

Isoniazid Preventive Therapy: Level of Adherence and Its Determinant Factors among HIV Positive Patients in Adama Hospital Medical College, Oromia, Ethiopia, 2016

Elias Abdulalim¹, Sileshi Garuma², Bekele Dibaba¹, and Tolossa E Chaka^{3*}

¹Department of Public Health, College of Health Sciences, Arsi University, Ethiopia

²Department of Public Health, Adama Hospital Medical College, Ethiopia

³Department of Paediatrics and Child Health, Adama Hospital Medical College, Ethiopia

*Corresponding author: Tolossa Eticha Chaka, Department of Paediatrics and Child Health, Adama Hospital Medical College, Ethiopia, Tel: +251911413135; E-mail: tecb2006@gmail.com

Received date: January 31, 2017; Accepted date: February 20, 2017; Published date: February 27, 2017

Copyright: ©2017 Abdulalim E, et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background: Tuberculosis is an airborne disease caused by *Mycobacterium Tuberculosis* (M.TB). *Mycobacterium bacilli* in the body will get destroyed or presented to white blood cell that could trigger immune response and ultimately establishes latent tuberculosis infection. Isoniazid preventive therapy (IPT) hinders the development of active TB in patients with latent TB infection. All HIV positive patients without contraindications are eligible for IPT.

Methods: A facility based cross-sectional study was conducted to assess the level of adherence to IPT and its determinant factors among HIV positive patients at Adama Hospital Medical College ART clinic. One hundred sixty eight patients who were ≥ 18 years of age and who took IPT at least for two months were consecutively interviewed. SPSS version 21 was used for data entry, cleaning and analysis. Descriptive and analytic statistics were utilized. Crude and adjusted odds ratio (COR & AOR respectively) with 95% confidence interval (CI) was used to interpret the findings.

Result: A total of 168 respondents were included in the study. The seven day self-reported adherence rate was 68.5%. The average number of doses missed in the past seven days prior to the study was 0.8 doses per day. Forgetfulness (59%, N=49), being away from home (25.3%, N=21) & being busy (15.7%, N=13) were the most common reasons for ever missing pills since the start isoniazid. Abdominal side effects [AOR 3.76 (1.38, 10.26)], unclear information from health care providers [AOR 3.59 (1.63, 7.93)], not using memory aiding tools for dose schedule [AOR, 2.15 (1.03,4.49)] and perceived lack of confidentiality [AOR 7.01 (2.71,18.12)] were the factors associated with the poor adherence of IPT.

Conclusion: IPT adherence rate is poor. Clear and targeted health education should be given by service providers. Medication side effects should be addressed promptly.

Keywords: Tuberculosis; IPT, Adherence; HIV positive; Adama

Background

Tuberculosis (TB) is an airborne disease caused by *Mycobacterium tuberculosis* (*M. tuberculosis*). Tubercle bacilli invades the alveoli of the lungs where it is ingested by macrophages to be partially destroyed and partially presented to white blood cell that could trigger immune response and ultimately establishing latent tuberculosis infection (LTBI) [1].

Without treatment, anyone who has LTBI can develop TB disease (10% life time risk) but some people are at higher risk than others. People living with untreated Human Immune Virus (PLWHA) are prone to 7-10% risk per only a year [1].

Global TB prevalence and annual death from the disease is estimated to be 11 million and 1.1 million respectively. TB is a major opportunistic infection frequently affecting people living with HIV/

AIDS [2]. Five deaths of estimated sixteen deaths per year per 100,000 from TB are reportedly occurring in HIV-positive individuals [3].

Africans suffer the burden of TB in highest degree when compared to other regions of the globe. More than three fourth of total TB deaths and 73% of TB deaths among HIV-negative individuals happen on African continent [3].

The first Ethiopian population based TB prevalence survey showed that prevalence of smear positive TB in Ethiopia was 63/100,000 and prevalence of bacteriologically confirmed TB cases were 156/100,000 [4].

As TB frequently infects people living with HIV (PLWHA), TB/HIV collaboration program comes into picture. Thus, Preventive activities that focus on HIV-positive individuals like screening for TB on every contact with health service and early initiation of Antiretroviral Therapy (ART) and enrolling to Isoniazid preventive Therapy (IPT) are international strategies which are complemented by national guidelines [2,5].

IPT is a treatment that is used to prevent the occurrence of active TB on individual who have latent infection with *Mycobacterium tuberculosis*. It is the most frequently used TB preventive treatment requiring self-administration of isoniazid for a minimum of six months [2,5].

Though IPT is recommended to PLWHA for TB prevention on the package, compliance of patients with IPT is expectedly a practical challenge on implementation. Accordingly, Ethiopian guideline recommends patients to be given one month supply of isoniazid and evaluated for adherence to treatment at each visit for six consecutive months [5].

Reports suggest that adherence to long term medications, including IPT, is seldom achieved. Adherence could be defined as the extent to which the patient follows medical instructions. Adherence could be measured subjectively by standardized patient administered questionnaires and patients' self-report on adherence behavior [6,7].

Though adherence to treatment regimens means taking all medicines (100%) as per prescribed doses, taking $\geq 85\%$ of prescribed doses, is mostly used as the threshold to define good adherence [8-13]. Poor-adherence to treatments across chronic diseases is a worldwide problem. It would be far more challenge in developing countries, like Africa [7]. It is undeniable that many patients experience difficulty following treatment course in chronic diseases where studies show that patient non-adherence to their treatment occurs at least occasionally [14-16].

Health outcomes cannot be accurately assessed if they are measured predominantly by resource utilization indicators and efficacy of interventions. Without a system that addresses the determinants of adherence, advancements in medicinal science will fail to realize their potential to reduce the burden of chronic illnesses [16]. Prolonged healing time which makes the patient away from productive functionality and repetitive visiting of health care facility for the same health problem could happen as a result of non-compliant behavior of patient that greatly affect the health care cost and the economy of a country in a wider prospect [17].

Studies identified higher chance of emergence of drug resistance when adherence rates to drugs fall between 50%-85%. Unfortunately, an important proportion of treated patients fall within this range [7]. Multi drug resistant tuberculosis(MDR-TB) and recently, extensively drug resistant tuberculosis (XDR-TB) are diseases caused by first line and second line TB drug regimen resistant strains of *Mycobacterium tuberculosis* respectively [3,18]. Resistance to drugs becomes more likely to occur in monotherapy than combined drug regimen. Accordingly, IPT could thus be public disadvantage if the users are not compliant enough to good adherence behavior [19].

Different studies show that adherence to IPT is also a challenge which is affected by different factors and requiring adoption and maintenance of a range of therapeutic behaviors and may include self-management of biological, behavioral and social factors that influence health and illness [11-13].

As patients are expected to take the dose daily for six months, they find it hard to always remember their medications: some get busy and forget to carry their medications with them, some have many other medications to take and they are tired of it and/or some decide to skip medications because they don't like how it makes them feel [20,21]. Therefore, the objective of this study is to assess the level and factors

affecting adherence to IPT in HIV infected patients at Adama Hospital Medical College, Adama, Ethiopia.

Materials and Methods

Facility based cross-sectional study was conducted from April 11 to May 10, 2016 at Adama Hospital College Medical, a teaching referral hospital with the largest ever enrolled HIV patients in the Oromia Regional Governmental State. The hospital has standalone ART clinic where the service runs six days a week. The service is run by ART trained clinical nurses, Health officers and General practitioners. The study participants were HIV infected patients (>18 years of age) who were on IPT for at least two months during the study period.

The sample size was determined by using single population proportion formula by assuming IPT adherence rate of (88.5%) from a study conducted in Ethiopia [13], 95% confidence interval, margin of error of 5% and 10% non-response rate yielding sample size of 172. All patients who met the inclusion criteria during the study period were consecutively interviewed up on their exit by trained data collectors until the required sample size was obtained. The collected data was entered into SPSS version 21 for cleaning and analysis. Descriptive and analytic studies were undertaken to identify adherence and associated factors. Crude and adjusted OR with 95% CI was used to interpret the findings. P-Value of less or equal to 0.05 was used as a cut-off point to determine significance. The assumptions for normality of continuous variables and multi-collinearity of independent variables were checked.

Results

Socio-demographic characteristics of the respondents

A total of 168 respondents were included in the study. The mean age of the respondents was 36.83 (+/-9.66 SD) years. The majority (73.2%) of the respondents were female. Over two thirds (70.8%) of the respondents were married and 38.7% of them were house wife by their occupation. About 8.3% of the respondents have other chronic health problems for which they should also take medications other than IPT during the study period (Table 1).

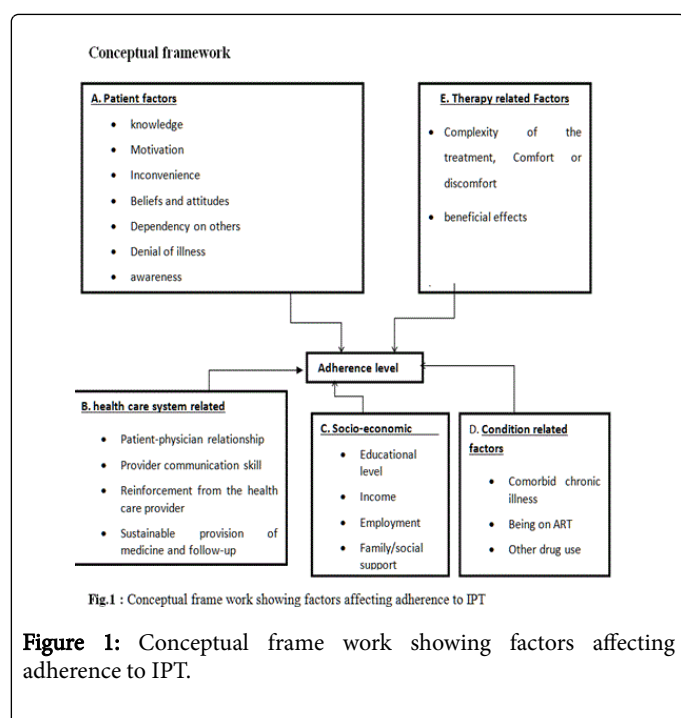
Socio-demographic Profiles		Number	Percentage (%)
Age group	20-30	45	26.8
	31-40	81	48.2
	41-50	27	16.1
	>/50	15	9.0
Sex	Male	45	26.8
	Female	123	73.2
Educational level	Illiterate	18	10.7
	Primary school	83	49.4
	Secondary school	47	28.0
	Diploma & above	20	11.9
Ethnic group	Oromo	82	48.8
	Amhara	58	34.5

	Others	28	16.7
Religion	Orthodox	125	74.4
	Protestant	22	13.1
	Others	21	12.5
	Married	119	70.8
Marital status	Divorced/ Separated	20	11.9
	Widowed/Widower	15	8.9
	Single	14	8.3
	Occupational Status	No occupation	65
Private employee		36	21.4
Govt. employee		30	17.9
Merchant		19	11.3
Day laborer		18	10.7
Income group	0-1000	112	66.7
	1001-2000	56	33.3

Table 1: Socio-demographic Characteristics of Patients on INH, AHMC ART Clinic, Adama, Ethiopia.

Adherence level

Overall, the seven day self-reported adherence rate was 68.5%. The average number of doses missed in the past seven days prior to the study was 0.8 doses per day. Only 56% and 50% of study participants have never missed a pill in the last 7 days and since the start respectively (Figure 1).



Forgetfulness (59%, being away from home (25.3%) and being busy (15.66%) were reasons for ever missing pills since INH started. Fifty two (31%) participants of this study have missed their clinical appointment sometime since enrolled on IPT. Forgetfulness (36.5%), being busy (26.9%), facility being far (21.2%) and being sleepy (15.4%) were common reasons to miss clinical appointments.

Participants that did not experience abdominal side effect were more likely to adhere (COR=3.07, 95% CI: 1.27-7.42) than who did have the side effects. Study Participants who felt that IPT schedule is convenient with their life were more likely to adhere (COR=1.96, 95% CI: 1.01-3.78). Perceived confidentiality of service favors adherence to IPT (COR=4.39, 95% CI: 1.96-9.81). Respondents who claimed the information from clinicians was clear were more likely to adhere too (COR=2.27, 95% CI: 1.17-4.41). Individuals who used memory aiding tools to remember the time of INH dose were more likely to adhere (COR=2.46, 95% CI: 1.26-4.79) than who did not use any memory aiding tools. Moreover, the study participants that had taken INH for five or more months were more likely to adhere than whom took for two or less months (COR=3.32, 95% CI: 0.28-8.61).

However, when the variables were adjusted, participants that did not experience abdominal side effect were more likely to be adherent (AOR=3.76, 95% CI: 1.38-10.26). Respondents that did not complain about the confidentiality of the service were also more adherent (AOR=7.01, 95% CI: 2.71-18.12). Those who got clear information from clinicians were more likely to adhere than who claimed unclear information (AOR=3.59, 95% CI: 1.63-7.93). Individuals who used memory aiding tool to stick to the time of INH dose were more likely to adhere (AOR=2.15, 95% CI: 1.03-4.49) than who did not use any memory aiding tool.

Discussion

Seven days self-reported adherence rate of this study was 68.5% which is less than the prevalence found in a study done at yekatit 12 Hospital (94%) [22]. Other two facility based cross sectional studies conducted at Addis Ababa also showed higher rates of IPT adherence (86.5% and 89.5%) [12,13]. But the current finding is comparable to adherence level among HIV-infected adults in South Africa (72%) [10].

Participants who didn't experience abdominal side effect were more likely to adhere than who did experience abdominal side effects. This result is in congruent to a result from cross sectional study conducted in four hospitals in Addis Ababa and Yekatit 12 Hospital where abdominal side effects affected adherence [2,12]. This may be due to discomfort on abdomen like abdominal pain, nausea, vomiting and loss of appetite that could seriously challenge intake of food, medicine and the overall state of mood of the patient towards his/her regimen which might end up to non-compliance.

Respondents who didn't complain the service privacy were more likely to adhere than who complained that could greatly compromise uptake of proper information, knowledge and behavior by the patient. This might arise from the stigma and perception by the patient. Stigma and perception as a factor affecting adherence was also shown by a study which indicated that patients who were not comfortable to take IPT in front of other people were less likely to adhere to IPT [12].

The current study pointed out that individuals who received explanation about IPT from health care providers were more likely to adhere to IPT. This finding is similar to the study by Miindachew et al. which also suggested that individuals who received explanation about

IPT from health care providers were more likely to adhere to IPT (OR=7.74; 95% CI: 3.144, 19.058) [12]. Comparably, respondents in the current study who claimed the information from clinicians was clear were more likely to adhere than their counter parts. This might be explained by betterment of patient involvement in the therapy

following clear communication between the health care provider and the client. Clear communication between clinician and patient is very important as a patient would get trust with every treatment procedures which potentially improve the patient level of adherence to his/her medication Table 2.

Variables		Adherence status		COR,(95% CI)	AOR(95% CI)	P values
		not-adherent	adherent			
Abdominal side effect	Yes	13 (7.73%)	11 (6.54)	1:00	1:00	
	No	40 (23.81)	104 (61.9)	3.07 (1.27-7.42)	3.763 (1.380-10.259)	0.010
IPT harmonized	No	30 (17.86)	46 (27.38)	1:00	1:00	
	Yes	23 (13.69)	69 (41.07)	1.96 (1.01-3.78)].	1.578 (0.646-3.858)	0.317
Dissatisfied b/c privacy	Yes	19 (41.07%)	13 (7.73%)	1:00	1:00	
	No	34 (20.24%)	102 (60.71)	4.39 (1.96-9.81)	7.008 (2.711-18.118)	0.000
Care provider communication unclear	Yes	31 (18.45%)	44 (26.19%)	1:00	1:00	
	No	22 (13.10%)	71 (42.26%)	2.27 (1.17-4.41)	3.590 (1.626-7.925)	0.002
Using memory aiding tool	No	32 (19.05%)	44 (26.19%)	1:00	1:00	
	Yes	21 (12.5%)	71 (42.26%)	2.46 (1.26-4.79)	2.150 (1.029-4.493)	0.042
Period since IPT	≤ 2 month	12 (7.14%)	10 (5.95%)	1:00	1:00	
	3-4months	15 (8.93%)	33 (19.64%)	2.640 (0.935-7.452)	1.787 (0.481-6.641)	0.386
	5-6months	26 (15.48%)	72 (42.86%)	3.32 (1.28-8.61)	1.656 (0.538-5.100)	0.380

Table 2: Factors Associated with Adherence Status of Patient to INH Prophylaxes at ART clinic of AHMC, Adama, Ethiopia.

This study identified that usage of memory aids improves IPT adherence where individuals who used memory aiding tool to stick to the time of INH dose were more likely to adhere to the drug. There is no study done, as to the best knowledge of the authors, which showed the effect of memory aids on IPT adherence.

Conclusion and Recommendations

The adherence rate in Adama Hospital Medical College is 68.5%. Abdominal side effects, unclear health provider's messages, not using memory aiding tool for dose schedule and service lacking confidentiality were the factors significantly associated with adherence to INH prophylaxis. The health workers, the hospital and regional health bureau as well as ministry of the health should design and deliver tailored health education messages on the aforementioned risk factors for clients and health service providers to promote better adherence.

References

- Core Curriculum on Tuberculosis (2013) What the Clinician Should Know. CDC sixth ed.
- Fujiwara PI, Dlodlo RA, Ferraoussier O, Nakanwagi-Mukwaya A, Cesari G, et al. (2012) Implementing Collaborative TB-HIV Activities: A Programmatic Guide. *Int J Tuberc Lung Dis*.
- World Health Organization (2014) Global Tuberculosis Report. France.
- Federal Democratic Republic of Ethiopia MoH, Ethiopian Health and Nutrition Research Institute (2011) First Ethiopian National Population Based Tuberculosis Prevalence Survey. Ethiopia: Federal Democratic Republic of Ethiopia, Ministry of Health.
- MOH (2007) Implementation Guideline for TB/HIV Collaborative Activities in Ethiopia.
- Burkhart PV, Sabaté E (2003) Adherence to Long-Term Therapies Evidence for action. *J Nurs Scholarsh* 35: 207.
- Yach D, Bengoa R, Sabaté E, Epping-Jordan J, Kawar R (2001) Adherence to long term therapies: policy for action. *Adherence Meeting: World Health Organization*.
- Makanjuola T, Taddese HB, Booth A (2014) Factors Associated with Adherence to Treatment with Isoniazid for the Prevention of Tuberculosis amongst People Living with HIV/AIDS: A Systematic Review of Qualitative Data. *PLoS* 1: 9.
- Kaona F, Tuba M, Siziya S, Sikaona L (2004) An assessment of factors contributing to treatment adherence and knowledge of TB transmission among patients on TB treatment. *BMC Public Health* 4: 28.
- Szakacs TA, Wilson D, Cameron DW, Clark M, Kocheleff PMFJ, et al. (2006) Adherence with isoniazid for prevention of tuberculosis among HIV-infected adults in South Africa. *BMC Infect Dis* 6: 97.
- Munseri PJ, Talbot EA, Mtei L, Fordham von Reyn C (2008) Completion of isoniazid preventive therapy among HIV-infected patients in Tanzania. *Int J Tuberc Lung Dis* 12: 1037-1041.
- Mindachew M, Deribew A, Tessema F, Biadgilign S (2011) Predictors of adherence to isoniazid preventive therapy among HIV positive adults in Addis Ababa, Ethiopia. *BMC Public Health* 11: 916.
- Berhe M, Demissie M, Tesfaye G (2014) Isoniazid Preventive Therapy Adherence and Associated Factors among HIV Positive Patients in Addis Ababa, Ethiopia. *Adv Epidemiol* 6.
- Garcia Popa-Lisseanu MG, Greisinger A, Richardson M, O'malley KJ, Janssen NM, et al. (2005) Determinants of Treatment Adherence in

-
- Ethnically Diverse, Economically Disadvantaged Patients with Rheumatic Disease. *J Rheumatol* 32: 913-919.
15. Rosner F (2006) Patient Noncompliance: Causes and Solutions. *Mt Sinai J Med* 73: 553-559.
 16. Chambers SA, Rahman A, Isenberg DA (2007) Treatment adherence and clinical outcome in systemic lupus erythematosus. *Rheumatology* 46: 895-898.
 17. Muszbek N, Brixner D, Benedict A, Keskinaslan A, Khan ZM (2008) The economic consequences of noncompliance in cardiovascular disease and related conditions: a literature review. *Int J Clin Pract* 62: 338-351.
 18. WHO (2001) Global Strategy for Containment of Antimicrobial Resistance.
 19. Bonhoeffer S, Lipsitch M, Levin BR (1997) Evaluating treatment protocols to prevent antibiotic resistance. *Proc Natl Acad Sci* 94: 12106-12111.
 20. Haynes RB, Mcdonald H, Garg AX, Montague P (2002) Interventions for helping patients to follow prescriptions for medications. *Cochrane Database Syst Rev* 2: CD000011.
 21. Schneider J, Kaplan SH, Greenfield S, Li W, WI B (2004) Better Physician-Patient Relationships Are Associated with Higher Reported Adherence to Antiretroviral Therapy in Patients with HIV Infection. *Journal of General Internal Medicine* 19: 1096-1103.
 22. Getachew Y, Mekonnen W (2015) Correlates of adherence and utilization of Isoniazid preventive therapy in HIV patients. *JMID* 5: 45-50.