

Isoniazid Preventive Therapy Adherence and Its Predictors Among Soldiers on HIV Antiretroviral Therapy at a General Military Hospital in Uganda

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Background: Uganda faces a significant dual challenge with tuberculosis (TB), ranking among these countries most affected by the disease worldwide. The World Health Organization (WHO) recommends isoniazid preventive therapy (IPT) for managing latent TB. However, the adherence to IPT in military settings remains under-explored in Uganda. This study aims to assess IPT adherence and identify its predictors among soldiers undergoing HIV antiretroviral therapy at a General Military Hospital in Uganda.

Methodology: We conducted a cross-sectional study involving 300 HIV-positive soldiers receiving antiretroviral therapy (ART) at the General Military Hospital in Uganda. Due to the small sample size, we employed a consecutive sampling method. We utilized descriptive statistics and modified Poisson regression model for prevalence of IPT adherence and associated factors respectively.

Results: Among the 300 clients, the prevalence of isoniazid preventive therapy (IPT) was 94.7%, 95% CI: 92.1–97.2; adherence to IPT was associated with being aged ≥ 50 years, with a prevalence ratio (PR) of 1.061 and 95% CI: 1.01–1.12; being married, with a PR of 1.438, 95% CI: 1.12–1.84; having social support, with a PR of 1.498, 95% CI: 1.17–1.92; and having social support played a significant role in IPT adherence among married participants, with a PR of 0.817, 95% CI: 0.72–0.93.

Conclusion: To enhance adherence to isoniazid preventive therapy among young soldiers with HIV, targeted interventions are crucial, as older individuals tend to adhere better. Implementing marital support programs and strengthening community engagement can bolster adherence through social support networks. Educational campaigns should focus on the importance of IPT, while regular follow-ups will ensure effective monitoring and support. Further research is needed to explore how social support can mitigate stigma associated with HIV. The findings highlight the importance of improving IPT adherence among married soldiers and suggest that this approach could be effective in other low-resource settings.

Keywords: IPT, adherence, TB, HIV, soldiers, ART

Introduction

Tuberculosis (TB) remains the leading cause of death among people living with HIV (PLHIV). In 2019, TB accounted for an estimated 30% of the 690,000 AIDS-related deaths in the world. These 208,000 deaths represented approximately 15% of the 1.4 million TB deaths that year.¹ The risk of developing TB among the millions of people living with HIV (PLHIV) is 18 times greater than among the rest of the global population.² An estimated eight percent of the reported TB cases in 2020 were among PLHIV, and 214,000 TB deaths were among HIV-positive people.³ Sub-Saharan Africa carries the greatest burden of HIV/TB co-infection, with 95% of global TB deaths and more than 70% of the global HIV burden.⁴ Uganda has a high burden of tuberculosis and HIV, and less than 2% of people with HIV had received IPT by 2018.⁵ Anti-retroviral therapy (ART) dramatically decreases the chances of developing TB.⁶ Nonetheless, individuals undergoing chronic ART care are still deemed highly susceptible to contracting TB.⁷ Isoniazid preventative therapy

(IPT), and antiretroviral therapy (ART), has been found to reduce the burden of TB in people living with HIV (PLWHIV).⁸

In 2018, the Uganda Ministry of Health (MOH) Uganda guidelines, recommended IPT for HIV positive children and adults who do not have TB in a dosage of 10mg/kg/day (max 300mg/kg) and 5mg/kg/day (maximum 300mg), respectively. Prophylaxis of isoniazid takes six months.⁹

The combination of IPT and ART may give rise to adherence issues. The extended duration of therapy, apprehension about a high pill burden, potential adverse effects and perceived low risk of TB may all contribute to challenges in adherence. However, it is crucial to emphasize that adherence to isoniazid preventive therapy (IPT) is essential for achieving optimal outcomes.¹⁰ Non adherence to IPT leads to substantial economic costs, as it contributes to a higher incidence of tuberculosis among soldiers. This in turn, results in increased expenditure on medical care, heightened morbidity rates, and ultimately leads to suboptimal health outcomes.¹¹ In South Africa, a cross-sectional study with an overall self-reported adherence rate of 72% was conducted. In contrast, a similar study on IPT adherence among HIV patients showed an adherence rate of 84% in Uganda.⁹ Expenses related to TB medication, difficulty obtaining medications, lengthy queues, drug shortages, pill burden, adverse side effects and the lack of service integration have all been identified as factors that can disrupt adherence to IPT guidelines among uniformed men and women in the military.¹² These individuals bear the crucial responsibilities of ensuring security, contributing to nation building, and maintaining peace, in various parts of sub-Saharan Africa. The co-infection of HIV and TB poses a substantial threat to military effectiveness in the region.¹³ While extensive research exists on IPT adherence in various high-burden settings, there remains a substantial gap in understanding adherence among military personnel. This study aims to address this gap by investigating IPT adherence specifically at the General Military Hospital in Bombo, Uganda. The novelty of this research lies in its focus on a unique population uniformed personnel who may face distinct challenges affecting their adherence to treatment. Thus, the primary objective is to assess IPT adherence and identify its predictors among soldiers undergoing HIV antiretroviral therapy at this military hospital, offering valuable insights that could inform tailored adherence strategies in similar contexts.

Methods

Study Design and Setting

The study design was a hospital based cross-sectional study that took place in the TB/HIV clinic at the General Military Hospital (GMH) in Bombo.

Study Area

The study area was the Bombo district, approximately 32km from Kampala, the capital of Uganda. The hospital is a referral centre for various health units within the Uganda Peoples Défense Forces (UPDF).¹⁴ The General Military Hospital boasts a capacity of 150 beds, catering to an annual population of approximately 15,000 inpatients. The hospital provides various services, including outpatient, inpatient and specialized care. The primary care recipients at the hospital include military personnel, their families, and civilian communities near the barracks.¹⁴ As of 2022, more than 5082 HIV-positive soldiers are under care at General Military Hospital, and more than 4000 soldiers are receiving IPT. The facility routinely records self-reported adherence data in the database during each client's clinic visit.

Study Population

Eligible participants consisted of soldiers living in and around Bombo barracks who were enrolled in IPT, receiving chronic care at Bombo General Military Hospital, and provided informed consent. Those who were seriously ill, transferred, or had completed their IPT treatment were excluded from the study. To enhance the small initial sample size, consecutive sampling was employed; thus, patient meeting the eligibility criteria during isoniazid refills at the TB/HIV clinic was invited to participate and gave their consent for the study.

Outcome Variables

Adherence was classified as “Yes=1” for good adherence and “No=0” for nonadherence. Various evaluation methods were outlined in the national HIV guidelines for chronic care patients. However, this study opted for a self-reporting approach because of its speed, cost-effectiveness, and common usage in military HIV and TB clinics for assessing isoniazid preventive therapy (IPT) adherence. The self-reporting involved asking clients about any missed doses to gauge adherence levels. Questions were designed to be non-threatening and sensitive, ensuring the collection of accurate information. This method was considered suitable for all clients.¹⁵

Adherence was assessed based on the previous 28 days of IPT intake. Missing fewer than 2 doses indicated $\geq 95\%$ adherence, classified as good adherence and coded as “Yes=1.” Conversely, missing 2 to 4 doses corresponded to 85–94% adherence, and missing 5 or more doses indicated $< 85\%$ adherence, both categorized as poor adherence and coded as “No=0.”

Predictor Variables

The study examined various independent demographic factors that influenced individuals’ decisions to adhere to isoniazid (INH) therapy. Key variables included age groups (18–39, 40–49, and 50+), sex (male and female), marital status (married or not), and education levels (never attended school, primary, secondary, and tertiary). Factors like fear of INH side effects, fear of IPT pill burden, and knowledge of IPT were also considered. Social support was assessed for its impact on treatment decisions. The study explored decision-making influences from healthcare providers, patients, and social circles. Additionally, it examined the effects of follow-up calls by caregivers and counseling on adherence, as well as factors related to deployments that affected accessibility and adherence. This analysis aimed to clarify the complex interplay of these variables in isoniazid (INH) therapy adherence.

Sample Size Estimation

We estimated the sample size using the Fleiss formula for two proportions.¹⁶

$$N = \frac{\left[z_a \sqrt{P(1-P) \left(\frac{1}{q_1} + \frac{1}{q_2} \right)} + z_\beta \sqrt{p_1(1-p_1) \frac{1}{q_1} + p_2(1-p_2) \frac{1}{q_2}} \right]^2}{(p_1 - p_2)^2}$$

where p_1 is the proportion of male patients who adhered to IPT in a prior study conducted in Ethiopia, which was 0.94; p_2 is the proportion of female patients who adhered to IPT in a previous study in Ethiopia, which was 0.88;¹⁷ q_1 is the assumed male proportion in the study (80%) and q_2 was the assumed proportion of females in the study (20%). $P = p_1q_1 + p_2q_2$, and N was the total calculated number of participants. We set the power at 80.0% ($z_\beta = 0.84$); and the alpha at 0.05 ($z_a = 1.96$). Therefore, the initial estimated sample size was approximately 472. However only 300 participants were interviewed, as some individuals were transferred to different stations. This resulted in a reduction in the number of available clients, corresponding to a study power of 77%.

Data Collection Procedures

The data were collected over a period of one month, from 10th September to 10th October 2022. All HIV-positive soldiers who came to the HIV/TB clinic site for services and were still active on IPT were informed about the study; those who were eligible and interested in the study consented and were consecutively enrolled. We interviewed approximately 8–10 participants daily at the clinic site. The eligibility criteria included being an adult soldier (18 years or older), being HIV-positive and receiving antiretroviral therapy (ART) and isoniazid preventive therapy (IPT) care at General Military Hospital, Bombo. Soldiers who were severely ill, those transferred to other stations, or those who had completed their isoniazid preventive therapy (IPT) treatment were excluded from the study. Each participant completed out a structured questionnaire providing self-reported information upon enrolment. The questionnaires were translated into Kiswahili and pretested with 10 randomly selected clients. The data were collected by registered nurses who were trained in the study procedures and had experience in TB/HIV treatment services.

The study endpoints were IPT adherence and its associated factors in the last 28 days of treatment. Participants who needed counselling services received support and assistance from the research team, including both the services themselves and social support.

The structured abstraction tool was pretested on 10 clients at Bombo General Military Hospital, especially the TB/HIV clinic to determine the problems that may be expected during data collection and how to overcome them. This helped to determine the appropriateness of the tool to capture every aspect of the study.

The research assistants underwent a minimum of two days of training before commencing the data collection. Regular cross-checking, inspection and scrutiny of the information were conducted to ensure the accuracy, consistency and uniformity of the data collected by the principal investigator.

Statistical Analysis

The data were collected using Epidata client (v4.6.0.6); and then transferred into an Excel spreadsheet and later to STATA 14.0 for analysis.¹⁸ The data were summarized using descriptive texts, tables and figures. Continuous variables, such as age, were presented as both the mean, standard deviation (SD) and the median. Categorical variables were summarized in terms of frequencies, confidence intervals, and proportions. In order to determine the population prevalence using descriptive analysis, the percentage of participants who adhered to isoniazid preventive therapy was calculated, along with the 95% confidence interval.

All variables with p-values < 0.2 and those known to influence isoniazid preventive therapy (IPT) adherence, such as fear of isoniazid side effects, social support, age 50+ years, sex, marital status and secondary education were entered into the multivariable modified Poisson regression model of family Poisson and link log with robust standard errors to adjust for overinflated variances. A p value of < 0.05 was considered to indicate statistical significance. The association between IPT adherence and the predictors was measured by the prevalence ratio (PR) with a 95.0% confidence interval (CI) at both the bivariate and multivariate levels. We assessed interactions and confounding factors, considering all variables that resulted in a $\geq 10.0\%$ change in the prevalence ratio of both the crude and adjusted models as confounders.

Ethical Considerations and Guidelines

This study was carried out in accordance with research guidelines and ethical standards of the Makerere University School of Medicine Research and Ethics Committee (SOMREC), accredited by the Uganda National Council for Science and Technology (UNCST) with approval number 2022–401. This study adhered to the SOMREC guidelines for human subjects research, which include: informed consent, confidentiality anonymity, respect for autonomy, non-maleficence, beneficence and justice. These guidelines align with international ethical principles, such as the Declaration of Helsinki and Belmont Report, ensuring the protection of the rights and dignity of participants.

Results

Description of Study Participants

A total of 300 participants were recruited into the study.

The mean age and age interquartile range (IQR) of the participants was 41.33(\pm SD 10.72) and 17(33–50) respectively; the majority were male, and were married and had attained primary education. [Table 1](#).

Individual Beliefs, Family and Social Factors, and Health Worker Related Factors

There was no fear of the side effects of isoniazid (INH), knowledge about IPT therapy, no fear of pill burden, no deployment or assignment of tasks at different stations during treatment, no social support, decisions made by the families to start INH, decisions by the doctors, follow-up calls by caregivers, and counselling on adherence to IPT. [Table 2](#)

Prevalence of Adherence to IPT

The prevalence of self-reported adherence to IPT among soldiers was 94.7%; 95% CI (92.1–97.2).

Table 1 Demographic Characteristics of 300 Soldiers on ART and IPT at General Military Hospital

Characteristics	Number or Median, % or IQR
Median (IQR) age in years	41(33–50)
Age in years	
18–39	139 (46.3)
40–49	83 (27.8)
50 above	78 (26.0)
Sex	
Male	185(61.7)
Female	115 (38.3)
Marital status	
Married	218 (72.7)
Not married	82 (27.3)
Education level	
Never	25(8.3)
Primary	126(42.0)
Secondary	110 (36.7)
Tertiary	39(13.0)

Table 2 Individual Personal Beliefs; Family and Social Factors of 300 Soldiers on ART and IPT at General Military Hospital

Characteristics	Number (Percentage)
Fear of INH side effects	
Yes	77 (25.7)
Knowledge on IPT	
Yes	244 (81.3)
Fear of IPT pill burden	
Yes	67(22.3)
Social support	
Yes	112(37.3)
Decision to take INH	
Doctor	76(25.3)
Patient	74(24.7)
Family	107(35.7)
Friends	43(14.3)
Follow up calls by the care givers	
Yes	213(71.0)
Counselled on adherence	
Yes	260(86.7)
Deployments	
Yes	44 (14.7)

Table 3 Multivariate Analysis of Factors Associated with IPT Among Soldiers on ART and IPT at the General Military Hospital

Factors	Prevalence Ratio	95% CI	P value
Age in years			
18–39	Ref	Ref	
40–49	0.981	0.91–1.06	0.613
50+	1.061	1.01–1.12	0.030
Social support			
Yes	1.498	1.17–1.92	0.001
Marital status			
Yes	1.438	1.12–1.84	0.004
Social support*Marital status	0.817	0.72–0.93	0.002

Notes: Bolded- indicates statistically significant variable.

Abbreviation: Ref- reference; CI-confidence interval.

Factors Associated with IPT Adherence

The factors that were independently associated with adherence to IPT in the last 28 days, were being 50 years and older, marital status, social support and an interaction factor between social support and marital status. [Table 3](#).

Discussion

Among HIV-positive soldiers receiving ART at Bombo Military Hospital in Uganda, our objective was to find out how common IPT adherence was and what factors were linked with it. Of the study participants, 94.7% had taken at least $\geq 95\%$ of the recommended isoniazid doses in the 28 days prior to the study, according to our findings. A number of factors, including age 50 and beyond, social support, availability of counselling services, marital status, and social standing particularly among married clients, are linked to IPT adherence.

This study revealed a greater prevalence of adherence to IPT. This suggests that the military excels in streamlining policies; the discipline instilled in soldiers to follow orders, may have contributed to the seamless implementation of IPT uptake among them. A study conducted in Thailand reported a low percentage of HIV-infected individuals (81.8% by pill count).¹⁹ This variation could be explained by the manual pill count monitoring used in Thailand which is more objective than self-reported adherence in this study, and differences in policy implementations because the countries are on different continents.

Participants aged 50+ years were significantly more likely to adhere to IPT. This finding implied that the older soldiers were more likely to adhere to IPT treatment than the younger soldiers were. This finding is in agreement with a study performed in Botswana, which found that the younger age group did not obey the norms of IPT policies.²⁰ Given these results, targeted interventions and education programs should be developed to specifically address relatively young age group's lack of adherence to IPT policies.

The study further revealed that having social support was independently associated with adherence to IPT. This finding implies that having social support increases the likelihood of adhering to IPT. This finding is consistent with a report from a study by Munseri et al that reported that family and other support systems significantly influence adherence.²¹ The study revealed that soldiers who adhered to IPT were more likely to have approval from both family and spouses for their decision to take IPT. This finding aligns with reports from a study by Gust et al, indicating that patients rely on the support of their families and friends. This suggests that personal connections and shared experiences play a significant role in motivating individuals to take proactive measures against TB. This highlights the need for increased awareness and education to combat the misconceptions surrounding TB and promote a supportive environment for those seeking treatment.

The study revealed that being married was associated with adherence. This finding implies that having a partner or spouse increases the likelihood of adherence to IPT. This finding aligns with a study conducted in South Africa across 14 public primary care clinics in Matlosana. The study revealed that participants with a partner or a spouse were motivated to

adhere to preventive therapies.²² These findings imply that social support from a partner significantly contributes to fostering adherence to IPT. It is conceivable that a supportive relationship offers individuals the essential encouragement and reminders needed to consistently follow their preventive therapies.

The study also revealed that the interaction between social support and marital status, was associated with adherence to IPT. This implies that, married soldiers living with HIV who received social support were more likely to adhere to IPT. However, no literature has shown, the role of social support for improving IPT adherence among married people living with HIV.²³ Understanding the available social support for married people living with HIV reveals the importance of people within their social network that could be pivotal to improving their retention in care and adherence to medications and direct links between disclosure and support within families and the broader community. The adherence of married clients to their treatment regimen can be attributed to the pivotal role of social support, particularly from their families, which encompasses various forms, notably emotional support.

Study Strengths and Limitations

This study is among the first to evaluate the prevalence of IPT adherence and related factors among soldiers living with HIV in a low-income country like Uganda. Our results, therefore, may be used as a baseline to inform the implementation of IPT programs among such populations in a similar setting.

Initially, adherence to IPT was measured using self-reported methods, which are often subject to recall and social desirability biases. To address this issue, adherence was assessed based on the previous 28 days of treatment, allowing clients to easily recall their experiences. This approach minimized recall biases and the tendency toward impression management, ultimately mitigating the impact of social desirability biases. The study faced limitations due to a small participant enrolment; however, adjustments to its power helped address this challenge. The reported findings offer valuable insights into the factors that affect adherence to IPT, highlighting the complex variables at play despite the obstacles encountered. The findings provide important insights into the factors influencing adherence to IPT, revealing the complexity of the issues involved. They underscore the necessity for additional research, particularly focusing on HIV-related factors not explored in the study. Future research should consider incorporating qualitative methods to better understand the experiences and perspectives of individuals facing challenges with treatment adherence. This approach could lead to more effective strategies for supporting people living with HIV in their treatment journey.

Conclusion

The adherence of IPT was notably high among soldiers. The factors associated with adherence to IPT among HIV-positive soldiers on ART included age, marital status, social support and the significant influence of social support, particularly in the case of married soldiers. These findings suggest that the emotional and practical support a spouse provides, can positively impact medication adherence. Married soldiers may benefit from their partner's encouragement and reminders to take their medications regularly. Age also played a role, with older soldiers, demonstrating higher adherence rates, perhaps due to increased maturity and responsibility. These results highlight the importance of considering psychological factors when designing interventions to improve adherence to IPT among HIV-positive soldiers on ART.

Recommendations

Military leaders should strengthen social support to improve adherence to IPT among young HIV-positive soldiers. Additionally, future longitudinal studies are necessary to explore the relationship between various factors, including the duration of IPT and HIV related factors, which were not addressed in this research. The cross-sectional study design in this investigation restricts the ability to assess these associations over time.

Data Sharing Statement

The data associated with this study are available at: <https://datadryad.org/stash/share/m8Qzp45tRa4VO9BXS2tQMNXs0prE9-DsOzv5pPRazPU>.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there are no conflicts of interest regarding the publication of this article.

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