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Prevalence of Human Immunodeficiency Virus in children with Tuberculosis

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Author`s Contribution

[1,2]Substantial contributions to the conception or design of the work; or the acquisition, [2,6]final approval of the study to be published [3]Drafting the work or revising it critically for important intellectual content, [4,5]Active participation in active methodology, literature review

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ABSTRACT

Objectives: To determine prevalence of HIV co-infection in children with TB visiting Tb center Children Hospital, PIMS.

Methodology: This cross sectional study was conducted in Children Hospital, Pakistan Institute of Medical Sciences, Islamabad. from March 2022 to February 2024 after approval from ethical review board. 170 participants were selected from TB center Children hospital PIMs. Written and informed consent was obtained from parents/attendants of all patients. HIV serology of all TB patients coming to TB center children hospital PIMs is advised in routine and HIV serology is available free of cost in our hospital. Demographic data of patients, information regarding type of TB, bacteriological evidence of TB and HIV serology results were entered in a standardized Performa created for our study.

Results: Out of the total 170 TB cases included in our study 5 patients were HIV positive. This represents 2.9% of our study population. Out of these 5 patients, 3 were male and 2 were female. Age of HIV positive patients was widely distributed with the youngest patient being 3 months only and the oldest 11yrs. 4 (80%) HIV positive patients had clinically diagnosed and 1 patient had MTB positive in gastric aspirates. All HIV positive cases had pulmonary TB.

Conclusion: Prevalence of HIV infection in children with Tb was much higher as compared to the prevalence of HIV in general population.

Keywords: Human Immunodeficiency Virus, Tuberculosis, HIV screening, Concentrate epidemic.

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Introduction

Tuberculosis (TB) is a communicable disease and remains among the top 10 causes of death globally. Following COVID-19, TB is the second leading infectious killer worldwide. Approximately one-quarter of the world's population is infected with tuberculosis. In 2022, an estimated 1.3 million people died from TB, including 167,000 individuals living with HIV. That same year, around 10.6 million people developed TB globally, comprising 5.8 million men, 3.5 million women, and 1.3 million children. TB affects individuals of all ages, but it is both treatable and preventable.[1]

In 2022, an estimated 39 million people were living with HIV, with 1.3 million new infections and 630,000 deaths due to HIV-related causes.[2] Of the 39 million individuals, about 1.5 million were children aged 0–14 years. Children under 15 represent 4% of all people living with HIV, accounting for 10% of new HIV cases and 13% of AIDS-related deaths. Infants under 1 year of age are the most vulnerable to HIV infection.[3]

Pakistan is one of four countries in Asia where the number of new HIV cases has continued to increase since 1990. A study conducted in Sindh, Pakistan, reported the highest estimated HIV prevalence among younger age groups: 7% in children aged 0–2 years and 6% in those

aged 3–5 years, compared to only 1% prevalence in adults aged 16–49 years.[4]

HIV infection in children with tuberculosis (TB) is a significant public health concern, particularly in regions with high burdens of both diseases. Although determining the exact global prevalence is challenging, estimates suggest that between 10% and 60% of children diagnosed with TB may also be HIV-positive.[5] Several studies conducted in Pakistan have reported a higher prevalence of HIV among children with TB compared to the general population, where HIV prevalence is approximately 0.1–0.34%.[6–7]

Tuberculosis weakens the immune system. *Mycobacterium tuberculosis* (Mtb), the causative agent of TB, has evolved sophisticated mechanisms to evade the host immune response in order to survive and disseminate infection. Mtb disrupts phagosome maturation within macrophages, impairing their ability to destroy the bacteria. It also suppresses the production of critical inflammatory cytokines that enhance immune responses. This persistent inflammatory state may ultimately impair the body's ability to control the infection.[8]

The immune system is further compromised by malnutrition, which commonly coexists with TB in children. Malnutrition impairs the production and function of key immune cells, such as T lymphocytes and macrophages, which are vital in controlling TB infection. Additionally, the synthesis of essential immune mediators, including cytokines and antibodies, may be disrupted by nutritional deficiencies, further weakening the immune response.[9] Consequently, children with TB, who already have compromised immune systems, are at greater risk of acquiring HIV infection.

HIV-infected children are more likely to have extra-pulmonary forms of tuberculosis. Co-infection with HIV/TB can worsen the course of both diseases. Children with HIV/TB co-infection experience more severe illness and have higher mortality rates compared to children with TB alone.[10] This mortality rate is higher among children under 5 years.[11] Children with HIV/TB co-infection might show less specific symptoms compared to children with TB alone. These could include: weight loss, fever, poor appetite, cough (may not be a prominent symptom), swollen lymph nodes. HIV positive children with TB infection, especially those newly infected with HIV, often present with atypical symptoms that differ from classic adult TB symptoms. This can make diagnosis of TB challenging and lead to delays.[12]

HIV weakens the immune system by depleting CD4+ T cells, crucial for fighting TB infection. This makes it harder for the body to respond effectively to TB medications, leading to slower recovery increased risk of treatment failure.[5,13] Co-infection increases the risk of developing resistance to both HIV and TB medications: Non-adherence to complex treatment regimens can contribute to drug resistance.[14] Treatment for TB in HIV-infected patients typically takes longer than in HIV-negative patients.

So it is crucial to find HIV status in patients with TB. Our study was conducted to find prevalence of HIV in children with TB visiting TB center children hospital PIMS.

Methodology

This was a cross-sectional, hospital-based study conducted over a period of two years at the Children's Hospital, PIMS, Islamabad. Ethical approval was obtained from the Institutional Review Board (Letter No. F.1-1/2015/ERB/SZABMU/942).

Using the WHO sample size calculator, a sample size of 170 was determined based on a 95% confidence level, an anticipated population proportion of 9.7%, and an absolute precision of 4.5%.[15] Participants were selected using non-probability consecutive sampling from among children presenting at the TB Center. Written informed consent was obtained from the parents or guardians of all study participants.

Inclusion criteria comprised all male and female children aged 0–12 years with a confirmed diagnosis of tuberculosis who visited the TB Center during the study period. Exclusion criteria included children previously diagnosed with HIV before their TB diagnosis, those with other systemic illnesses or comorbidities, and those on immunosuppressive therapy.

At our hospital, routine HIV serology is advised for all TB patients, and testing is available free of charge. Demographic data, clinical information including the type of TB, evidence of TB infection, and HIV serology results were recorded using a standardized proforma developed for this study. All collected data were entered and analyzed using SPSS version 23.

Results

Total 170 children with TB were included in the study out of which 89 (52.4%) were males and 81 (47.6%)

females. Youngest patient included in the study was only 2 months old and maximum age limit was 12 yrs. Majority of the patients visiting TB center were clinically diagnosed and out of 170 patients only 67 patients (39.4%) had bacteriological evidence of TB (MTB positive in either sputum, gastric aspirates, CSF, pleural fluid or any other body fluid).

Out of total 170 patients, 64 (37.6%) had pulmonary TB, 91 (53.5%) had extra-pulmonary TB and 15 (8.8%) had both pulmonary TB and extra-pulmonary TB; as shown in table 1.

Specific site of extra-pulmonary TB in patients were also noted. Pulmonary TB was the most frequent type in our study, with 64 cases (37.6% of the total). This means almost 4 out of 10 cases have TB located primarily in the lungs.

Patients with extra-pulmonary TB (TB affecting sites other than the lungs) had either abdominal TB, Tuberculous meningitis, lymph nodes, spinal TB, pleural effusion, osteomyelitis and TB arthritis. Of all these extra-pulmonary sites Tuberculous meningitis was the most common in our patients, accounting for 28 cases (16.5% of total cases and 30.7 % of extra-pulmonary TB cases) with lymph node TB being second most common having 22 cases (12.9% of total and 24.2% of all extra-pulmonary cases). Out of the remaining extra-pulmonary cases, 10% were abdominal TB, 4.7% osteomyelitis, 4.1% pleural effusion, 2.9% spinal TB, and 2.4% TB arthritis cases. (Table I)

Table I: Gender and TB site distribution of TB patients. (n=170)

		N	%
Gender	Male	89	52.4%
	Female	81	47.6%
Site of TB	Pulmonary	64	37.6%
	Both Pulmonary and Extra-pulmonary	15	8.8%
	Tuberculous Meningitis	28	16.5%
	Lymph Nodes	22	12.9%
	Abdominal	17	10%
	Osteomyelitis	8	4.7%
	Pleural Effusion	7	4.1%
	Spinal	5	2.9%
	TB Arthritis	4	2.4%

15 patients (8.8%) in our study had both pulmonary and extra-pulmonary TB, either having 2 sites involved or having disseminated TB.

Out of the total 170 TB cases included in our study 5 patients were HIV positive. This represents 2.9% of our study population (table II). Out of these 5 patients, 3 were male and 2 were female. Age of HIV positive patients was widely distributed with the youngest patient being 3 months only and the oldest 11yrs. 4 (80%) HIV positive patients had clinically diagnosed and 1 patient had MTB positive in gastric aspirates. All HIV positive cases had pulmonary TB (table III).

Table II: Prevalence of HIV in patients with TB. (n=170)

		Frequency	Percentage
HIV status	negative	165	97.1
	positive	5	2.9

Table III: Gender, Age and TB site distribution of HIV positive cases.

		HIV positive	HIV negative
Gender	Male	3	86
	Female	2	79
Ages	3 months	1	2months-12yrs
	10 months	1	
	3.5yrs	1	
	8yrs	1	
	11yrs	1	
Site of TB	Pulmonary	5	59
	Extra-pulmonary	0	15
	Both pulmonary and extra-pulmonary	0	91
Gene expert	MTB detected	1	66
	MTB not detected	4	99
Total		5 (2.9%)	165

Discussion

There is a scarcity of studies investigating the parameters of HIV co-infection among children with tuberculosis. Our study provides valuable new insights into this area. The findings reveal that the prevalence of HIV among pediatric TB patients was 2.9%, with a slightly higher male-to-female ratio observed among HIV-positive cases. This prevalence is significantly higher than the HIV prevalence in the general population of Pakistan, which was reported to be 0.1% in 2019.[16] Compared to other national studies, our results indicate a marginally elevated rate of HIV co-infection in children with TB, underscoring the need for routine HIV screening in this high-risk group.

Safdar et al. (2018) found that 145 (0.66%) TB patients were found positive for HIV infection out of 21,644 patients included in study. The prevalence of HIV was higher among Extra-pulmonary TB patients than pulmonary TB patients (1.02% vs 0.55%). The prevalence among bacteriologically positive was slightly

increased as compared to clinically diagnosed (0.32% vs 0.23%). The prevalence of HIV was higher among males (1.23%) than female (0.09%) TB patients.[6] Compared to this study our study found out a prevalence of 2.9% which is much higher, the prevalence was higher in clinically diagnosed cases of TB and in male children with TB. Safdar et al. (2018) conducted the study in 17 different TB registration centers with a large study population while our study included only 1 such center with study population of only 170. But our study is one of its kind in Pakistan as it looked for prevalence of HIV in children with Tb and no such study has been done so far in children younger than 12yrs.

Hasnain et al. (2012) conducted a similar study in Sindh in 12,552 with TB, aged 16-60yrs. Study showed that out of total 12,552 TB patients tested, 42 were HIV-positive (0.34%). Prevalence of HIV among male patients was 0.67% which was higher than prevalence among female patients (0.03%). Even though out of total 42 HIV positive patients' majority(n=28) had pulmonary TB, prevalence of HIV among extra-pulmonary TB patients was higher 0.48% compared to pulmonary TB (0.29%).[7] Compared to this study as well, our study shows a much higher prevalence of HIV in children with TB and only patients with pulmonary TB were HIV positive.

A study conducted in India found that among children with tuberculosis, the HIV prevalence rate was 9.7% which is much higher than HIV prevalence in general population of 0.22%. Most prevalent was pulmonary TB 61.1%. among HIV positive TB patients and a higher prevalence was found among male children.[17] These results are comparable to our study in which we found majority HIV positive in male TB patients and all HIV patients had pulmonary TB.

HIV and TB co-infection creates a complex interplay that worsens the course of both diseases. Some of the mechanisms involved include Immune System Weakening, increased bacterial burden and dysregulated inflammation. HIV weakens the immune system by depleting CD4+ T cells, which are vital for fighting TB infection. This makes it harder for the body to control the TB bacteria. HIV infection can increase bacterial burden and lead to a higher number of Mycobacterium tuberculosis bacteria multiplying inside infected cells.

HIV can trigger chronic inflammation, further damaging tissues and hindering the body's ability to fight TB effectively thus dysregulating inflammation.[18] TB Impacts HIV infection negatively by either increasing HIV replication, Immune activation, or increasing risk of transmission.[18] TB infection can activate HIV replication within infected cells, leading to a higher viral load. TB bacteria trigger immune responses that can further activate HIV, creating a vicious cycle.[19,20] Co-infection can increase the risk of transmitting HIV to others, particularly through coughing.[18] Macrophages are crucial for fighting both HIV and TB. However, HIV can infect macrophages, making them less effective against both pathogens. HIV can also infect monocytes, another type of immune cell, further weakening the immune response[18,21]

HIV/TB Co-Infection not only leads to severe TB disease, but also causes diagnostic and treatment challenges. HIV co-infection often leads to a more severe and aggressive form of TB, with faster progression and higher mortality rates. Weakened immune response can make it harder to diagnose TB using traditional methods. Co-infection can complicate treatment because some medications used for TB can interact with HIV medications.[22] Overall, HIV and TB co-infection creates a synergistic effect, where each disease worsens the other.[23] Understanding this complex interplay is crucial for developing effective prevention, diagnosis, and treatment strategies.

Since it might be difficult to manage both infections at the same time, treating HIV in children who are also TB-positive calls for a cautious, integrated strategy. Treatment needs to be customized to treat both HIV and TB infections while taking side effects, immunological reactions, and possible medication interactions into account, particularly in children.[24] Thus there is need to find HIV status in all patients with TB and larger multicenter studies are required to find HIV prevalence in children with TB

Conclusion

Prevalence of HIV infection in children with Tb was much higher as compared to the prevalence of HIV in general population (2.9% vs 0.1%). It was also much higher than that found in other studies done in Pakistan. And so far, no such studies have been done in children less than 12 years of age.

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