



ORIGINAL ARTICLE

Determinants of Isoniazid Preventive Therapy Completion among People Living with HIV in Oyo and Ogun States, Southwest Nigeria

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Keywords

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ABSTRACT

Background: The World Health Organization (WHO) recommends the use of Isoniazid Preventive Therapy (IPT) among People Living with HIV (PLHIV) to reduce morbidity and mortality from Tuberculosis (TB). This study assessed the rate of IPT completion and its associated factors among PLHIV in South West Nigeria.

Methods: A review of records of 1526 PLHIV who commenced IPT between October 2017 and December 2018 was done. Data were extracted from facility level IPT service documentation tools using study-developed data abstraction template. The chi-square test was used to assess the association between the independent variables and the patient's IPT completion status at 0.05 significance level. Logistic regression was used to determine the predictors of IPT completion.

Results: The mean age of the study population was 42.3±11.3 years and 1154 (75.6%) of them were females. About 1342 (87.9%) completed IPT within six months of initiation. Major reasons for non-completion of IPT were lost to follow up 86 (46.7%) and non-adherence to IPT 60 (32.6%). Higher proportion of respondents who were Igbo (92.9%), ART-naïve (97.6%) or active on ART regimen (94.8%) completed their IPT regimen within 6 months of initiation when compared to those of other tribes ($p=0.023$), ART experienced (87.7%), ($p=0.023$) or inactive on treatment (0.9%), ($p<0.001$) respectively. Traders/farmers were 6 times more likely to complete IPT compared to public/civil servants (AOR=6.110, 95%CI=2.180-17.112, $p=0.001$).

Conclusion: IPT completion rate was high among study participants. Intensified counselling on IPT benefits among ART patients with focus on civil/public servants might further improve IPT completion.

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INTRODUCTION

Globally, tuberculosis (TB) is the leading opportunistic infection (OI) among people living with HIV

(PLHIV).¹ The risk of developing TB among PLHIV is between 20 and 37 times greater than those without the infection.² The World Health

Organization (WHO) in response to the dual Human Immunodeficiency Virus (HIV) and TB epidemics recommended various TB/HIV collaborative activities, which include interventions such as Isoniazid Preventive Therapy (IPT), intensified TB case findings and TB infection control.³ These interventions aim to reduce morbidity and mortality from TB among PLHIV.²

Isoniazid preventive therapy has been known to prevent TB among PLHIV for many years. According to the WHO, PLHIV who screen negative to any of the TB symptoms, namely current cough, fever, weight loss and night sweat are unlikely to have TB and therefore should receive at least 6 months of IPT as part of a comprehensive package of HIV care.^{2,3} Several literature have documented the benefits of IPT in preventing TB among PLHIV and this has been proven to be enormous.^{4,5,6} A study conducted in the Northwest Ethiopia showed that provision of IPT for 6 months was significantly associated with reduction in the incidence of TB with individuals who were never on IPT to be 20 times more likely to develop TB compared with individuals who had IPT in the course of their ART⁷ while among pediatric age

group, a meta-analysis has also shown that IPT for 6 months will reduce incidence of TB by about 60%⁸ which could be higher if IPT uptake among PLHIVs is complemented with TB infection prevention and control.¹⁰

Despite its known benefit and efficacy, IPT uptake has remained low in most high burden TB countries.⁹ In 2016, out of 2.2 million PLHIVs newly enrolled on treatment, only about 940,000 were initiated on IPT globally.¹¹ Even though this figure is an improvement on the figures reported in previous years, IPT coverage is still less than 45% of PLHIV enrolled in care globally.¹¹ According to the 2017 global tuberculosis report, IPT coverage rate among newly enrolled PLHIV ranged from 2.4% to 73% among the 12 high TB burden countries that reported IPT data in 2016.¹¹ In the same report, Nigeria newly enrolled about 216,000 PLHIV in care in 2016 out of which approximately 62,000 were initiated on IPT giving a coverage rate of about 29%.¹¹ Coupled with the challenge of poor uptake is the low completion rate among the few PLHIV that were initiated on IPT. Documented evidence from the literatures shows an IPT completion rate of between 40-46%

among PLHIV, ^{9,12} which is grossly inadequate and could lead to the development of resistance to Isoniazid (INH) among PLHIV.¹³

Evidence from the TEMPRANO study, revealed that IPT and early ART initiation independently reduced the risk of developing serious HIV complications, most especially tuberculosis, and that receiving both early ART and IPT provided the best protection from HIV-related diseases.¹⁴ Findings from the post-trial phase of the TEMPRANO study showed that 6-month of IPT administered early in the course of HIV infection provides a durable survival benefit of about 40% reduction in mortality risk that was independent of the antiretroviral treatment during the period of follow-up.¹⁴

Studies on IPT implementation in Nigeria is still limited compared to some African countries where many processes of IPT implementation for PLHIVs have been explored.^{15,16,17} In 2018, a study conducted in a secondary health facility in Ogun State looked into the use of Quality Improvement (QI) approach to improve uptake and completion of IPT; the study outcomes demonstrated

tremendous improvement in IPT initiation and completion over a period of six-month among PLHIVs who received care and treatment services in the facility.¹⁸ This study however, found out that stock out of Isoniazid in the country at that time was a major barrier to the QI project performance while the concept of QI to improve IPT uptake and completion may be difficult in many facilities where there were no adequate human and financial resources.^{18,19} Furthermore, a study conducted in Oyo State explored challenges confronting IPT implementation for PLHIVs in a tertiary facility without exploring factors associated with IPT completion.¹⁹ Another study carried out in north-western Nigeria employed the concept of pharmacist-led patient education at service delivery points which revealed a significant improvement in IPT treatment adherence and treatment completion rates.²⁰ Though the study suggested that health care system and hospitals have opportunities to expand the role of pharmacists to improve the care of PLHIV with latent TB infection but it failed to also explore factors that are likely to determine IPT completion among PLHIVs.²⁰

This study therefore, aimed to assess rate of IPT completion among PLHIVs and explore factors that determine IPT completion among PLHIV in a development partner supported comprehensive ART sites in South West Nigeria. Findings from this study will help in the design of quality improvement initiatives to bridge identified gaps in HIV program to optimize IPT completion among PLHIVs. In addition, this study will inform evidence-based health policy on TB-HIV control and the design and implementation of context-specific interventions that will improve access and utilization of IPT among PLHIV in the national HIV program. Furthermore, it will inform evidence-based policy on TB control among PLHIV in the country and similar settings in sub-Saharan Africa.

METHODOLOGY

This was a cross-sectional study design that involved a review of service delivery records of PLHIVs on antiretroviral therapy who were commenced on 6 months Isoniazid Preventive Therapy (IPT) in eight selected sites in Oyo (4 sites) and Ogun (4 sites) states between October 2017 and December 2018. Oyo and

Ogun states are among the six Southwestern states carved out of the old Western region of Nigeria. While Oyo state had an estimated population of 7,840,864 as at 2016, with annual growth rate of 3.5%, Ogun State population was estimated to be 5,217,716 as at 2016 with annual growth rate of 3.5%.²¹ The vast majority of residents in both states are Yoruba, with Yoruba language being the dominant language. Oyo and Ogun states had a total of 14,500 and 12,600 PLHIVs active on antiretroviral treatment as at 1st October 2017 respectively. HIV prevalence in the states were 0.9 % and 1.4% for Oyo and Ogun states, respectively.²² HIV program in both states are being supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), with APIN Public Health Initiatives acting as the implementing partner in the states. Oyo State has 11 comprehensive ART sites comprising of 6 secondary health facilities, 2 tertiary health facilities, 3 mission hospitals while Ogun State has 13 comprehensive ART sites; 7 secondary health facilities, 2 tertiary health facilities, 2 mission hospitals and 2 Primary Health care centers. Comprehensive ART sites are health facilities providing full complement of

ART services including adult and paediatric ART, and Prevention of Mother to Child Transmission of HIV (PMTCT) services.

The first four high-volume comprehensive ART sites were selected from each state for the study. These health facilities constituted approximately 80% of PLHIVs accessing comprehensive ART services from each state. The study population were PLHIV on antiretroviral therapy who were commenced on IPT between October 2017 and December 2018. PLHIV who had no documentation of IPT initiation as written in the IPT register were excluded from the study. A total of one thousand, five hundred and twenty-six (1526) records of PLHIV who commenced INH between October 2017 and December 2018 were reviewed 6 months after initiation for IPT completion. IPT completion was defined as the number of PLHIVs on care and treatment that were eligible and placed on IPT with documented evidence of successful completion of the WHO recommended 6-months course of 300mg daily dose of Isoniazid (INH) for adults and 10mg/kg for the pediatric age group.²³

Based on standard of care for tuberculosis (TB) prevention in HIV positive population and as also recommended in the Nigeria National Guideline for HIV prevention, treatment and care, all PLHIVs on antiretroviral therapy are screened for TB at every clinic visit using a four-symptom-based algorithm at every clinic visit; history of fever, cough, weight loss, and night sweats, with a score of “1” assigned to each symptom.²⁴ PLHIV with score of “0” (i.e., with no symptoms) are termed non-presumptive for TB and are commenced on 300mg daily or 10mg/kg (pediatric) of INH prophylaxis for a period of 6 months, every 2 years. Presumptive patients, that is with score of 1 to 4, are referred for TB diagnostic test and commenced on anti-tuberculous treatment if confirmed TB positive while those that were negative commenced 6-months INH prophylaxis.

The study participants’ data were extracted from the electronic medical records (EMR) of selected facilities and the patients care cards/case folders using study designed excel-based data abstraction tool that elicited information on study outcome “patient’s INH completion status” and

covariates such as patients' sociodemographic characteristics such as sex, age, functional status, marital status, ethnicity, occupation; and patients' ART care history. The outcome of interest (patient's INH completion status) was defined as patients who started IPT within the review period and completed it within stipulated 6 months after initiation as stated in the 2016 Nigeria National Guideline for HIV Treatment and Prevention.²⁴

Data were collected by trained data clerk working in the facility under the supervision of the facility ART clinician. Data collected were entered, cleaned, and analyzed using SPSS IBM version 21. Data were summarized using summary statistics such as means, standard deviation and median for continuous variables, and using frequency and proportion for categorical variables. Association between outcome variable and exploratory variables were measured using independent chi-square statistical test at a p value < 0.05 significance level. Furthermore, logistic regression was done to ascertain predictors of IPT completion.

Ethical approval for the study was sought and obtained from the Oyo State Ministry of Health Ethical Review Committee through the office of the State AIDS & STI Program Coordinator (SAPC) with reference number AD 13/479 4277^A. The study involved analysis of secondary data and there was no contact with human subjects.

RESULTS

Table 1 shows the background characteristics of 1526 PLHIVs that were commenced on INH between October 2017 and December 2018 whose records were reviewed across eight selected sites in Oyo and Ogun states. The respondents mean age was 42.3 ± 11.3 years. A larger percentage of the respondents were female 1154 (75.6%) and of Yoruba ethnicity 1404 (92.0%). The majority were old ART experienced patients previously on care 1485 (97.3%) and active on ART drugs 1415 (92.7%). The majority of the respondents, 1342 (87.9%) completed Isoniazid preventive therapy (IPT) within six months of initiation while 184 (12.1%) did not complete the therapy. Of the 184 that did not complete the INH therapy, 86 (46.7%) had treatment interruption

(IIT) and 60 (32.6%) were due to non-adherence to IPT despite being active on ART. (Table 2)

Higher proportion of respondents who were Igbo (92.9%), ART-naïve (97.6%) or active on ART regimen (94.8%) as at the time of assessment, completed their IPT regimen within 6 months of initiation when compared to their colleagues that were of other tribes (p = 0.023), ART experienced (87.7%) (p = 0.023) or inactive on treatment

(0.9%), (p < 0.001) respectively. (Table 3) Logistic regression showed that traders/farmers were 6 times more likely to complete IPT compared to patients that were public/civil servants (OR = 6.110, 95% CI = 2.182 – 17.112, p = 0.001). Artisans and unemployed/Student also had a higher likelihood of completing IPT compared to Public/Civil servants although this was not statistically. (Table 4)

Table 1: Background characteristics of the respondents

Variables	Frequency (n=1526)	Percent
Age group (years)		
0-9	10	0.7
10-19	23	1.5
20-29	107	7.0
30-39	512	33.6
40-49	518	33.9
≥ 50	356	23.3
Sex		
Female	1154	75.6
Male	372	24.4
Ethnicity		
Yoruba	1404	92.0
Igbo	84	5.5
Hausa	9	0.6
*Others	29	1.9
**Occupation (n=1152)		
Public/Civil servant	711	61.7
Trading/Farming	364	31.6
Artisan	40	3.5
Unemployed/Housewife	37	3.2
ART Experience		
Previously on care	1485	97.3
ART Naïve	41	2.7
ART Retention Status		
Active	1415	92.7
Loss to follow up	88	5.8
Transferred Out	11	0.7
Dead	12	0.8

*Others include Tiv, Fulani.

** Patients occupation missing in some records

Table 2: IPT Completion rate and reasons for non-completion

Variables	Frequency	Percent
Completed IPT (n=1526)		
Yes	1342	87.9
No	184	12.1
Reasons for non-completion (n=184)		
Loss to follow up	86	46.7
Non-Adherence	60	32.6
Dead	13	7.1
Transferred Out	11	6.0
*Others	14	7.6

*Others – Adverse effect, drug misplacement, stopped (due to acute illness)

Table 3: Association between respondents' background characteristics and IPT completion

Variables	IPT Completed		Total	Statistical Indices
	No (n = 184)	Yes (n = 1342)		
	n (%)	n (%)		
Age group (years)				
0-9	2 (20.0)	8 (80.0)	10	$\chi^2 = 7.796,$ df = 5, p = 0.168
10-19	6 (26.1)	17 (73.9)	23	
20-29	17 (15.9)	90 (84.1)	107	
30-39	59 (11.5)	453 (88.5)	512	
40-49	64 (12.4)	454 (87.6)	518	
≥ 50	36 (10.1)	320 (89.9)	356	
Sex				
Male	51 (13.7)	321 (86.3)	372	$\chi^2 = 1.266,$ df = 1, p = 0.261
Female	133 (11.5)	1021 (88.5)	1154	
Ethnicity				
Yoruba	168 (12.0)	1236 (88.0)	1404	LR = 9.514, df = 3, p = 0.023
Igbo	6 (7.1)	78 (92.9)	84	
Hausa	1 (11.1)	8 (88.9)	9	
Others	9 (31.0)	20 (69.0)	29	
Occupation (n = 139, 1013)				
Public/Civil servant	94 (13.2)	617 (86.8)	711	LR = 8.507, df = 3, p = 0.037
Artisan	1 (2.5)	39 (97.5)	40	
Trading/Farming	37 (10.2)	327 (89.8)	364	
Unemployed/Student	7 (18.9)	30 (81.1)	16	
ART Experience				
Previously on care	183 (12.3)	1302 (87.7)	1485	LR = 5.206, df = 1, p = 0.023
ART naïve	1 (2.4)	40 (97.6)	41	
Active on Treatment				
Yes	74 (5.2)	1341 (94.8)	1415	$\chi^2 = 855.287,$ df = 1, p < 0.001
No	110 (99.1)	1 (0.9)	111	

Table 4: Predictors of IPT completion rate

Variables	Adjusted OR	95% C.I.		p-value
		Lower	Upper	
Ethnicity				
Yoruba*	1			0.905
Igbo	0.694	0.264	1.820	0.457
Hausa	0	0.000		0.997
Others	0	0.000		0.995
Occupation				
Public Servant *	1			0.005
Artisan	2.978	0.400	22.178	0.287
Trading/Farming	6.110	2.182	17.112	0.001
Unemployed/Student	1.106	0.273	4.479	0.887
ART Experience				
ART Naïve *	1			
Previously on Care	0.000	0.000		0.996
Active on Treatment				
No*	1			
Yes	0	0.000		0.994

*Reference group

DISCUSSION

This study assessed rate of IPT completion and factors that determine IPT completion among PLHIV in some selected APIN/PEPFAR supported comprehensive ART sites in Oyo and Ogun States, Southwest Nigeria. It is of note that 87.9% of respondents completed IPT within the stipulated six-month duration as recommended in the 2016 Nigeria National HIV guidelines for treatment and prevention.²⁴ IPT completion was higher in this study which was far above a similar study conducted in Tanzania where IPT completion was 58% which could be as a result of the National HIV test and treat program which culminated in deliberate demand creation for INH prophylaxis

in the study locations.²⁵ However, a significantly high IPT completion rate among PLHIV on ART is in keeping with findings obtained in studies from Kenya,¹⁷ Tanzania,²⁵ Ethiopia^{27, 30} and Brazil.²⁶ The high IPT completion rate in the study would surely reduce incidence of TB among PLHIVs and its associated morbidity and mortality while likelihood of PLHIVs developing INH resistance which is associated with poor IPT completion would as well reduce.

Furthermore, this study found many reasons responsible for failure to complete six-month INH prophylaxis which included development of treatment interruption (IIT), Non-adherence to INH prophylaxis, death, transfer out among others. Of all these

reasons for non-completion of INH, high lost to follow up and non-adherence constituted almost 80% of obstacles for IPT prophylaxis. Many studies allude to our findings of poor adherence to be among major barriers to INH prophylaxis completion^{12,27} but our study did not consider WHO HIV clinical stage, CD4 count and being on ART as variables of interest for poor INH prophylaxis completion during the study.^{9,12,27}

This study also explored the association between IPT completion and patients' background characteristics such as age of the patients, sex, ethnicity, occupation, ART experience and retention on ART. However, ethnicity, occupation and being newly initiated on ART were found to be associated with IPT completion among the study population which is different from a Tanzanian study in which the results indicated that patients who were already linked with ART services have an increased prevalence of IPT completion.¹⁶ In addition, lower prevalence of IPT completion was found among patients age 10-19 years in this study compared with older age groups which may be connected with the fact that most adolescents and young people

depend on parents or care givers for financial support to access health care services. This allude to a study that revealed higher IPT completion among patients age 25-34 year compared to 15-24 years which is in line with a study in Uganda,¹⁵ but contrary to the results found in Malawi²⁸ and Rwanda.²⁹

Furthermore, finding from the multivariate analysis showed that PLHIVs who engaged in trading/farming jobs were six times more likely to complete IPT within stipulated six months duration compared with public/civil servants. Other potential predictors of IPT completion such as ethnicity, ART regimen exposure and retention on ART before IPT commencement were not statistically significant. This is in keeping with a study conducted in Ethiopia in which subject age, sex, occupation, HIV stigma and discrimination and level of education on TB were not found to predict IPT adherence and completion among PLHIV.³⁰ The findings are also similar to other studies where adherence to IPT was predicted by patients on ART compared with patients yet to commence ART.^{28,31}

This study is not without some limitations. First, the findings of this study may not be generally applicable even in Nigeria as this study was carried out in Southwestern with relatively better-quality health services and good health indices compared to some other geopolitical zones.³² In addition, the study was conducted in facilities that are supported by implementing partners, which means they have access to financial and technical support from foreign donor agencies. Furthermore, other variables such as socioeconomic status, educational status and marital status (and couple's seropositive status) which all influence adherence were not measured in this study. Despite the limitations, this study can be of great use in national policy development and implementation. It shows the importance of proper documentation and, monitoring and evaluation. We recommend further studies both prospective and qualitative studies to explore long-term outcomes and the perspectives / experience of clients on IPT and comprehensive HIV service providers.

Conclusion: IPT completion rate was relatively high in the surveyed states which is as a result of the ongoing

deliberate program efforts to improve INH prophylaxis for PLHIVs. Patients working in government establishments or other private sectors have a lower likelihood of completing IPT compared to the self-employed patients (Artisans, farmers, etc.). Ethnicity, ART experience, and ART retention were significantly associated with IPT completion while farmers / traders were six times likely to complete INH compared to Public Servants. This study can be of great use in national policy development and implementation on TB prevention among PLHIV. It is very important to maintain increase in IPT completion to ensure PLHIVs are protected against TB disease. There should also be a targeted intervention to be developed to assist patients with lower IPT completion especially adolescents and young people living with HIV.

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