዲሁም በተፈለገው ሰአት ለታካሚዎች መጠኑ መጨመሩ እና የስኳር በሽታ በሽተኞች በሽታቸውን በግል ለመቆጣጠር የሚያደርጉት ጥረት በበሽታው ላይ የሚያሳድረው ተጽእኖ ምን እንደሚመስል መረጃ ለመሰብሰብ ነው፡፡

የሚሰበሰበው መረጃ ሙሉ በሙሉ በምስጢር የሚያዝ መሆኑን አረጋግጥለዎለታለሁ፡፡ የእርስዎም ስምና መለያ አድራሻ አይመዘገቡም፡፡

መረጃ መስጠት ካልፈለጉ መብትዎ ነው፡፡ መመለስ ያልፈለጉትንም ጥያቄ መዝለል/ ማለፍ ይችላሉ፡፡

ይሁን እንጂ የእርስዎ ትብብር ትክክለኛ ምላሽ ምርምሩ እንዲሳካ ያደርገዋል፡፡ ስለዚህ ለሚቀርብልዎት ጥያቄ ትክክለኛና ፍቃደኛ ሆነው፣ በትዕግስት እንዲመልሱልን እጠይቀዎታለሁ፡፡ መጠይቁ ከ 10- 15 ደቂቃ ሊወስድ ይችላል፡፡

በዚህ ጥናት ላይ በመሳተፍ ላደረጉልን አስተዋፅዖ በቅድሚያ ታላቅ ምስጋና እናቀርባለን፡፡

በጥናቱ ውስጥ ለመሳተፍ ፍቃደኛ ነዎት? አዎ_____ወደሚቀጥለው ገፅ ይለፉ

አይደለሁም_____አመስግነው መጠይቁን ያቋርጡ፡፡

የመጠይቁ ዉጤት፡- 1. የተሟላ_____ 2. በከፊል የተሟላ _____

3. ፍቃደኛ ያልሆኑ _____ 4. ሌላ_____

የመረጃ ሰብሳቢ ስም_____ ፊርማ_____

የቆጣጣሪ ስም_____ ፊርማ_____

ነ.የተሳታፊው/ዋ ማህበራዊና ኢኮኖሚያዊ ሁኔታ

ተ.ቁ	ጥያቄዎች	መልስ
101	የተሳታፊዉ /ዋ ፆታ	ነ. ወንድ 2. ሴት
102	እድሜዎ/ህ/ሽ ስንት ነው?	_____ አመት
103	ያጠናቀቁት ከፍተኛ የትምርት ደረጃ ስንት ነዉ?	ነ. መደበኛ ትምህርት ያልተማሩ 2. የመጀመሪ ደረጃ (ነ-8ኛ ክፍል) 3. ሁለተኛ ደረጃ (9-12ኛ ክፍል) 4. ከፍተኛ ደረጃ (ዲፕሎማና ከዚያ በላይ)
104	በአሁኑ ሰዓት ሥራዎት/ህ/ሽ ምንድነው?	ነ. የመንግስት ሠራተኛ 2. ነጋዴ 3. ገበሬ 4. ጡረተኛ 5. የቤት እመቤት 6. ሌላ (ይገለፅ)_____
105	ወርሀዊ ገቢዎት/ህ/ሽ በብር ምንያህል ይሆናል?	_____ ብር
106	የስኳር በሽታ ህመምተኛ እንደሆኑ/ህ/ሽ በምርመራ ካወቁ/ህ/ሽ ስንትጊዜ ሆነዎት/ህ/ሽ?	_____አመት
107	መድኃኒቶችህን/ሽን እንዴት ታኛለሽ?	ነ.በነጻ 2.በክፍያ

፲፲. የስኳር በሽታን በራስ ስለመቆጣጠር ክህሎት

ተ.ቁ	ጥያቄዎች	መልስ
201	የስኳር በሽታዎን/ህ/ሽ ለመቆጣጠር የአመገጋገብ ለውጥ ያደርጋሉ/ህ/ሽ ?	፩. አዎ 2. አላደርግም
202	ዘውትር የአካል ብቃት እንቅስቃሴ ያደርጋሉ/ህ/ሽ?	፩. አዎ 2. አላደርግም
203	በየጊዜው የእግርዎትን/ህ/ሽ ጤንነት ያረጋጣሉ?	፩. አዎ 2. አላረጋግጥም
204	ጫማዎትን/ህ/ሽ ከመጫማትዎ/ህ/ሽ በፊት ከስሩ እግርዎትን ሊጎዳ የሚችል ባዕድ ነገር አለመኖሩን ያረጋግጣሉ?	፩. አዎ 2. አላረጋግጥም
205	በአብዛኛው ጊዜ በባዶ እግርዎት/ህ/ሽ ይሄዳሉ?	፩. አዎ 2. አልሄድም
206	የኢትዮጵያ የስኳር በሽተኞች አባል ነዎትን/ ነህን/ሽን?	፩. አዎ 2. አይደለሁም
207	ስለ ስኳር በሽታ የሚሰጠውን ትምህርት ብዙ ጊዜ ይከታተላሉን/ ትከታተላለህ/ትከታተያለሽ?	፩. አዎ 2. አልከታተልም
208	የባህል መድኃኒቶችን ይጠቀማሉን /ትጠቀማለህን/ትጠቀሚያለሽን?	፩. አዎ 2. አልጠቀምም
209	ሱስ አምጭ መደኃኒቶችን የመጠቀም ልማድ አለዎትን/ አለህ/ አለሽ?	፩. አዎ 2. የለኝም
210	መድሃኒትዎን/ህን/ሽን መዉሰድ እረስተዉ/ህ/ሽ ያዉቃሉ/ታዉቃለህ/ታዉቂለሽ?	፩. አዎ 2. አላውቅም
211	አንዳንድ ጊዜ መድሃኒትዎን/ህን/ሽን ሲወስዱ/ስትወስድ/ስትወስጅ ጥንቃቄ የማያደርጉበት/የማታደርግበት/የማታደርጊበት ጊዜ አለ?	፩. አዎ 2. የለም
212	ህመምዎ/ህ/ሽ ሲሻለዎት/ሲሻልህ/ሽ አንዳንድ ጊዜ መድሃኒትዎን/ህን/ሽን መዉሰድ ያቆማሉ/ታቆማለህ/ታቆሚያልሽ?	፩. አዎ 2. አላቆምም
213	አንዳንድ ጊዜ ህመምዎ/ህ/ሽ ሲብስብዎ/ህ/ሽ መድሃኒትዎን/ህን/ሽን መዉሰድ ያቆማሉ/ታቆማለህ/ታቆሚያልሽ?	፩. አዎ 2. አላቆምም

A. **Pattern of Dose Titration and Glycemic Control in the First Twelve Months of Metformin Use**

Date of Visit	Glycemic Level (FPG) (mg/dl)	Dose of Metformin (mg)	Antidiabetic Drugs	Comorbid Conditions	Medications for Comorbid Conditions