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Efficacy and Safety of Anti-Tuberculosis Drugs in HIV Positive Patients

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A B S T R A C T

Background: HIV infection is the single greatest risk factor for developing tuberculosis, proving the existence of a synergy between the two diseases. The risk of tuberculosis (TB) infection is more than ten times higher for those living with HIV than it is for people who do not have the virus. Since the emergence and widespread dissemination of HIV, the world has seen a dramatic shift in the prevalence of tuberculosis.

Objective: The main purpose of this prospective study was to examine the efficacy and safety of anti-tuberculosis medications in a cohort of individuals who are HIV-positive and also have tuberculosis.

Methodology: The study took place between September 2021 and February 2022 at Liaquat University of Health Sciences, Jamshoro - Pakistan. Our attention shifted to the treatment of individuals suffering from tuberculosis, specifically regarding its efficacy and safety, as an essential aspect of an ongoing study evaluating opportunistic infections (OIs) among HIV-positive patients. In order to carefully choose suitable participants for our study, we used purposive sampling and one year's prevalence data. This single-center trial was designed to prospectively follow patients for a year while examining clinical development, OI outcomes, and the precise safety and efficacy profile of the medications delivered.

Results: Only 69 of the 100 patients who voluntarily participated tested positive for tuberculosis, with the vast majority (59) being adults and the remaining (10) being children. When comparing both genders, men made up a larger share (66.6%). The abdominal form of tuberculosis was the most prevalent extrapulmonary form, affecting 45 individuals (65.2%). All patients received medical treatment in accordance with NTP guidelines, as suggested by the National AIDS Control Programme (NACP) of Pakistan. Of the 60 patients (86.1%) who had evaluable outcomes for their TB therapy, the vast majority were successful, whereas 10 patients unfortunately passed away. The most common adverse drug response (ADR) in this group was urine staining, which occurred in 57 individuals (82.6%) out of a total of 129 ADRs.

Conclusion: Abdominal tuberculosis is the most prevalent form of this opportunistic illness in HIV-positive people. Anti-tuberculosis medications were shown to be safe and effective for the vast majority of individuals in this research.

Key Words: Tuberculosis, Safety, HIV, Anti-tuberculosis, Medications

Introduction

The ancient and anticipated tuberculosis (TB) was once thought to be on the verge of extinction in many regions of the world[1]. In countries where both HIV and TB are prevalent, however, the spread of the Human Immunodeficiency Virus (HIV) epidemic has sparked a comeback of this deadly disease[2]. HIV infection is the single greatest risk factor for developing tuberculosis, proving the existence of a synergy between the two diseases[3]. The risk of tuberculosis (TB) infection is more than ten times higher for those living with HIV than it is for people who do not have the virus[4]. Since the emergence and widespread dissemination of HIV, the world has seen a dramatic shift in the prevalence of tuberculosis[5]. Although tuberculosis (TB) was thought to be on the decline, it has recently reappeared as one of the most common opportunistic infections (OIs) affecting HIV-positive people in TB-endemic areas[6]. A striking example is Pakistan, that is fighting off a severe HIV/TB epidemic. Nearly 1.5 million people in the country were anticipated to be living with HIV/AIDS by the end of 2022, and this number was aggravated by the annual addition of about 510,000 new cases of tuberculosis[7]. As of the year 2021, the rate of AIDS-related fatalities per 100,000 people in Pakistan is a shocking 19 for the country due to the combined effects of HIV and tuberculosis[8].

Active tuberculosis adds an additional risk to an already catastrophic scenario by accelerating the spread of HIV and eventually AIDS[9]. The National AIDS Control Programme (NACP) in Pakistan has developed crucial protocols for the management of both the tuberculosis and AIDS pandemics[10]. The National Tuberculosis Control Programme (NTP) guidelines are recommended for the treatment of tuberculosis in HIV-positive patients in this document. However, data about the efficacy and safety of anti-tuberculosis treatments in HIV-positive individuals remains limited despite the vital necessity of these guidelines. In light of this, the current study set out to fill a significant informative gap about the administration of anti-tuberculosis drugs in the presence of HIV co-infection.

Objective

Our major aim was to conduct a thorough analysis of the effectiveness and safety of anti-tuberculosis medications in a group of individuals who are combating tuberculosis while also bearing the extra strain of HIV.

Methodology

This extensive study was an integral aspect of a larger inquiry of prescription medication use. Outpatient and hospitalized HIV-positive patients' opportunistic infections (OIs) were the primary emphasis, as were the utilization patterns and medication safety of the pharmaceuticals used to treat them. The research was done at Liaquat University of Health Sciences, Jamshoro - Pakistan between September 2021 and February 2022 using a thorough, prospective, and single-center design. Minister Nadeem Jan of Pakistan's Federal Ministry of Health gave us his absolute permission for the study's ethical execution. The OPD at the hospital was regularly visited by our dedicated research team, who conducted thorough OI screenings on each and every patient. Patients who had recently been diagnosed with an OI and readily given written informed permission were considered for inclusion, regardless of whether they were new to the hospital or continuing with therapy. We assembled our research population using purposive sampling, capitalizing on the significant insights gained from prior data regarding the incidence of various OIs in these patients during the last two years. Our study's enrollment period lasted seven months, and patients were monitored for another five months after enrollment.

Using conventional case record forms, we systematically gathered all of the relevant information. Intricate details of OIs (including clinical symptoms, laboratory tests, and outcomes) were included among this rich tapestry of data, which also included demographic variables (age and gender) and the method of HIV transmission. In addition, our rigorous data collectors recorded extensive information on the medications used to treat OIs and the side effects that occurred as a result of these therapies. Additionally, we conducted a comprehensive analysis of data collected from TB patients, looking at factors such as demographics, HIV transmission routes, TB subtypes, baseline CD4 counts, treatment outcomes, side effects, and adherence to National AIDS Control Programme (NACP) standards. Adverse drug reactions (ADRs) were a crucial aspect of our research; therefore, we rated their severity using a modified Hartwig and Siegel scale and determined whether or not they were drug-related using criteria established by the World Health Organization (WHO). Additionally, we used Fischer's Exact test to investigate if there were any significant variations in the death rate from TB based on gender.

Results

The course of 200 opportunistic infections (OIs) in 100 patients was meticulously documented in our study. Of these OIs, TB was certainly the most common, affecting 69 people, out of which 10 passed away. We observed that most of these occurrences were among adults as we explored further into the data. Specifically, TB was found in 59 people (30 men and 29 women). These people had a mean CD4 count at baseline of 122.33 cells/microliter and a mean age of 29.05 years (Table 1). Every single adult patient had a CD4 count of less than 500 cells/microliter, which is alarming. 10 young people, 5 males and 5 females, were found to have TB in the paediatric

Table 1. Demographic Characteristics of Patients with Tuberculosis

Demographic Characteristics	Adults (n=49)	Pediatrics (n=10)	Total (n=59)
Gender			
Male	30	5	35
Female	19	5	24
Age (years)	29.05	7.4	29.05
CD4 Count (cells/microliter)	122.33	526.5	122.33

population (Table 1). The average age was 7.4 years, and their CD4 count was 526.5 cells/microliter at the start (Table 1). According to our findings, the most common way HIV is spread between adult patients is through heterosexual contact (40 cases), followed by blood transfusion (10 patients). The route of infection was unknown in just a small number of instances (5 individuals). Vertical transmission had a prominent role among paediatric patients (4 patients), with one incidence linked to blood transfusion and the routes of transmission in 2 children remaining unclear. Of the 69 patients seen in the ART clinic at the hospital, 38 were initially untreated.

The symptoms of TB demonstrated remarkable variability, with abdominal TB dominating the charge (50.7%), followed by pulmonary TB (11.5%), and a mix of both pulmonary and extrapulmonary TB (4.3%). Pleural effusion (7.2%), cervical lymphadenitis (2.8%), and meningitis (1.4%) all manifested themselves in this complicated tapestry of TB symptoms. The administration of anti-tuberculosis medications rigorously followed to the rules set out by the National Tuberculosis Control Programme (NTP) in accordance with the guidelines of the National AIDS Control Programme (NACP). Specifically, individuals encountering TB for the first time (45 cases) were treated with category I medications (isoniazid, rifampicin, pyrazinamide, and ethambutol), all within the indicated dosages. On the other hand, individuals with treatment relapse, treatment failure, or a history of defaulting (24 cases) got category II medications (isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin) in the usual amounts (Table 2). We identified a solitary patient who chose for treatment from a private specialist, encouraged by the reduced pill load that came from the doctor's recommendation of fixed medication combinations. Unfortunately, one example of non-compliance surfaced when a patient first defaulted category I medication and was then transferred to category II treatment. Additionally, pyridoxine was provided to all patients at the indicated amounts.

9 of 69 patients had uncertain treatment results. After the research, these people were either lost, transferred, or remained in therapy. A remarkable 83.3% of the remaining 60 patients were healed, while 16.6% died. After investigating further, we found that women had a 37.9% mortality rate compared to 26.6% for men. This gender discrepancy raises significant concerns. ATB was detected in 40 people—29 adults and 11 children. One patient received Forcox and AKT-3 at a private facility. Abdominal TB was connected to 5 of 10 fatalities after additional analysis. Four of eight adult pulmonary TB cases had positive sputum for acid-fast bacilli (AFB), three had negative results, and one had no results. One patient died, while two recovered. In two of three sputum-negative pulmonary TB cases evaluated, both patients were cured. The ultimate case was favourable despite missing sputum reports. Patients with pulmonary TB had considerably lower CD4 counts than those with extrapulmonary TB. Sputum-negative TB is more prevalent in adults with severe immunosuppression, and research showed that these patients had significantly lower mean CD4 counts than sputum-positive patients. Moreover, four adults and one child under five had pulmonary and extrapulmonary TB. The treatment helped all four patients, surprising them. The investigation identified eight tuberculous pleural effusion instances, three adults and a 12-year-old. The third patient died, but two found a therapy. After treatment, two tuberculous meningitis patients—an adult and a child—recovered. Cervical tuberculous lymphadenitis afflicted three adults and one seven-year-old. Three recovered, one died.

Safety evaluation relies on adverse drug reactions (ADRs). 129 ADRs were found in 57 individuals, indicating that 8.26% of research participants had them. Urine colour change was the most prevalent side effect of rifampicin. Most of these ADRs (98.4%) were mild on the Modified Hartwig and Siegel scale. Interestingly, two ADRs had severity ratings of 2 and 3. A severe widespread skin rash that peeled in one case was attributed to rifampicin. Stopping the medication and managing the symptoms promptly resolved the adverse drug response (ADR). One patient had hepatitis and elevated SGPT (216 IU/L), thus isoniazid and rifampicin were stopped. After quitting these drugs, side effects decreased. According to the

Table 2. Modes of HIV Transmission and Treatment Categories for TB Patients

Modes of Transmission	Adults (n=49)	Pediatrics (n=10)	Total (n=59)
Heterosexual	40	-	40
Blood Transfusion	10	1	11
Unknown	5	2	7
Vertical Transmission	-	4	4
Treatment Categories			
Category I	45	-	45
Category II	24	-	24
Non-Compliance	1	-	1

WHO ADR causation scale, the suspected medicine was connected with a probable causal relationship in 80% cases, a likely correlation in 49 cases, and the definitive cause in one case.

Discussion

Since the HIV epidemic began, experts have known the two illnesses are interconnected. HIV dramatically increases TB worldwide. Tuberculosis (TB) kills many HIV-positive people[11]. As expected, TB was the most common opportunistic infection (OI) among HIV-positive persons in places where it is widespread. The safety and efficacy of anti-tuberculosis medication for these patients must be assessed. We started this research to evaluate HIV-positive people's anti-tuberculosis drugs' safety and efficacy. According to our figures, adults had the most TB cases. Paediatric patients' higher mean baseline CD4 count may explain their lower OI rate. We found that most treatment-naive people were adults, suggesting that the in-patient setting reduced TB risk. Early ART start in HIV-TB co-infected people reduces mortality[12]. Our study indicated that many patients responded well to treatment, supporting this crucial outcome. TB treatment in AIDS patients benefits from NTP regimens. However, co-occurring illnesses and HIV-positive patients' overall health can greatly increase mortality risk[13]. Death rates also differed by gender, which is significant and warrants more study.

It is important to note that some patients had their ART regimens altered to avoid negative medication interactions, such as moving from nevirapine to efavirenz to avoid rifampicin's interaction with nevirapine[14]. In example, rifampicin can cause a decrease in plasma levels of nevirapine by inducing the metabolism of nevirapine. Furthermore, there appears to be little to no reduction in nevirapine's antiviral activity when used in conjunction with rifampicin[15]. Our findings call attention to the need for more research into the effects of co-administering nevirapine with rifampicin, which may help make it easier to choose an ART regimen for these individuals.

Conclusion

Our results highlight the continued importance of detecting and treating tuberculosis (TB), the leading opportunistic illness in the HIV-positive population. In addition, we have discovered an intriguing epidemiological trend by determining that extrapulmonary TB is more common than pulmonary TB in our group. Anti-tuberculosis drugs are prescribed with a level head in this healthcare system. Patients are always cared for in accordance with national rules, demonstrating the significance of sticking to norms. In addition, the excellent results of therapy in the vast majority of our patients shows that the anti-tuberculosis medications we used were successful. Overall tolerability was also shown by the low occurrence of significant adverse drug reactions (ADRs) with these medications. Patients taking antiretroviral therapy (ART) and additional drugs, such as cotrimoxazole for PCP prophylaxis, nutritional supplements, and others, may experience a significant pill load due to their treatment regimens. With so many pills to take, it's easy to see how noncompliance with HIV and TB treatments may spiral into the emergence of drug resistance. Therefore, we encourage additional studies into the correlation between CD4 count and TB subtype in adults, as well as the unique pattern of TB in HIV-positive children. Further research is needed to determine the

effects of co-administering nevirapine and rifampicin in these individuals.

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