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ORIGINAL RESEARCH

Determinants of Statin Initiation Among Adult Diabetic Patients in Bonga, Ethiopia

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Background: Diabetes mellitus (DM) is a chronic degenerative disease associated with a high risk of chronic complications and comorbidities. According t the World Health Organization, 16.7 million people worldwide die of cardiovascular diseases each year.

Aim of the Study: The aim of this study is to evaluate determinants of statin initiation among diabetic patients.

Methods: A hospital-based cross-sectional study was conducted to evaluate statin initiation and determinants in Gebre Tsadik Shewa General Hospital, Bonga, Ethiopia. This hospital covers a catchment population of about 1.4 million and offers diagnosis and treatment in outpatient and inpatient settings in different departments. Epi data 4.0.2.49 and STATA 14.2 were used for data entry and analysis. Before analysis, presence of co-linearity and model fitness were checked. Chi-square statistics were used to check adequacy of cells for binary logistic regression. Bivariate analysis was done and p <0.25 was included in a multivariate model. Finally p-value less than 0.05 was considered a significant predictor.

Results: A total of 120 patients were included in this study, of which 77 (64.17%) were males. The mean age and standard deviation was 47.04 ± 12.13 years with 75% of patients ≥40 years. The mean duration of illness was 10.26 ± 0.6 years. Ninety-eight (81.67%) patients had varying comorbidities. Sixty-four (53.33%) patients developed complications. The majority of patients were evaluated by a general practitioner (GP). Fifty-one (42.5%) patients started statins. Of them, 31 (60.78%) started for secondary prevention. The majority of patients had atorvastatin with moderate dosage. Government insurance (p=0.029), polypharmacy (0.008), physician level of training (0.023) and previous counseling of patients about the importance of statins (p<001) were significantly associated with initiation of statins.

Conclusion: Only near to 40% of patients started statins. Physician reluctance and unavailability of drugs were the most common reasons not to initiate statins. The hospital tries to provide medication. Physicians should evaluate patients in need of cardio-protective drugs.

Keywords: diabetes, statin initiation, determinants, primary prevention, secondary prevention, general hospital

Plain Language Summary

What is Known: The importance of statins as primary and secondary prevention of CVDs patients with DM.

What is Added: What the statin utilization pattern looks like and what factors negatively affect statin initiation.

Introduction

Diabetes mellitus (DM) is a chronic degenerative disease associated with a high risk of chronic complications (especially cardiac complications like atherosclerosis) and

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comorbidities.[1] According to World Health Organization estimates, 16.7 million people worldwide die of cardiovascular diseases each year.[2] Guideline recommended preventive measures can reduce cardiovascular disease (CVD) risk in adults with diabetes and CVD, yet the degree to which these high-risk adults are achieving guideline indicated secondary prevention interventions has been under-studied globally.[3] The prevalence of cardiovascular (CV) risk factors continues to rise and globalization seems to have contributed to a higher prevalence in developing countries.[4]

The economic burden with hospitalizations and consultations were 22%, and costs related to the loss of productivity related to the disease were 15%. Health expenditures in Brazil are estimated at 9.5% of gross domestic product and the average cost of CVD was estimated at 0.7% of gross domestic product.[5]

CV risk reduction is critically important for the care of patients with diabetes, with or without known CVD and CV risk factors. Use of statins, aspirin, glucose-lowering therapies, and intensive lifestyle management are important to prevent CVD.[6] Statins reduce the risk of CVD-associated morbidity and mortality through their lipid lowering, anti-inflammatory, plaque-stabilization and anti-thrombosis effects. Although statin therapy for patients with prior CV events is widely supported, use in patients without prior CV events is controversial.[7] A case control study showed that statins use is also associated with reduced risk of hepatocellular carcinoma development compared with non-users. The reduction in risk was significant in the presence and absence of DM.[8]

Although there are no nationwide data on CV burden in Ethiopia, DM and associated CV burden is high as evidenced by clinical practice. Studies show that statins prevent the occurrence and complications of CVD.[9] However, in Ethiopia, statins use in diabetes patients is suboptimal.[10] Therefore, there is an urgent need for evaluation of statin initiation and its determinants to prevent CVD. The aim of this study is to evaluate statin utilization patterns and determinant factors.

Method

Study Setting and Period

This study was done at Gebre Tsadik Shewa General Hospital, Bonga, Ethiopia. It is one of the governmentally established hospitals in Ethiopia. It covers a catchment population of about 1.4 million and offers diagnosis and treatment for nearby populations. In this hospital a total of 145 DM patients were on follow up. The hospital serves outpatient and inpatient settings in different departments. The study was conducted specifically at an outpatient department service which is a DM clinic, from November 1, 2019–December 22, 2019.

Study Design

Hospital-based cross-sectional study was used to evaluate statin initiation and contributing factors for statin initiation in general hospital of diabetic clinic.

Population and Sample Size Determination

All diabetes patients who have follow-up at this hospital were taken as the source population. Patients who had follow-up during the data collection period were treated as the sample population. Since the numbers of DM patients on follow-up were small (145), all subjects who fulfilled inclusion criteria were the subject of this study.

Inclusion and Exclusion Criteria

Inclusion criteria were confirmed cases of DM aged between 18 and 75 years, patients aged less than 40 years with suboptimal lipid profile (including TG>150 mg/dl, TC>200 mg/dl, and LDL >100 mg/dl) and patients with age greater than 40 years irrespective of lipid profile and who attended a follow-up DM clinic. Patients who had known heart failure class II–IV, patients unwilling to participate or on dialysis were excluded.

Study Variables

Statin initiation is the dependent variable, and sociodemographic, comorbidity, complication, duration of illness, number of comorbidities, number of complications, laboratory indices (lipid profile), type of statin, physician level of training and experience are independent variables.

Data Collection Tool and Procedures

Relevant patient data were collected via face to face interview and medical cards using a data abstracting form. The questionnaire included socio-demographic data, responsible physician for statin initiation (obtained from patient medical records) and clinical details (diabetes complications, comorbidities, duration of diabetes, laboratory values and statin medication profiles). The questionnaire was translated to the local language and retranslated to English for consistency. Data were collected by two

pharmacists (B. Pharm) after one day of training. Supplementary information and clarifications on some patients' medical information was obtained through discussion with respective nurses, physicians and care-givers. Statin initiation was dichotomized; patients who had statins and those who are not initiated based on the current guideline recommendations.[11]

Analysis

Data were entered using Epi data 4.0.2.49 and analyzed using STATA 14.2. Before data analysis, presence of colinearity between independent factors (having less than 2.5 variance inflation factor or all variables have tolerance greater than 0.77) and model fitness (with Hosmer–Lemeshow test p-value greater than 0.54 for binary logistic models) were checked.

Continuous variables/data were checked for the presence of deviation from normal distribution. All the data were normally distributed as evidenced with Shapiro–Wilk test, p >0.07. In all of the analyses, significance testing was conducted using two-sided p-values and 95% confidence intervals. Chi-square statistics were used to check adequacy of cells for binary logistic regression.

The association of independent predictors and statin initiation was evaluated using a multivariate binary logistic regression model. Finally, categorical variables are presented as percentages and continuous variables as means (standard deviations) or their 95% confidence intervals as appropriate. A p value < 0.05 was considered significant.

Results

Background Characteristics of Participants

One hundred and twenty patients fulfilled inclusion criteria and were included in this study, of which 77 (64.17%) were males. The mean age was 47.04 ± 12.13 years with 75% of patients ≥40 years. Eighty-six (71.67%) patients had type 2 DM and slightly more than half of the patients lived in an urban area. The mean duration of physician experience was 8.78 ± 2.67 years. Regarding educational status, 40 (33.33%) patients had attained secondary school and 37 patients were illiterate (30.83%). The majority of patients attended their appointment every two months and only 7 (5.83%) were currently smokers. Fifty-three (44.17%) patients consumed alcohol sometimes, especially during holidays. The majority of patients had no insurance coverage (Table 1). The mean total cholesterol and low density lipoprotein levels were 198 and 173.35 respectively (Table 2).

Disease and Medication Related Characteristics

Patient mean duration of illness was 10.26 ± 0.6 years. Ninety-eight (81.67%) patients had comorbidities. Sixty-four (53.33%) patients developed complications and the majority of patients were evaluated by a general practitioner (GP). Fifty-one (42.5%) patients started on statins and 31 (60.78%) started for secondary prevention (treatment for complications). The majority of patients were put on atorvastatin with moderate dosage. Sixty-five patients developed medication side effects (obtained from patient medical record) in their life time (Table 3).

As shown in Figure 1, 21 (30.43%) patients had not started statins because their physicians had not prescribed them, despite the patients being candidates for primary or secondary prevention, followed by 20 (28.99%) patients who had stopped taking statins due to unavailability of the drugs in the hospital.

From the total of patients who were exposed to statins in previous or current therapy regimes, 13 (41.94%) reported right upper quadrant pain followed by muscular pains (12; 38.71%). The proportions of patients reporting nausea and vomiting (NV) and fatigue were similar and 55.0% patients were taking simvastatin (Figure 2). Ninety-eight patients had comorbidity in addition to DM, 40 (40.82%) had hypertension and 24 (24.49%) had congestive heart failure (Figure 3).

Statin Initiation

Only 51 (42.5%, 95% CI: 28.35–45.8) of the patients had started statins for primary or secondary prevention. Thirty-one (60.78%) patients had initiated statins for secondary prevention (treatment of CV complications) whereas 20 (39.22%) patients were treated for primary prevention of CV complication. Among patients who were on statins, 31 (60.78%) were evaluated by a medical internist. Thirty-two (62.74%) patients on statins had government insurance for their health service. Patient frequency of follow-up varied from every month to every three months. From the total of patients who were on statins, more than half (54.9%) patients visited their physician every two months. However, only 5.88% of participants followed their appointment every three months. Of the patients who were on statins, 34 (62.74%) and 39 (76.47%) had

Table 1 Socio-Demographic Characteristics of Patients, in General Hospital, Ethiopia, 2020

Socio-Demographic Characteristics of Patients	Category	Number	Percent	Mean + SD	Range
Sex	Male Female	77 43	64.17 35.83		
Age group	Mean (±SD)			47.04±12.12	22–75
Educational status	Illiterate Primary school Secondary school Tertiary school	37 21 40 22	30.83 17.5 33.33 18.33		
Type of DM	I II	34 86	28.33 71.67		
Residence	Urban Rural	64 56	53.33 46.67		
Frequency of follow up	Every one month Every two month Every three month	27 66 27	22.5 55.0 22.5		
Smoking	Yes No	7 113	5.83 94.17		
Government insurance	Yes No	43 77	35.83 64.17		
Marital status	Married Single Divorced Widow	103 14 2 1	85.83 11.67 1.67 0.83		
Khat chewing	Yes No	26 94	21.67 78.33		
Alcohol	Yes No	53 67	44.17 55.83		

a family history of CVD and DM respectively and only 15 (29.41%) live in a rural area.

Bivariate analysis showed that statins were prescribed significantly more in patients who have a family history of DM compared with those who do not (COR=1.36, 95% CI: 1.14–1.61, p=0.001). Patients evaluated by a GP were less likely to be initiated with statins as compared with those evaluated by medical internists (COR=0.739, 95% CI: 0.61–0.89, p=0.002). Patients who had received counseling previously about the importance of statins were more likely to initiate statins as compared with those who had no previous counseling (COR=1.95, 95% CI: 1.71–2.23, p<0.001). In addition, government insurance was correlated with initiation of statins; patients under government insurance were more likely to be started on statins compared with those who had no government insurance (COR=1.28, 95CI: 1.06–1.53, p=0.009). Moreover, polypharmacy (COR=1.25, 95% CI: 1.04–1.51, p=0.019), presence of complications (COR=1.25, 95% CI: 1.05–-1.49, p=0.012) and type of residence of the patient (COR=1.34, 95% CI: 1.13–1.59, p=0.001) were highly correlated with statin initiation (Table 2).

After adjusting confounding factors using multivariate binary logistic regression analysis, only four variables were significantly associated with statin initiation. Patients with government insurance were significantly associated with statin initiation as compared with those who had no insurance (AOR=1.11, 95% CI: 1.33–1.87, p=0.029). Statin initiation was significantly associated with patients having polypharmacy compared with those

Table 2 Bivariate and Multivariate Binary Logistic Regression Analysis for Predictors of Statin Initiation, General Hospital, Ethiopia, 2020

Variables		Current Statin		Bivariate Analysis		Multivariate Analysis	
		Yes	No	COR (CI)	P-value	AOR (CI)	P-value
Sex	Male Female	34(66.67) 17(33.33)	43(62.31) 26(37.69)	1.04(0.868–1.26)	0.627		
Age Duration of illness TC LDL HDL	Mean (±SD) Mean (±SD) Mean (±SD) Mean (±SD) Mean (±SD)	47.04±12.12 10.26±2.62 198±16.62 173.37±14.88 43.49±8.58		0.993(0.991–1.00) 1.01(0.998–1.025) 0.99(0.97–1.24) 0.998(0.998–1.00) 1.00(0.997–1.01)	0.869 0.086 0.472 0.174 0.189	 1.00(0.998–1.01) 1.00(0.99–1.6)	 0.933 0.342
Comorbidity	Yes No	44(86.27) 7(13.73)	54(78.26) 15(21.74)	1.14(0.9–1.43)	0.266		
DM type	I II	14(27.45) 37(72.55)	20(28.98) 49(71.02)	 0.98(0.80–1.19)	 0.855		
Types of comorbidity	HTN CHF CKD Ischemia	10(22.72) 12(27.27) 10(22.72) 12(27.27)	30(55.55) 12(22.22) 5(9.25) 9(12.96)	0.5(0.43–1.58) 1.54(1.24–1.94) 2.18(0.56–4.38)	0.241 0.054 0.19	0.67(0.54–2.66) 2.96(1.67–3.43) 1.67(1.05–3.17)	0.31 0.085 0.094
Complication	Yes No	34(66.67) 17(33.33)	30(43.47) 39(56.53)	1.25(1.05–1.49)	0.012	0.94(0.79–1.12)	0.476
Residence	Urban Rural	36(70.58) 15(29.42)	28(40.57) 41(59.43)	1.34(1.13–1.595)	0.001	0.88(0.73–1.06)	0.184
Insurance	Yes No	32(62.74) 19(37.26)	18(20.1) 51(79.9)	1.28(1,06–1.53)	0.009	1.11(1.33–1.87)	0.029
Educational status	Illiterate Primary Secondary Tertiary	6(11.76) 8(15.68) 13(25.49) 24(47.07)	31(44.92) 17(24.63) 16(23.18) 5(7.27)	0.31(0.16–0.95) 1.89(0.43–2.18) 0.92(0.57–1.23)	0.043 0.06 0.34	2.15(2.05–2.97) 2.10(1.82–2.186)	0.091 0.07
Polypharmacy	Yes No	40(78.43) 11(21.57)	40(59.97) 29(40.03)	1.25(1.04–1.51)	0.019	1.28(1.07–1.53)	0.008
Counseling about statin	Yes No	46(90.19) 5(9.81)	15(21.74) 54(78.26)	1.95(1.71–2.23)	<0.001	1.61(1.34–1.94)	<0.001
Frequency of follow-up	Every 1 month Every 2 month Every 3 month	20(39.21) 28(54.9) 4(5.88)	7(10.14) 38(55.1) 27(34.76)	2.16(1.74–2.94) 1.87(1.23–2.17)	0.235 0.95	1.32(0.49–1.82)	0.06
Who Evaluated you?	GP Internist	20(39.22) 31(60.78)	39(56.53) 30(43.47)	0.739(0.61–0.89)	0.002	0.9(0.77–0.997)	0.023
Family hx of CVD	Yes No	32(62.74) 19(37.26)	31(44.92) 38(55.08)	0.9(0.75–1.08)	0.269		
Family hx of DM	Yes No	39(76.47) 12(23.53)	32(46.37) 37(53.63)	1.36(1.14–1.61)	0.001	1.14(0.994–1.31)	0.059
Physician experience	Mean (±SD)	8.78±2.32		1.97(1.026–2.981)	0.007	0.99(0.98–1.00)	0.538

Abbreviations: COR, crude odds ration; CI, confidence interval; AOR, adjusted odds ratio; CVD, cardiovascular disease; DM, diabetes mellitus; hx, history; CKD, chronic kidney disease; TC, total cholesterol; LDL, low density lipoprotein; HDL, high density lipoprotein.

Table 3 Disease and Medication Related Characteristics of Patients, General Hospital, Ethiopia, 2020

Variables	Category	Number	Percent
Comorbidity	Yes No	98 22	81.67 18.33
Complications	Yes No	64 56	53.33 46.67
Evaluator	GP Internist	82 38	68.33 31.67
Side effect	Yes No	31 34	47.69 52.31
Current statin therapy	Yes No	51 69	42.5 57.5
Type of statin	Atorvastatin Simvastatin Lovastatin	19 26 6	37.25 50.98 11.76
Intensity	Low Moderate High	14 22 15	27.45 43.13 29.42
Polypharmacy	Yes No	80 40	66.67 33.33
Previous statin therapy	Yes No	41 79	34.17 65.83

Notes: Evaluator: Health professionals who evaluate/diagnose the patient during data collection period.

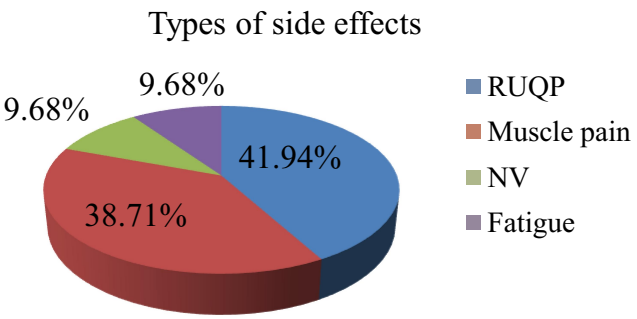

Figure 2 Types of suspected SE the patient developed, General Hospital, Ethiopia, 2020.
Abbreviations: RUQP, right upper quadrant pain, NV, nausea and vomiting.

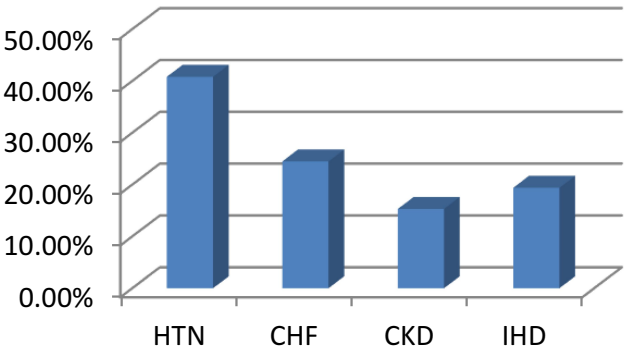

Figure 3 Types of comorbidity of participants in general hospital, Ethiopia, 2020.
Abbreviations: HTN, hypertension; CHF, congestive heart failure; CKD, chronic kidney disease; IHD, ischemic heart disease.

who had no multiple medications (≥3 medications) (AOR=1.28, 95% CI: 1.07–1.53, p=0.008). Previous counseling was significantly associated with statin initiation; patients who had received counseling about cardioprotective effects of statins were more likely to be associated with station initiation (AOR=1.61, 95% CI: 1.34–1.94, p<0.001). Moreover, patients who were evaluated by a GP were less likely to start statins compared with who were evaluated by a medical internist (AOR=0.9, 95% CI: 0.77–0.997, p=0.023) (Table 2).

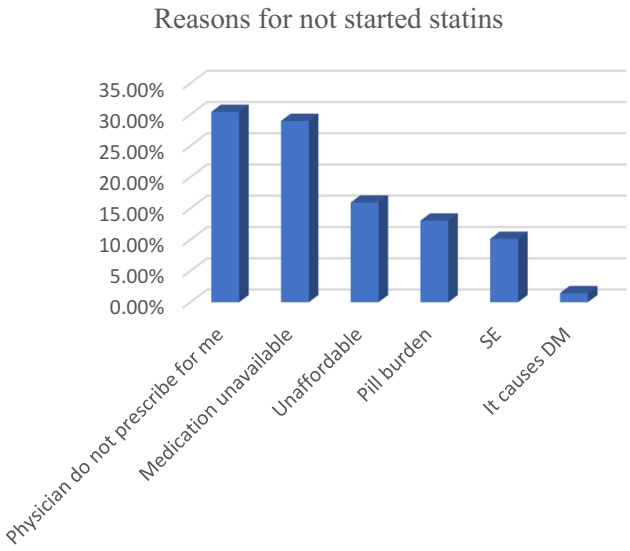

Figure 1 Reasons that the patient did not start statins, General hospital, Ethiopia, 2020.

Discussion

To our knowledge, no sufficient previous published research has explored initiation of statins and determinants for patients with DM in Ethiopia. This study describes the overall rate of statin initiation and associated factors among DM patients. The current study suggested that less than half of the patients (42.5%) were treated with statins. This is less than found previously in Ethiopia by Demoz et al.[10] and from the USA[12] in which 68.3% and 58.4% received moderate- to high-intensity statin therapy, respectively. This difference could be due to the availability of statins and the presence of a sufficient number of specialists in the previous study set up.

The majority of patients initiated statins for secondary prevention (i.e. for treatment of complication). Similar results were reported in Italy[13] where statin use was higher for acute coronary syndrome than for patients having DM alone. This is also similar with the previous finding[14] that less than 5% of the primary prevention and less than 30% of the secondary prevention population had received statins from healthcare providers.

More than half of the patients were evaluated by a GP. Patients evaluated with specialists were more likely to use statins as compared with those who were evaluated by a GP. Similar evidence has shown previously[13] that patients evaluated with cardiologists were more likely to initiate statins as compared with others. As medical staff specialize, they become familiar with guidelines to optimize patient health and prevent unnecessary cost, complications associated with medications and promote the health status of patients.

The majority of patients had comorbidity with most of these patients suffering with hypertension. This result is the same as a previous study[14] showing that the most common condition coexisting with type 2 diabetes is hypertension. The most commonly prescribed statins were simvastatin, atorvastatin and lovastatin. Moderate, high and low intensity doses of statins were prescribed more frequently respectively.

Different reasons were reported by patients as to why they did not start statins for prevention of cardiovascular complications. The first reason was physicians had not prescribed statins, followed by the unavailability of appropriate medication at the healthcare institution. Drug acquisition cost was another reason. Patients who had insurance coverage were more likely to be on statins as compared to with those who have no government insurance. Moreover, side-effects of medication was a reason that discouraged patients from starting statins, with the most common side-effects reported being right upper quadrant pain and rhabdomyolysis (a form of muscle toxicity involving muscle breakdown).

Regarding lipid profiles, levels of total cholesterol were ≥200 mg/dL in more than 50%, LDL ≥100 mg/dL in about 60.0%, triglycerides ≥150 mg/dL in 55.0%, and low HDL ≤ 40 for females in 36.67% and for males in 52.5%. However, in the current study, lipid profile was not significantly associated with the initiation of statins. This is not similar with a previous study done in India.[17]

Most of the patients' TC, TG, LDL and HDL levels were beyond the standard. In our study, less than 40% of patients received high dosage statins. However, the American College of Cardiology/American Heart Association task force on practice guidelines recommended high dose statins in all patients with diabetes with age 40–75 or with suboptimal lipid profile.[14] Anther review showed that diabetic patients between the age of 40–75 years and LDL-C > 70 mg/dL should be treated with a moderate-intensity statin.[9,15–17] Although some patients were on moderate intensity statins, overall prescriptions of statins as well as high intensity statins were suboptimal and much lower than the guidelines. Evidence shows that patients who do not start or have low adherence with statin therapy were more likely at risk for CVD.[21]

Although, polypharmacy was one of the reasons for not initiating statins, patients on multiple medications were more likely to start statins compared with those on less than three drugs. This could be becausepatients taking multiple drugs were suffering with complications which should be treated with statins. A second reason could be that patients with polypharmacy received more attention from their physicians, who can counsel them about the drugs and evaluate their conditions thoroughly.

Patients having family history of DM, physician duration of experience, patient residence and presence of complications, were correlated with statin initiation. However, after controlling confounding factors using multivariate binary logistic regression, these variables were not statistically associated with initiation of statins. Patients having family history of CVD, duration of illness, comorbidity and type of comorbidity were not correlated with statin initiation.

In this study the majority of patients were males. However, sex difference had no significant impact on the initiation of statins. The current finding is not in line with previous reports[11,12] that men with DM were prescribed statins more than women. The discrepancy could be explained if women the previous study had lower coronary artery disease incidence than men.

Limitation of the Study

This study was conducted in a single health institution and with a small sample size, so it is difficult to give inferences for the general population.

Conclusion

In conclusion, only near to 40% of patients started statins. The most common reasons not to initiate statins were physician reluctance to prescribe and unavailability of drugs in the health institution. Insurance, polypharmacy,

counseling patients about importance of statins for cardiac disease prevention and physicians' level of training were statically significant predictors for initiation of statins. The hospital tries to provide medication. Physicians should evaluate their patients' need for cardioprotective drugs and counsel them on the importance of statins.

Data Sharing Statement

All data analyzed during this study are available for publication.

Ethics and Consent

The study was done in accordance with Helsinki declaration (October 2000). Ethical approval was obtained from institutional review board of college of health science, Mizan-Tepi University and sent to Bonga Hospital. Written letter was obtained from drug and therapeutics committee of Bonga Hospital to collect data from the patients. Verbal informed consent from respective physicians and nurses (working in the outpatient department) was secured to extract data from medical charts if necessary. Written informed consent has been given for every patient to participate. Privacy and confidentiality were ensured during patient interview and review of patient charts.

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Author Contributions

Both authors played a significant role on the work submitted including in conception, methodology, data acquisition, data analysis, drafting and revising of articles. Finally, both authors agreed for submission as the current format to the journal has been submitted. In addition, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest for this work.

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