

Research Article

Tuberculosis Co-infection among HIV/AIDS Cases Attending an Anti-retroviral Therapy Center: A Retrospective Cohort Study from Pakistan

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Abstract

Objective: The co-occurrence of tuberculosis (TB) and human immunodeficiency virus (HIV) results in heightened morbidity and mortality, placing an increased burden on healthcare systems. This study aims to assess the incidence and identify associated risk factors for TB/HIV co-infection, with the objective of enhancing the survival rates of co-infected patients in Pakistan.

Methods: This retrospective cohort investigation took place at the Anti-Retroviral Treatment Center in Islamabad, Pakistan. Data spanning a decade (January 2006 to December 2016) were extracted from 2,542 people living with HIV using a pre-tested data extraction tool.

Results: Following the exclusion of 156 ineligible participants, records of 2,386 individuals were analyzed over 4,433 person-years. The cumulative incidence and incidence rate of TB among HIV/AIDS patients were 446 (18.7%) and 0.001 cases/10,000 person-years, respectively. The majority (81%) of incident TB cases occurred within one year, predominantly manifesting as pulmonary TB. Of the TB-infected individuals, 98.6% received TB medication, with 0.7% prescribed Isoniazid prophylaxis. Significant associations with TB were identified in relation to work abroad history, patient age, and current HIV stage ($P < 0.05$). Binary logistic regression indicated a 3.1 times higher likelihood of TB infection in the anemic group compared to the non-anemic group. HIV/AIDS infection emerged as a consistent TB risk factor irrespective of CD4 count and WHO HIV staging.

Conclusion: This study highlights a substantial incidence of TB co-infection among HIV patients in Pakistan, emphasizing the need for comprehensive efforts by the National AIDS Control and National TB Control Programs to effectively manage co-infection.

Keywords: person-year, association, risk factors, people living with HIV, low-middle income country

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1 INTRODUCTION

It is estimated that the risk of acquiring tuberculosis (TB) is 26 to 31 times higher in patients with human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) than in those without HIV/AIDS^[1]. HIV infection poses susceptibility towards active TB disease, and

itself is a risk factor for recurrence of latent TB to active TB state^[2]. By the end of 2013, globally, around one and a half million people died due to HIV/AIDS-associated disease complex, 35 million people were living with HIV/AIDS, and about two million new cases had been detected^[3].

TB has been documented being moderately high among

the patients suffering from HIV/AIDS, killing one out of every three persons infected with HIV/AIDS. Children having TB and HIV together had 47% more chances of dying as compared to HIV negative TB children. A few studies have documented 13% case fatality rate (CFR) among those who had TB-HIV/AIDS co-infection^[4-7]. For TB alone, WHO reports that 1/3 of the global population is infected with latent TB, and on an average, about three million people die from TB every year^[8,9]. Among 22 high endemic countries, Pakistan remained at fifth place for the last a few years^[10]. Out of 27 high-burden drug-resistant tuberculosis countries, Pakistan ranks eighth among them^[11].

Worldwide, the prevalence of HIV and TB co-infection is on a rise. Ninety percent (90%) of the co-infected people are living in developing countries^[12,13]. TB is the frequent opportunistic infection, and a cause of mortality for those people who have had concomitant HIV/AIDS (up to 28% among those who are infected with HIV/AIDS)^[13,14]. Once infected with HIV, the lifetime risk of developing TB ranges between 10-20%^[15,16]. While in people co-infected with HIV and TB, the annual risk could exceed 10%^[17-19]. The threat of developing TB is estimated to be between 26-31 times more among people living with HIV (PLWHA) than those living without HIV/AIDS infection^[20].

At CD4⁺ lymphocyte count <200/mm³, there is high likelihood of acquiring TB, making the person with HIV/AIDS most susceptible to the concomitant infection of tuberculosis^[21]. Clinical picture of Tuberculosis in HIV/AIDS infected people depends on the immune-suppression level-results of the patients. In individuals with comparatively intact immune function with CD4⁺ lymphocyte count of more than 200/mm³, pulmonary tuberculosis is more frequent than extra pulmonary TB^[22,23].

Among people who have recently acquired TB, and within those with the latent disease, HIV/AIDS is the most prominent risk factor for emergence of latent TB infection into active TB disease. HIV/AIDS infected TB patients suffer from other HIV/AIDS-related health issues as well^[24].

Countries with high burden of tuberculosis have been reporting an excess CFR among both the smear positive and smear negative cases of TB with varying percentages^[25]. Latest diagnostic methods, such as geneXpert could improve diagnostic sensitivity and specificity among PLWHA^[26].

During 2011, the USA saw 9% new cases of TB, and 13% of cases of TB worldwide, which were co-infected with HIV/AIDS infection^[27]. Of the 15 countries with the highest numbers of HIV and TB co-infection among adults, 12 are in Africa and the rest are in Asia^[24-28]. Africa alone has recorded 50% of HIV/AIDS infection among TB patients^[28]. According to WHO, almost 45,000 people had

developed drug-resistant TB around the world by 2012. Out of which, 9.6% of cases were of multi-drug resistance TB (MDR-TB). Among 27 high-burden and drug-resistant TB countries, Pakistan is ranked eighth^[11]. We conducted this retrospective cohort study to calculate incidence and incidence rates of HIV/AIDS and HIV/AIDS TB co-infection, and to determine its associated risk factors for TB among PLWHA.

2 METHODS

Our study design was the retrospective cohort study. We analysed data for the past 10 years from January 2006 to December 2016 of Anti-Retroviral Therapy (ART) Center at a major tertiary care hospital in Islamabad, Pakistan. We developed "Data Extraction Tool" consisting of socio-demographic indices, TB co-infection, and its associated risk factors such as patient age, gender, marital status, spouse HIV/AIDS status, patient education, occupation, HIV/AIDS exposure, history of use of substance of abuse (intravenous drug use), and history of sexually transmitted infections; laboratory diagnostics such as TB diagnostic tests, viral load, CD4 level; WHO clinical stage of HIV/AIDS, sputum test, treatment received, use of Isoniazid (INH) prophylaxis, ART regimen, overall health status defined as "*health is a state of complete physical, mental, and social well-being, and not the mere absence of disease or infirmity (WHO), and being alive at the last visit (survived).*" Records with incomplete information were excluded. Data were entered and cleaned in MS Excel. Analysis was done by using the statistical software SPSS version 21. We calculated frequencies, used Chi-squared test and logistic regression to find any association between independent and dependent variables while controlling for any potential confounders at the same time. We used a *P* less than 0.05 being significant at 95% confidence level.

3 RESULTS

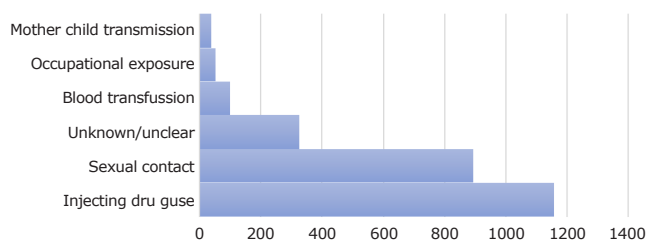
3.1 Summary of Results

We reviewed a total of 2,542 PLWHA medical records from January 2006 to December 2016. One hundred fifty-six (156) were excluded from the analysis due to incomplete information. The cumulative incidence and incidence rate of TB among HIV/AIDS patients was 446 (18.7%) with an incidence rate of 10 cases/100 Person Years, respectively.

Socio-Demographic Indices and Economic Characteristics of PLWHA: Table 1 gives the details of the socio-demographic profile of the patients. There were more males than females, and a few were transgender. Most of them were either unemployed or had a history of working abroad. Table 2 gives the percentage of the respondents by place of work abroad. Substance abuse was common. About one-fourth had a partner with known HIV status, and a few also had children infected

Table 1. Socio-Demographic Incidences of PLWHA

Variables	Number (n)	Percentage (%)	Variables	Number (n)	Percentage (%)
Gender			History of working abroad		
Male	2,017	84.5	Yes	481	20.2
Female	360	15.1	No	1,905	79.8
Transgender	9	0.4	Current work status		
Age group			Unemployed	1,800	75.4
≤15	65	2.7	Employed	338	14.2
16-30	1,035	43.4	Housewife	248	10.4
31-45	989	41.5	H/O substance use		
46-55	221	9.3	Yes	1,645	68.9
>55	76	3.2	No	741	31.1
Marital status			Spouse HIV/AIDS status		
Single	863	36.2	HIV+	396	26
Married	1,339	56.1	HIV-	377	24.8
Divorce/Separated/ Widow	184	7.7	Unknown	750	49.2
Education			No of kids		
Illiterate	881	36.9	≤4	2,132	89.4
Primary	807	33.8	>4	254	10.6
Secondary	481	20.2	Kids infected with HIV/AIDS		
College level	217	9.1	Yes	30	1.3
Work status when diagnosed with HIV/AIDS			No	2,356	98.7
Unemployed	1,684	70.6			
Employed	438	18.4			
Housewife	264	11.1			

**Figure 1. Exposure to HIV/AIDS.**

with the HIV infection. Majority of those had the working abroad history of the UAE.

Injecting Drug Users and the sexual contact were the most frequent exposures to the HIV/AIDS among the study participants: 1157(48.5%) and 893(37.4%)(Figure 1).

3.2 Base Line Clinical and HIV-related Characteristics of PLWHA

Out of the total, 2,065 (86.5%) of the study participants, HIV/AIDS diagnosis was made by ELISA. 850 (35.6%) of the participants had a baseline WHO clinical stage I or II, while, for 385 (16.1%) the disease stage was undocumented or unknown. Overall, the clinical stage for 1405 (58.9%) of the patients was missing in the records. The baseline CD4 lymphocyte count in 795 (33.3%) of the

patients was 200 to 500 (cells/mm³). For 269 (15.5%), it was not done. At the time of registration, 1,128 (47.3%) of PLWHA were found anemic. The average baseline median viral load of respondents at the enrolment was 26,731 (IQR 2,60,098), [range 55-35,777,633]. By the end time of follow-up of the patient, it was 10,733 (IQR 1,66,342), [range f53 to 14,862,985]. It was observed that initial viral records were recorded in 410 patients, while at the end of follow-up, the record was found for 133 of the patients only (Table 3).

Adherence to Therapy: Co-trimoxazole was recommended for one-third (33.2%) of the respondents. Approximately half (55.4%) were provided with an Antiretroviral Therapy (ART) regimen, with the majority (93.4%) being on first-line drugs. Among the respondents, 1,265 (53%) were able to correctly identify their ART regimen dose. Proper intake of the regimen without missing a dose was observed in 37.3% of them. Only one-fourth (24.1%) of the respondents adhered to their scheduled visits.

The lost-to-follow-up rate for drug therapy was 61.8%. The primary reasons for being lost to follow-up were relapse (followed by transfer out at 13.5% and death at 10.6%) as indicated in Table 4.

Table 2. Percentage of PLWHA Worked Abroad

Place of work abroad	n (%)	Place of work abroad	n (%)	Place of work abroad	n (%)
Afghanistan	5 (1.05)	India	1 (0.21)	Oman	3 (0.63)
Africa	41(8.61)	Iran	6 (1.26)	Portugal	1 (0.21)
America	9 (1.89)	Iraq	1 (0.21)	Qatar	6 (1.26)
Bahrain	7 (1.47)	Ireland	1 (0.21)	Spain	1 (0.21)
Canada	3 (0.63)	Italy	1 (0.21)	Thailand	6 (1.26)
China	3 (0.63)	Japan	2 (0.42)	Turkey	2 (0.42)
France	2 (0.42)	Kango	1 (0.21)	UAE	324(68.07)
Germany	2 (0.42)	Korea	4 (0.84)	UK	15 (3.15)
Greece	2(0.42)	Kuwait	6 (1.26)		
Hong Kong	6 (1.26)	Malaysia	15 (3.15)		

Table 3. Base Line Clinical and HIV Related Characteristics of PLWHA

Variable	Number (n)	Percentage (%)	Variable	Number (n)	Percentage (%)
Test for HIV diagnosis			Current HIV stage		
Elisa	2,065	86.5	I or II	537	22.5
Rapid test	89	3.7	III	265	11.1
Other	232	9.7	IV	179	7.5
Initial CD4 count (cells/mm ³)			Not known	1,405	58.9
>500	670	28.1	Initial HB level		
200-500	795	33.3	Anemic	1,128	47.3
<200	552	23.1	Non anemic	555	23.3
Not done	269	15.5	Not done	703	29.5
Current CD4 count (cells/mm ³)			Current HB level		
>500	438	18.4	Anemic	267	11.2
200-500	383	16.1	Non anemic	150	6.3
<200	171	7.2	Not done	1,969	82.5
Not done	1,394	58.4	Blood glucose		
Initial HIV stage			Normal	76	3.2
I or II	850	35.6	Low	23	1
III	551	23.1	Diabetic	26	1.1
IV	600	25.1	Not done	2,261	94.8
Not known	385	16.1			

3.3 TB Incidence in People Living with HIV/AIDS

Cumulative incidence of TB among people living with HIV/AIDS: Cumulative incidence of TB among HIV/AIDS patients was 446/2,386 (18.7%) over the follow-up duration.

Follow-up Person Years of people living with HIV/AIDS: We found that more than half of 1,474 (61.8%) of the participants dropped out of the records due to death, relapse, non-adherence, transferred out, and some other reasons. Only for 912 (38.2%) patients, records were found complete. 2,386 study participants were followed for different periods in the follow-up for a total of 4,433 years. The mean observation period was 1.86±1.93 years. Study participants stayed in the follow-up for a minimum of <1 year and a maximum of 10 years.

The Incidence rate of TB among people living with HIV/AIDS: We calculated the TB incidence rate for the follow-up period as 0.001 cases per 10,000 person-years. Out of a total of 446 new TB cases, 362 (81%) occurred within one year of registration in the record. The total incident rate for TB cases was calculated as person years.

Table 5 shows disaggregated data showing majority (87%) of the incident TB cases being males. Out of the total, 423 (94.8%) of the chest X-Rays were positive, while 256 (57.3%) had positive sputum AFB smear. 327 (73.3%) were having confirmed pulmonary TB. Out of 446 TB-infected persons, 440 (98.6%) received medication for TB. During the follow-up, INH prophylaxis was prescribed to 17 (0.7%) of the respondents.

Associated factors for TB in PLWHA: Cross-tabulation between TB status and associated factors (Table 6)

Table 4. Adherence to the Treatment Regimen of PLWHA

Variable	Number (n)	Percentage (%)
Co-trimoxazole prescribed		
Yes	792	33.2
No	1,594	66.8
Used ART regimen		
Yes	1,299	54.4s
No	1,087	45.6
Regimen line		
1 st line	1,213	93.4
2 nd line	86	6.6
The number of missed doses in the last month (395), (Not missed=889)		
≤7 (doses)	41	1.7
>7 (doses)	344	14.4
Patient can identify ART regimen dosing		
Yes	1,265	53
No	1,121	47
Followed schedule visits		
Yes	1,474	61.8
No	912	38.2
Lost to F/U		
Yes	1,474	61.8
No	912	38.2
Reasons lost to F/U		
Death	254	10.6
Relapse	488	20.5
Non-adherence	106	4.4
Transfer out	321	13.5
Other	305	12.8

Table 5. TB incidence in People Living with HIV/AIDS

Variables		n	%
Type of TB	Pulmonary	327	73.3
	Extra pulmonary	119	26.7
	Chest X-Ray +ve	423	94.8
TB diagnostics	Sputum AFB smear & culture +ve	256	57.3
Received TB treatment	Yes	440	98.6
	Yes	17	0.7
INH prophylaxis use	No	2369	99.3
TB incidence among PLWHA	TB cumulative incidence, 18.70%		
	TB incidence rate, 0.001 cases/10,000 person years		

revealed that HIV patients with TB (either pulmonary or extra-pulmonary) and no experience of working abroad exhibited a significant association (Chi-squared=9.71, $P=0.0008$). Similarly, individuals in the age bracket of 16-45 years were highly likely to be recently diagnosed with HIV

and have unknown HIV/AIDS staging (Chi-square=51.47, $P<0.001$ and Chi-square=110.5, $P<0.001$, respectively). However, other factors such as patient education, occupational status at the time of HIV/AIDS diagnosis, family size, and patient gender did not show a significant association with TB among HIV patients (Table 6).

3.4 Univariate Analysis of “Initial CD4 Count” and of Initial HB Level

The univariate analysis of the initial CD4 count showed that among those in which the counts were done, most of those patients had a CD4 count ranging from 200-500 and more than 500 (16.0% to 18.4%) (Table 7).

Initially, majority of the patients’ initial hemoglobin level was optimal i.e., they were not anemic (47.3%), though a lesser number was found to be having confirmed lab-based anemia based on their Hb levels (Table 8).

Binary logistic regression of the factors associated with TB disease among the HIV/AIDS patients: In the simple logistic regression model, four variables were significantly associated with Tuberculosis disease among HIV/AIDS infected people. The anemic group had a 3.1 times greater chance of TB infection than the non-anemic group. Being infected with HIV/AIDS was a risk factor for TB regardless of the CD4 count and WHO’s HIV stage. Those who did not use ART had a greater chance of TB infection with OR 3.1(CI 1.4-6.9) at 0.05 significant level (Table 9).

4 DISCUSSION

Pakistan stands out as a country with a high prevalence of TB. Despite official figures of HIV/AIDS cases being confined to high-risk groups, our findings, revealing TB in less than a quarter of PLWHA, underscore the urgent need for robust efforts to enhance primary, secondary, and tertiary care for HIV/AIDS patients with TB co-infection. These results contribute to the collective rates of TB-HIV/AIDS co-infection observed in the region and across developing countries in Asia and Africa, where HIV/AIDS and TB coexist within fragile health systems and living conditions. Studies in India (17%)^[29], Nigeria (16.8%)^[30], Ethiopia (18.2%), and Nepal (27.3%)^[31,32] reflect similar challenges.

In contrast to studies with larger sample sizes conducted in countries where anti-retroviral treatment is not restricted to high-risk groups, our study, limited by the absence of surveillance in the general population, reported lower rates of co-infection. For example, Nigeria (22.7%)^[33] and India (38.4%)^[34] demonstrated comparatively higher incidence rates. Our results also differed from studies conducted in single hospitals, likely influenced by selection bias^[35-38]. Notably, 81% of incident TB cases in our study occurred within one year of registration, surpassing findings from other local studies^[37]. This rapid onset necessitates early interventions.

Despite the majority of TB cases being pulmonary in our

Table 6. Associated Factors for TB in PLWHA

Variables		No, n (%)	Yes, n (%)		Chi square value	P
			Pulmonary	Extra pulmonary		
History of work in abroad	Yes	368 (19)	80 (24.5)	33 (27.7)	9.71	0.008
	No	1572 (81)	247 (75.5)	86 (72.3)		
Patient education	Illiterate	724 (37.3)	117 (35.8)	40 (33.6)	6.57	0.36
	Primary	660 (34)	113 (34.6)	34 (28.6)		
	Secondary	377 (19.4)	72 (22)	32 (26.9)		
	College	179 (9.2)	25 (7.6)	13 (10.9)		
	Unemployed	1366 (70.4)	233 (71.3)	85 (71.4)		
Pt. occupation	Employed	254 (18.2)	66 (20.2)	18 (15.1)	3.91	0.41
	Housewife	220 (11.3)	28 (8.6)	16 (13.4)		
Family size	<4	1746 (90)	284 (86.9)	102 (85.7)	4.6	0.1
	>4	194 (10)	43 (13.1)	17 (14.3)		
	≤15	48 (2.5)	14 (4.3)	3 (2.5)		
	16-30	893 (46)	107 (32.7)	35 (29.4)		
Patient age	31-45	791 (804.1)	143 (43.7)	55 (46.2)	51.47	<0.001
	46-55	159 (179.7)	46 (14.1)	16 (13.4)		
	>55	49 (2.5)	17 (5.2)	10 (8.4)		
	1 or 2	443 (22.8)	68 (20.8)	26 (21.8)		
Current HIV stage	Three	201 (10.4)	44 (13.5)	20 (16.8)	110.5	<0.001
	Four	97 (5)	94 (19.6)	18 (15.1)		
	Not known	1199 (61.8)	151 (46.2)	55 (46.2)		
	Male	1628 (83.9)	289 (88.4)	100 (84)		
Patient gender	Female	304 (15.7)	37 (11.3)	19 (16)	4.8	0.28
	Transgender	8 (0.4)	1 (0.3)	0		

Table 7. Frequency Distribution of Initial CD4 Count of the Study Participants- (n=2,386)

CD4 Count	Number (n)	Percentage (%)
Not done	1,394	58.4
> 500	438	18.4
200-500	383	16
< 200	171	7.2
Total	2,386	100

Table 8. Frequency Distribution of Initial Hb Level of the Study Participants (n=2,386)

Hb level	Number (n)	Percentage (%)
Not done	703	29.5
Anemic	555	23.3
Non-anemic	1,128	47.3
Total	2,386	100

study, addressing the challenge of MDR-TB and extremely drug-resistant TB is crucial in Pakistan. Nepal similarly reported a majority of co-infected patients having pulmonary TB, while India showed a higher prevalence of extra-pulmonary TB among PLWHA^[34,39]. The subcontinent bears a significant burden of HIV/AIDS and TB co-infection.

Our study highlighted a lower provision of INH prophylaxis

compared to other regions. Given that prophylaxis significantly reduces TB risk in HIV/AIDS patients, its provision and adherence should be emphasized in Pakistan. Additionally, those not using Antiretroviral Therapy (ART) had a higher chance of TB infection, aligning with findings in Nepal and Ethiopia^[32,40]. A concerted effort to promote adherence to both ART and INH treatment is imperative.

Cultural norms and limited access resulted in a predominantly male participant group in our study. This aligns with literature linking female sex, WHO clinical stages III and IV, to TB-HIV co-infection^[31]. Our findings also associated WHO clinical staging with HIV/AIDS-TB co-infection, consistent with broader trends in low-middle income countries^[41].

Limitation of the study: Due to secondary data used for the study, it was not possible to control other risk factors for developing TB in the target population. Selection bias could have been potentially induced due to accessing data of ART centre and is usual for retrospective studies. We have used maximum cautiousness by using data extraction tool to limit any further bias in extraction of data, and also included all the patients attending the centre.

Table 9. Binary logistic regression of the factors associated with TB disease among the HIV/AIDS patients

Variables		TB (No), n (%)	TB (Yes), n (%)	Odds ratio (95% CI)	P
Initial CD4 count (cells/mm ³)	>500	607 (25.4)	63 (2.6)	3.3 (1.5-7.4)	0.002
	200-500	675 (28.3)	120 (5)	7.3 (3.6-14.7)	<0.001
	<200	325 (13.6)	227 (9.5)	2.6 (1.4-4.6)	0.001
	Not done	333 (14)	36 (1.5)		<0.001
Initial HIV stage	1 or 2	798 (33.4)	52 (2.2)	0.06 (0.02-0.13)	<0.001
	Three	458 (19.2)	93 (3.9)	0.02 (0.01-0.05)	<0.001
	Four	326 (13.7)	274 (11.5)	0.12 (0.06-0.22)	<0.001
	Not know	358 (15)	27 (1.1)		<0.001
Initial HB level	Anemic	343 (14.4)	212 (8.9)	3.1 (2.1-4.4)	<0.001
	Non-anemic	957 (40.1)	171 (7.2)	1.2 (0.8-1.8)	0.17
	Not done	640 (26.8)	63 (2.6)		<0.001
Used ART regimen	No	972 (40.7)	349 (14.6)	3.1 (1.4-6.9)	0.004

5 CONCLUSION

In conclusion, Pakistan faces significant challenges in combating the co-epidemics of HIV/AIDS and TB. Comprehensive strategies addressing prevention, early diagnosis, and integrated treatment for both infections, along with targeted efforts for marginalized populations, are essential in curbing the burden of co-infection. Our study revealed a high incidence of TBco-infection among PLWHA, with the majority of cases presenting with pulmonary TB. Notably, significant associations with TB were identified in relation to a history of working abroad, patient age, time elapsed since developing the disease, and the current HIV stage. Importantly, being infected with HIV/AIDS emerged as a critical risk factor for TB, irrespective of the CD4 count and WHO HIV stage. These findings underscore the importance of active screening for TB among HIV/AIDS patients and vice versa, emphasizing the need for joint efforts by the two vertical public health programs responsible for managing these infectious diseases. Early initiation of ART and INH is crucial for the effective management of co-infection and underscores the necessity for integrated approaches in public health interventions targeting both HIV/AIDS and TB.

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Ethical Approval

Formal IRB approval was obtained from the Health Services Academy, and permission to access data was acquired from the National AIDS Control Program in Pakistan.

Availability of Data and Materials

All generated data is included in this published article.

Conflicts of Interest

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

Author Contribution

Malik MS and Khan EA were responsible for conceptualization and formal analysis. Malik MS, Khan EA, Abbasi MMJ, and Javaid MM were responsible for data curation, methodology design, original draft writing, review, and editing. All authors have read and approved the final manuscript.

Abbreviation List

ART, Anti-retroviral treatment
HIV, Human immunodeficiency virus
INH, Isoniazid
PLWHA, People living with HIV
TB, Tuberculosis

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