Initiation appropriateness, adverse drug reaction and adherence of isoniazid prophylaxis therapy among people living with human immune virus in Eastern Ethiopia: A cross-sectional study

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INTRODUCTION: Tuberculosis (TB) is a communicable infectious disease caused by Mycobacterium Tuberculosis (MTB). Treatment for latent TB infection (LTBI) is an important strategy to reduce socioeconomic burden of HIV/TB coinfection by providing Isoniazid prophylaxis therapy (IPT) for people living with HIV (PLHIV). Appropriate initiation and good patient adherence are crucial to achieve this.

OBJECTIVES: The main aim of this study was to assess level of IPT initiation appropriateness, ADR and patient adherence in HIV patients on IPT during follow up in university of Gondar referral hospital.

METHODS: A facility based cross sectional study design was conducted and simple random sampling technique was used for selected populations. A structured questionnaire was used and IPT initiation appropriateness was determined against WHO guideline; patient adherence was evaluated according to Morisky adherence scale and self reported ADR was also assessed. Data was analyzed using SPSS version 21 for windows and statistically significance considered when $p<0.05$.

RESULTS: According to Morisky adherence scale 121 (81.2%) HIV patients were having good adherence with 95% CI (77.8–84.6). IPT adherence having statistically significant association with pill burden (<5pills per day, COR 10.14 (4.03-25.52) and duration of therapy (>2 hour, AOR 31.7 (3.37-298)). Out of a total of 52 patients who took IPT and experienced ADR, 21 patients (40.38%) were on INH for less than 3 month and the majority (59.62%) took IPT longer. The most common ADR encountered was constipation (30.8%). The obtained appropriateness level was 116 (77.9%) and the remaining 33 (22.1 %) initiation of isoniazid prophylaxis therapy was found to be inappropriate.

CONCLUSION: The level of adherence to IPT was generally high in PLHIV. Participants who need <2 hours to reach hospital had good adherence than those who need more than 2 hours. Patient who had baseline active TB symptom and contraindication at initiation suffer more from ADR and associated non adherence through therapy than those with appropriate initiation at baseline. Most ADRs were occurred in the last three month of therapy. Overall IPT initiation appropriateness was high.

Key Words: *Initiation*; *Appropriateness*; *IPT*; *Adverse drug reaction*; *Patient adherence*; *Harar*; *Ethiopia*

List of Abbreviations: *IPT: Isoniazid Prophylaxis Therapy*; *PLHIV: People Living with HIV*; *CI: Confidence Interval*; *SPSS: Statistical Packages for Social Sciences*; *ART: Antiretroviral Therapy*; *HIV: Human Immunodeficiency Virus*; *WHO: World Health Organization*; *HC: Health Center*; *TB: Tuberculosis*; *UNAIDs: Joint United Nations Programme on HIV/AIDS*; *ADR: Adverse Drug Reaction*

INTRODUCTION

Tuberculosis (TB) is a communicable infectious disease caused by Mycobacterium Tuberculosis (MTB). Its common site of infection is lung even though it can affect remaining parts of the body (1). TB and HIV have remained critical public health Problems for the last three decades. HIV and TB have a synergic effect. HIV suppresses immune system and maximizes the risk of tuberculosis infection among people living with HIV (PLHIVs). Similarly, TB increases HIV replication which further causes increased viral load. TB, though curable, is one of the most common causes of HIV-related illness and death (2-4).

Worldwide prevalence of TB/HIV co-infection is high and developing nations constitute 90% of co-infection cases. Among this, 79% of TB/HIV co-infection burden is found in SubSaharan Africa. Ethiopia is ranked 7thamong the 22 listed high burden countries with estimated incidence at 579 per 100,000 for all forms of TB and it accounts for 7% of all type of deaths in country. Sub Saharan Africa including Ethiopia are the leading nations who suffer from socio economic burden of TB/HIV co infection which affect the most economically productive age group attributed to HIV pandemic in these area (2,5,6).

As a result, tuberculosis is still the leading cause of morbidity and mortality among PLHIVs,despite significant progress on CPT and ART (7). Prevention of active TB is a vital strategy to reduce these burdens (8). Providing isoniazid preventive therapy (IPT) for people living with HIV, who do not have active TB and contraindication is a key intervention recommended by the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) to enable the effective prevention, diagnosis and treatment of TB in PLWHA (9).

There are many barriers for practical implementation of IPT program. Among many obstacles, Lack of experience, knowledge, and clarity on the benefits of IPT and lack of string adherence to existing guidelines and associated inappropriate initiation and utilization by health workers were cited as common barriers for effective and safe IPT provision beside patient-related factors (10). Inappropriate initiation involves the provision of IPT for patient with at least one active TB symptom or contraindication to IPT. Presence of contraindication at baseline may lead the patient to develop of severe ADR. Similarly, patients with active TB symptom would not benefit from INH monotherapy (11). Patient non-adherence is a significant barrier to effective IPT implementation from patient perspective (2,8,12).

Another obstacle to implementation is concern about adverse events attributable to isoniazid. According to study in south Africa the prevalence of ADR is only 0.54% in which headache and itchy skin are the most common ADR in first three month of therapy (13,14).

The Ethiopian national TB guideline recommends that Isoniazid (INH) should be given to patients daily at a dose of 5 mg/kg, a maximum dose of 300 mg/day for a period of 6 months. Pyridoxine at a fixed daily dose of

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25 mg is indicated in order to reduce the risk of developing INH-induced peripheral neuropathy (15).

Awareness of IPT initiation appropriateness level allow health care professional to provide effective and safe IPT service in line with WHO guideline recommendation, that influence health expenses, save lives, improves health, reduces morbidity and increases quality of life. Awareness of adherence level and IPT related ADR may also contribute to diminishing drugrelated morbidity and mortality. The present study aimed, therefore, to assess IPT initiation appropriateness, ADR and patient adherence in HIV patient on ART during follow up in Hiwot Fana Referal and Teaching Hospital.

MATERIALS AND METHODS

Study design and setting

An institution-based cross-sectional study was conducted on 149 HIV patients attending ART clinic from 12 April to 12 May 2018 at Hiwot Fana Referal and Teaching Hospital. The hospital is found in Harar city which is 526 km away in Eastern direction from Addis Ababa the capital city of the country. The hospital has many specialty departments, including HIV/AIDS care unit, obstetrics, surgery, psychiatry, internal medicine, pediatric, gynecology and outpatient clinic. Source populations was all HIV patients who visit ART clinic for follow up in Hiwot Fana hospital while the Patients with HIV and on IPT who were visiting ART clinic for follow up in the hospital during data collection period were considered as study populations.

Sample size determination

The sample size depended on the number of patients who visited follow up clinic during data collection time. Convenient sampling technique was used as per data collection period and inclusion criteria.

Data collection method and survey instrument

The data was collected by using cross-sectional study which involved interview of HIV patients who fulfill the criteria of the study and review their chart. A standardized data abstraction tool was developed after extensive review of published studies. The tool had two main parts. The first section was focusing on socioeconomic and clinical profile of study participants. The second part aimed at assessing IPT initiation appropriateness, ADR and adherence level among HIV patients. Data collection tool used for appropriateness was developed by using WHO IPT initiation criteria for resource constrained area or in area where Tuberculin Skin Test (TST) is not available (16). Adherence was assessed by using Morisky 8-item medication adherence scale which is standardized for this purpose. ADR was determined by using period prevalence of ever having experienced a specific symptom while on IPT which adopted from previous study (13). The tool was initially prepared in English then translated to Amharic local language for good

TABLE 1

Socio demographic and clinical characteristics of the study participants, Harar, April-May 2018

Socio demographic and clinical characteristic		Frequency	Percent
Age	18-30	34	22.8%
	31–40	50	33.6%
	41-50	43	28.8%
	Above 50	22	14.8%
Sex	Male	78	52.3%
	Female	71	47.7%
Ethnicity	Amhara	142	95.3%
	Other	7	4.7%
Religion	Orthodox	123	82.6%
	Protestant	8	5.4%
	Muslim	12	10.7%
	Others (catholic, Hawariat)	2	1.3%
Marital status	Single	37	24.8%
	Married	88	59.1%
	Divorced	11	7.4%
	Widow	13	8.7 %
Occupation	Student	1	0.7%
	Farmer	13	8.7%
	Government employee	66	44.3%
	Merchant (business man/woman)	31	20.8%
	Daily labour	32	21.5%
	Other (NGO, unemployment, house wife)	6	4.0%
Residence	Rural	114	76.5%
	Urban	35	23.5%
Education	Illiterate (not educated)	57	38.3%
	Primary	39	26.2%
	Secondary	37	24.8%
	University/college	16	10.7%
Monthly income	<500	24	16.1%
	500-1000	30	20.1%
	1001-2000	56	37.6%
	>2000	39	26.2%
Dose (300 mg)		149	100%
comorbidity	No	140	94.0%
	Yes	9	6.0%
Concurrent medication	No	140	94.0%
	Yes	9	6.0%
Alcohol use	None	122	81.9%
	1-14 unit per week	21	14%
	15 and above unit per week	6	4%
Patient on ART	Yes	140	94.0%
	No	9	6.0%

patient understanding and then translated back to English to ensure that the translated version give correct meaning. Inappropriateness was identified by assessing the presence of baseline contraindication and symptom of active TB symptom by reviewing chart and interviewing the patient as well. Adherence was determined by investigator administered questionnaires. Adequate training was provided for data collectors on how to approach the patients and abstract data.

Data processing and analysis

The final data collection tool was checked for completeness, and the response from each respondent was coded, entered and analyzed in SPSS 21.0 version. Data is presented in frequencies and percentages. Bivariate and multi-variate logistic regression was used to identify factor associated with adherence. CI 95% and p-value <0.05 were used as cut points for determining the significance of association.

RESULTS

Socio-demographic and clinical characteristics of study participants

A total of 149 HIV patients were interviewed with a mean age of 38.72 with a standard deviation of ±10. Majority of the respondents were Orthodox Christians 123 (82.6 %). Among the total respondents, 114 (76.5%) of them were urban residents and 142(95.3%) were Amhara in ethnicity. 104 (68.8%) of participant need less than 2 hours to get to the treatment setting. Majority of the study participants, 116(77.9%) had a pill burden of less than 5 pills per day including INH and 16(10.7%) of respondent had previous TB incident were all of them had a successful treatment (Table 1).

Adherence level among HIV positive patients on isoniazid prophylaxis therapy

Using accepted criterion of the Morisky 8 item medication adherence questionnaire, the level of self-reported adherence (good adherence) rate of IPT was found to be 121(81.2%) with 95% CI (77.8–84.6) and the remaining 28(18.8%) were classified as non-adherent to medication (medium adherent (7%) and poor adherent (11.8%)) with adherence score of one or more on the Morisky 8 item medication adherence questionnaire.

Reason for non-adherence reported by respondents

The most common reasons for non-adherence were forgetfulness to take medication 3 (7.1%) and poor or irregular drug supply 6(21.4%) even though others less common factors were also reported by the patients (Table 2).

Adherence and associated factor

In the bivariate logistic regression, respondents who have taken IPT for >3 months were more likely to be adherent than those who took only for 1-3 months [95% CI, AOR 25.5(3.37– 130.8)]. The likelihood of adherence was higher in patients who took less than 5 pills per day than those who took 5 pills and above per day [95% CI, COR 10.14 (4.03-25.52)] (Table 3).

Appropriateness of IPT initiation

Appropriateness level of IPT initiation was rated on WHO and Ethiopian guide line criteria to initiate IPT. Based on these criteria, the obtained appropriateness level was 116(77.9%) and the remaining 33(22.1 %) initiation of isoniazid prophylaxis therapy were inappropriate (Figure 1).

Predictors of inappropriate initiation

The highest number of inappropriateness attributes to initiation of IPT for patients with combined fever and night sweat from categories of active TB symptom 10(30.3%) and presence of previous hypersensitivity to INH before initiation of IPT among contraindication categories 6(4.7%). Presence of both active TB symptom and contraindication to INH were depicted in 5(15.1%) patients (Tables 4 and 5).

Adverse drug reaction frequency and periodic prevalence

Out of a total of 52 respondents who experienced ADR after IPT initiation or during the prophylactic course, 9 patients had co morbidities of which ADR occurred in six. Two patients with hypertension and on an anti-hypertensive medication and 3 patients with diabetes mellitus on hypoglycamic agents claimed to have constipation while on IPT. 1 epileptic patient receiving anticonvulsant had convulsion once in the duration of IPT, perhaps attributed to INH ADR. Constipation was the most prevalent adverse effect (33.8%). 16 patients were contraindicated to IPT before initiation. Regardless, they were put on it and eleven of them developed ADR, making presence of contraindication as probable predisposing factor (Figure 2).

DISCUSSION

This study was attempted to assess the IPT adherence and associated factors, IPT initiation appropriateness level and adverse drug reaction among HIV positive patients on isoniazid in university of Gondar referral hospital. This study was found an adherence rate of 81.2%. which was almost similar with study done in Diredawa, and Cambodia, where the levels were 86%, and 86.5%, respectively (17,18). However, it was lower than adherence level reported from previous study in Addis Ababa and Gondar health center,89.9% and 90.3% respectively (8,19). which could be due to use of standard questioner to measure adherence in this study and isoniazid (INH) stock out that was met the hospital 2 weeks prior to study period that last for 1 month.

Age, distance from the hospital, duration of IPT treatment, number of pills per day, ADR and inappropriate initiation were the most important factors that affect adherence. In the binary logistic regression analysis, patients who took IPT for >3 month were 30.46 times (COR=30.46;95 CI 10.44-88.41) and 25.5 times (AOR=25.5;CI4.9-130) more likely adherent than their counterpart who took it only for 1–3 months, respectively. Which is consistent with study done in Addis Ababa and Gondar health center which stated that patient who take IPT for longer time were more adherent than who were in first half of therapy period (8,19). This could be partially explained by the fact that repeated exposure to health care providers and their counselling improve adherence, which could be augmented by high prevalence of the most common annoying ADRs such as itchy skin which significantly affect adherence in first half of therapy that subsides in second half of therapy, which can be justified by this study finding. Personal factors related to people's characteristics such as age are believed to have a major influence on their adherence behaviour. Gust and colleagues observed that the case non adherent group was younger (t=58.2, p<0.0001) according to report from meta-analysis by Henok etal,which was consistent with this study finding that patient within 31-40 years age were 1.65 times(COR=1.65;95% CI 6.2-7.56) and 1.27 times(AOR=1.27;95% CI 2.7-5.19) 18-30 more likely adherent than their counter parts who were within 18-30 years (9).

According to study done in Addis Ababa, being away from home was among factors associated with poor adherence to IPT among people living with HIV (20). This was in agreement with this study finding that patients who need 2 or less hour to reach hospital were 3.55 times adherent than those who need more than 2 hours. Conversely, report for systemic review in Nigeria, Abuja reported higher adherence among patients with longer distance from treatment setting due to freedom to follow care with reduced stigmatization. This might be due to lack of sufficient patient counselling by health professionals about fear of stigmatization, in Nigeria [5]. Another report by this meta-analysis was that HIV treatment and concurrent use of HAART posed further contributing factors towards non-adherence to IPT. Similarly, in our finding, odd of adherence among HIV patient on IPT were 10.14 times higher among those who took <5 pill per day compared with those who took more than 5 pill per day (9,19). This could be justified by patient's lack of motivation to take two regimens at the same time due to high numbers of pill count.

A recent meta-analysis in Rio, brazil reported a 1.66-fold increased risk of adverse events leading to stoppage of treatment among HIV-infected patients receiving IPT compared with placebo (10). Similarly, a study in Gondar reported that respondents who experienced side effects had lower odds of being adherent compared to those who experienced none (19). Both confirm our study finding that patients who had not experienced ADR through therapy were 6.66 times adherent compared to those who had experienced ADR through therapy. In this study, the most common ADR associated with poor adherence is itchy skins that occur mostly in first 3 month of therapy which perhaps attribute to lower adherence rate in first half of therapy. In bivariate regression analysis patients who had active TB symptom and contraindication at initiation had lower adherence level compared to patients with appropriate initiation of IPT.

In this study, the predominant reason for not adhering to IPT was forgetting to take pills. This finding is consistent with several other studies conducted on adherence for long term treatments and also for tuberculosis preventive therapy. According to study in Dire Dawa,

21.2% of the study participants were reported to have missed doses as a result of forgetting (17). Similarly, in Addis Ababa, 24.24% of the study participants mentioned forgetfulness as a reason for missing doses (8). This implies that there is a requirement for a program that strengthen the adherence of patient through memory aids.

TABLE 2
Reason for non-adherence among HIV patient on IPT, Harar, April-May 2018

Variable	Frequency	percent
Patient related factors		
Schedule of your work make it impossible	2	7.1%
Forget to take medication	3	10.8%
Medication related factors		
Number of pill are high	4	14.4%
Medication related side effect	6	21.4%
Health system related factors		
Poor or irregular drug supply	6	21.4%
Lack of education about IPT	2	7.1%
Others		
Forgetfulness	2	7.1%
Distance from treatment setting	3	10.7%
Total	28	100%

TABLE 3
Isoniazid prophylaxis therapy adherence and associated factor among HIV patient on ART follow up in Hiwot Fana referral hospital, Ethiopia, April-May 2018

Variable		Adherent	Non-adherent	COR (CI)	AOR (CI)
Age	18-30	26	8	1	1
	31-40	44	6	2.25 (1.2-7.563)	1.27 (1.05-5.19)
	41-50	37	6	1.89 (0.166-6.628)	1.84 (0.053-4.40)
	Above 50	14	8	0.53 (0.054-6.67)	2.7 (0.003-8.12)
Duration of IPT treatment	≤ 3 month	t 13	22	1	1
	Above 3 month	108	6	30.46 (10.44-88.84)	25.5 (4.9-130.8)
Number of pill per day	<5 pills per day	105	11	10.14 (4.03-25.52)	2.74 (0.65-11.5)
	>5 pills per day	16	17	1	1
Previous TB treatment	No	110	23	2.17 (1.68-6.853)	5.2 (0.62-43.7)
	Yes	11	5	1	1
Active TB symptom	No	108	16	6.23 (2.42-16.01)	2.69 (0.63-11.4)
	Yes	13	12	1	1
Contraindication	No	112	21	4.14 (1.39-12.3)	2.81 (0.483-16.4)
	Yes	9	7	1	1
Adverse drug reaction	No	88	8	6.66 (2.67-16.6)	3.04 (0.78-11.74)
	Yes	33	20	1	1
Distance from hospital	≤ 2 hour	92	13	3.55 (1.51-8.51)	1.03 (0.235-4.57)
	Above 2 hours	29	15	1	1

In this study, the other reason for non-adherence reported by patients was unavailability of the medication at the hospital due to poor or irregular supply. This was in agreement with South African study which reported that 4.7% patients were forced to miss doses due to INH stock out in peripheral pharmacy (21). In this study, 4 % of the respondents had reported that they missed doses because of the side effects of the drug. Which was in line with study in Tanzania, 14% of individuals had side effects and as a result they were forced to miss doses and considered as non-adherent (22).

Appropriate initiation and regular supply of drug were among the most important factors to ensure good adherence of patient, and most of the adherent participants had no baseline active TB symptom and contraindication to IPT. This implies that appropriate initiation of IPT by making correct diagnosis prior to initiation significantly improve adherence. Many participants mention, they forced to miss dose due to unavailability of INH in the Hospital due to irregular or poor drug supply. As a result, adherence can be improved by ensuring regular sufficient supply of INH.

The other aim of this study was to assess appropriateness of IPT initiation; evaluation of initiation appropriateness is one among the way to ensure rational use of drug. If the use deemed inappropriate, intervention with patients and providers was necessary to optimize the drug therapy (23). The goal of IPT therapy is to achieve the best possible clinical outcomes with a reduced risk for developing resistance while consuming the least amount of hospital resources. Therefore, studying the initiation of INH as a preventive therapy among PLWHA helps to understand initiation appropriateness level in this hospital.

Appropriateness mainly evaluated by using WHO guide line for tuberculosis intensified case finding and isoniazid preventive therapy for people living with HIV in resource constrained setting. TST is not a requirement for initiating IPT in people living with HIV in resource constrained area. Adults and adolescents living with HIV should be screened for TB with a clinical algorithm and those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT in patient with no contraindication (16). Accordingly, the found appropriateness level is 116 (77.9%) and the remaining 33(22.1 %) initiation of isoniazid prophylaxis therapy is inappropriate. That means about three-fourth of patients initiated IPT has no any active TB symptom and no contraindication to it. This was in agreement with WHO guideline for isoniazid preventive therapy in resource constrained setting. The remaining

TABLE 4
Predictors of inappropriate initiation among HIV patient on IPT in Hiwot Fana Hospital, Harar, Ethiopia, April-May 2018

Variable	frequency	Percent
Active TB symptom		
Cough >2 weeks	4	12.1%
Loosing weight	1	3.0%
Fever	2	6.1%
fever and night sweet	10	30.3%
Contraindication		
Hepatitis	2	2%
INH hypersensitivity	6	4.7%
Alcoholism	3	4%
Having both predictors	5	15.1%
Total	33	22.1%

TABLE 5
Frequency of ADR in relation to other factors in HIV patients on ART and taking IPT at UOG ART clinic from April-May 2017

Frequency	Itchy skin	Appetite	Hepatotoxicity	Peripheral Convulsion	Headache	Constipation	Combination	disturbance neuropathy
Duration of IPT								
<3 mth	6	0	0	2	2	3	4	4
3-6 mth	3	2	1	2	2	2	12	7
Co-morbidity	0	0	0	0	1	0	5	0
Concurrent	0	0	0	0	0	0	2	0
medication	5	2	1	3	0	4	11	8
No of pills per day with IPT	4	0	0	0	0	0	0	0
<5								
≥ 5								
Adherence	5	2	1	2	3	0	13	7
adherent	4	0	0	2	1	5	3	4
Non-adherent	2	0	0	0	0	3	1	5
Contraindication Active TB symptom	5	0	0	3	2	1	10	4

33(22.1%) patient has either active TB symptom or contraindication to INH at initiation which is not in line with WHO guideline. This might have resulted because of the lack of health professionals paying attention to contraindications and non-adherence to the available updated guidelines, such as WHO guideline for tuberculosis intensified case finding and isoniazid preventive therapy for people living with HIV in resource constrained setting. Among 149 participant all (100%) took 300 mg per day which is appropriate dose recommended by WHO guide line. As a result, the finding regarding dose was in line with world health organization (WHO).

WHO guideline recommends that Adults and adolescents living with HIV and screened with a clinical algorithm for TB, and who report any one of the symptoms of current cough, fever, weight loss or night sweats may have active TB and should be further investigated for active TB. They are not eligible for TB preventive therapy until active TB disease has been excluded on the basis of sputum smear Microscopy, chest x-ray and mycobacterial culture. In this study from all participants who report one and above active TB symptom, confirmatory test was not done even for one patient in contrary with WHO recommendation. This can be justified by lack of independent confirmatory investigation in ART clinic and lack of health professional attention toward importance of confirmatory investigation.

ADR report was obtained through patient interrogation and review of their medical chart carried along during follow up. Death was not included as there was no sustained and accurate record on the database or even chart. A total of 34.9% of the patients were found to have experienced INH-related common side effects which was in agreement with a previous study from north west Ethiopia that reported ADR of 31.2% (19). However, there was a large variation with the report of ADR from another study in South Africa, recording ADR of 0.54%. This may be attributable to their large sample size, exclusion of active TB symptoms and contraindications before initiation of IPT. In this study, headache and itchy skin were more prevalent in first three month of therapy. Unlikely in South African study, headache (5.6%) and itchy skin (4.3%) occurred after 1 month increased to 5.7% and 5.4% respectively at 3 and 6 months (13).

Among patients contraindicated to IPT but started INH, 11 of them (68.75%) progressed to ADR most of them within 1-3 months (N=4) (66.67%). No patients with alcohol use and previous hepatitis co morbidity had hepatotoxicity as an ADR on initiation although hepatitis was developed 1-3 months after initiation in patients who had no history of hepatitis. A study in Botswana corroborates this study finding, there is no association between INH-hepatitis and prior hepatitis infection but occurrence of hepatitis in 1.1% of the study participants within 1-3 months of initiation was attributable to INH. Alcohol use also had no significant association [RR: 95%CI:(0.57-3.51)] (7). However, study in south Africa report an association

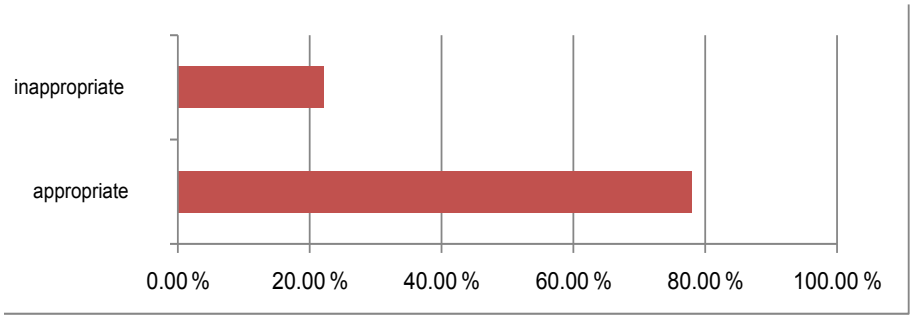

Figure 1) *Level of IPT initiation appropriateness among HIV patient on ART follow up in Hiwot Fana Referral Hospital, Harar, Ethiopia, April -May 2018*

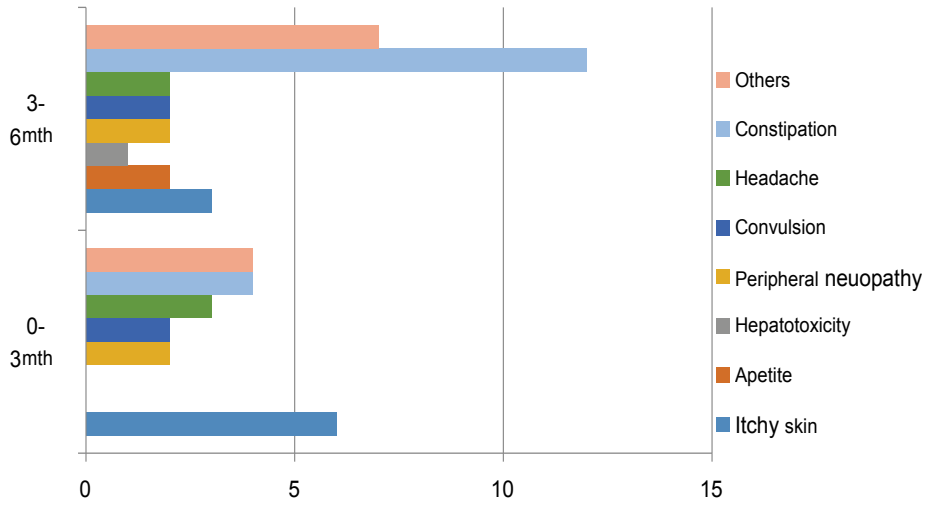

Figure 2) *Frequency and periodic prevalence of ADR in HIV patients on ART and taking IPT at Hiwot Fana Hospital ART clinic from April -May, 2018*

between alcohol and INH related hepatotoxicity in contrary to this study finding (13).

Out of 22% patients with symptoms of active TB before initiation, 17 faced ADR of which the majority (N=8) had both fever and night sweat who after being put on the therapy reported constipation, itchy skin and peripheral neuropathy. This implies that putting the patient on IPT in presence of active TB symptom would increase patient chance of developing ADR.

ADR was also shown to be more prevalent with milder and most common side effects of INH than severe. One epileptic patient reported that convulsion occurred once during IPT period but there was no evidence to associate it with INH side effect. Constipation was an ADR that had not been reported in any of previous researches conducted locally or at international level but counted for the majority of complaints (30.77%) in this study.

Limitation and strength of the study

The strength of the study is that since there is no study done on appropriate initiation and only few previous studies on adherence and ADR, the result of this study could be used as a reference for other studies on this topic and the results could serve as baseline for program implementation. As a limitation this study tried to assess the level of IPT adherence and ADR using a self-reported survey, which may be subjected to recall and social desirability biases. This may lead to under estimation of adherence and difficult to associate ADR with IPT. This study being cross sectional has limitation of determining the exact cause and outcome relationships genuinely.

CONCLUSION

The level of adherence to IPT was high among PLHIV on ART. Patients who took INH for >3 months were found more likely to be adherent than those who took it for ≤ 3 months. Patients who need ≤ 2 hour to reach the hospital had good adherence than those who need more than 2 hours. Patients who had baseline active TB symptom and contraindication at initiation suffer more from ADR and associated non-adherence through therapy than those with appropriate initiation at baseline. The overall use of isoniazid as a prophylaxis therapy among patients living with HIV/AIDS was consistent with WHO guidelines on appropriate initiation. ADR was more prevalent in the last 3 month of therapy than in first half of therapy. Forgetfulness and irregular drug supply were among the most important reason for non-adherence in this study.

RECOMMENDATION

Health care professionals should focus on adequate counselling of patients who are in first and second months of IPT along with provision of memory aid. Those involved in hospital management should ensure regular drug supply and provide independent confirmatory investigation in ART clinic.

ETHICAL CONSIDERATIONS

In conducting the study ethical clearance was secured from School of Pharmacy, College of Medicine and Health Sciences, University of Gondar and Hiwot Fana specialty Hospital. Verbal informed consent was obtained from the respondents for the interview and data was maintained with confidentiality.

CONSENT FOR PUBLICATION

Not applicable

AVAILABILITY OF DATA AND MATERIALS

Questionnaire used for adherence, ADR and appropriateness.

AUTHORS CONTRIBUTION

Both authors contributed from conceptualization of the study to making first draft of the manuscript.

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CONFLICTS OF INTEREST

The authors have declared no conflict of interest for this work.

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