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Epidemiological Study of Tuberculosis Among HIV-Positive Patients in the Osh Region of Kyrgyz Republic

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ABSTRACT
Tuberculosis (TB) and HIV represent two of the most critical worldwide public health concerns, primarily owing to their synergistic connections. In 2022, over 671,000 persons with HIV contracted tuberculosis, making it one of the most widespread illnesses and a primary cause of death among this demographic. Co-infection with TB and HIV led to around 167,000 fatalities worldwide in that year. Individuals with HIV possess a 20 to 30-fold increased likelihood of developing tuberculosis as a result of their compromised immune systems. Nonetheless, prophylactic TB therapy in HIV-positive patients has shown efficacy in substantially reducing this risk. Data from 2022 indicate that 80% of those diagnosed with tuberculosis had HIV testing, highlighting the essential importance of early diagnosis in enhancing survival rates via prompt treatment. This research examines the clinical features of TB/HIV co-infection in the Osh area of Kyrgyzstan, evaluating outcomes according to the stage of HIV infection and the patients' age groups. The studies seek to improve early diagnosis methods for both illnesses, therefore improving patient outcomes via earlier and more precise therapies.

Keywords: TB/HIV Co-Infection, Tuberculosis Prevention. HIV Testing, Immunity and Tuberculosis risk, Public Health Impact

BACKGROUND

Two of the most major public health concerns globally are HIV and tuberculosis (TB), particularly in low- and middle-income nations where both illnesses' burden is significant. Because HIV impairs the immune system, those living with HIV (PLHIV) are much more susceptible to TB, so the connection between TB and HIV is very challenging (Magee et al., 2018). Actually, persons with HIV are 20 to 30 times more likely than those without HIV to get TB (Ad et al., 2024). With approximately 167,000 fatalities estimated worldwide in 2022, this co-infection is the main cause of mortality in PLHIV. Although preventative treatment and diagnosis have advanced, TB/HIV co-infection remains a major issue particularly in areas with inadequate healthcare resources and increasing HIV rates (Mirrakhimov et al., 2014; Pc et al., 2016).

TB/HIV co-infection is a rising problem in Kyrgyzstan and especially in the Osh area. The area suffers from poor access to healthcare, migratory problems, and socioeconomic challenges all of which help to spread both TB and HIV. HIV infections in Kyrgyzstan have been rising steadily over years, which has aggravated the already major TB issue. Like elsewhere, HIV-positive Kyrgyzstan residents are more likely to get TB; co-infection sometimes results in more severe health problems. This emphasizes the need of early identification and appropriate treatment, which are very essential for raising patient results (Bergman et al., 2024).

This research is to investigate the clinical features of TB/HIV co-infection in the Osh area with an emphasis on how these features change depending on the stage of HIV infection and patient age group. Controlling these illnesses depends on early diagnosis and therapy being improved by an awareness of these trends. The results will also provide light on how Kyrgyzstan's healthcare systems may better control HIV and TB,

therefore lowering the population's burden of these diseases and enhancing general health results.

METHODOLOGY

This retrospective cohort study was conducted to analyze HIV/tuberculosis (TB) co-infection cases over a 10-year period, from 2012 to 2022. The study utilized medical records data from both inpatient and outpatient settings in the Osh region, Kyrgyzstan. The data collection was carried out from hospital records, TB dispensaries, and HIV clinics, focusing on patients with confirmed diagnoses of both HIV and tuberculosis during the year 2012 to 2022. Patient data were extracted from the medical records maintained by healthcare institutions in the Osh region, including both paper and electronic health records. The records were sourced from the Department of Infectious Diseases and the Osh Regional Hospital. We collected information on patient demographics (age, gender), clinical parameters (stage of HIV infection, presence of TB symptoms), laboratory findings (CD4 count, viral load, sputum smear results), and treatment outcomes. The study subjects were all patients who had confirmed HIV and TB co-infection between 2012 and 2022. The patient cohort was stratified by age group and the stage of HIV infection. This stratification allowed for a more focused analysis of how co-infection manifested across different populations and disease stages.

The data collected from medical records and laboratory databases were entered into an electronic database specifically created for this study. This database was then used for statistical analysis. Descriptive statistics were employed to analyze the variables, with categorical variables (e.g., gender, HIV stage) presented as percentages, and continuous variables (e.g., age, time to treatment) presented as means or medians where appropriate. Statistical analyses were conducted using Excel software package. Qualitative data were presented in both absolute numbers and percentages, while graphical representations (e.g., bar graphs, pie charts) were used to illustrate the epidemiological trends of TB/HIV co-infection.

The study was conducted in accordance with ethical standards for retrospective studies. Patient confidentiality was maintained by anonymizing all medical records and using unique identifiers for data analysis.

Classification of and Clinical Stages of HIV infection

Based on CD4+ T-cell counts, the World Health Organisation (WHO) divides HIV infection into four clinical phases that represent the course of the illness and the matching immunological response. Appropriate diagnosis and treatment of HIV depend on a comprehension of these phases (Ad et al., 2024).

Stage I: Asymptomatic Illness

Usually showing no symptoms, the early stage of HIV infection is often difficult to diagnose. Still, chronic systemic lymphadenopathy—which is marked by lymph node enlargement all across the body—may be present. Still somewhat high, the CD4+ T-cell count is over 500 cells/µl according to laboratory testing. Although the virus is actively multiplying during this stage, which lasts many years, the person is healthy and uninformed of their infection (An et al., 2024).

Stage II: Moderate Illness

Mild symptoms start becoming apparent when the condition progresses into Stage 2. Patients may have recurrent upper respiratory tract infections and modest weight loss—less than 10% of their total weight—which would indicate a decrease in immunological function. Apart from these symptoms, certain dermatological disorders like psoriasis or seborrheic dermatitis might develop. The CD4+ T-cell count falls between 499 and 350 cells/µl at this stage, suggesting a further immune system impairment and more susceptibility to opportunistic infections (Vidya Vijayan et al., 2017).

Stage III : Development of Symptoms

Stage 3 marks a notable rise in the degree of symptoms and medical consequences. Many times experiencing more than 10% of their body weight, patients may also acquire major oral mucosal diseases like ulcers or oral candidiasis. Extended diarrhea lasting more than one month without a clear reason becomes somewhat prevalent, which further contributes to nutritional deficits and general poor health. Furthermore more common at this period are severe systemic bacterial infections and pulmonary TB, which points to a clear decline in immunological capacity. Emphasizing the requirement of medical intervention, CD4+ T-cell counts at this

stage vary from 349 to 200 cells/µl (Younas et al., 2016).

Stage IV: AIDS

Acquired immunodeficiency syndrome (AIDS) defines the last stage of HIV infection. People at this level have severe clinical symptoms including Pneumocystis pneumonia, cachexia syndrome—extreme weight loss and muscle wasting—and recurring, severe bacterial pneumonia. Extrapulmonary TB becomes a major issue as it may compromise organs outside of the lungs. Complications in the neurological system might potentially develop including central nervous system toxoplasmosis and HIV encephalopathy. Moreover, persistent herpes simplex virus infections as well as the development of Kaposi's sarcoma, a malignancy connected with HIV might arise. Counts of CD4+ T-cells below 200 cells/µl indicate a key threshold wherein the risk of life-threatening infections and consequences greatly rises (Deeks et al., 2013).

This classification emphasizes the requirement of early diagnosis and continuous monitoring of people living with HIV as well as the need of prompt antiretroviral medication to properly control the illness and stop advancement through various clinical phases.

Classification and Forms of Tuberculosis

Based on the location of infection, the World Health Organisation (WHO) classifies two main kinds of tuberculosis (TB): extrapulmonary tuberculosis and pulmonary tuberculosis. Guiding diagnostic, treatment, and management plans need this categorization.

***1. Pulmonary Tuberculosis*:** Any bacteriologically proven or clinically diagnosed illness affecting the lung paredgy or the tracheobronchial tree defines pulmonary TB. This kind of TB involves involvement of the intrathoracic lymph nodes, which could develop without any radiological abnormalities in the lungs. From chronic coughing, chest discomfort, and hemoptysis to systemic signs including fever and weight loss, pulmonary TB may present itself. Reducing morbidity and death as well as stopping the spread of pulmonary tuberculosis depend on early detection and treatment of it (Li et al., 2024).

***2. Tuberculosis Extrapulmonary*:** Extrapulmonary TB is any clinically diagnosed or bacteriologically examined case affecting organs other than the lungs (Mert et al., 2024). This may cover a range of spots, including:

A. Pleura: Involving the pleural cavity, leading to pleurisy or pleural effusion.

B. Peripheral Lymph Nodes: Affecting lymphatic tissue outside of the thoracic region.

C. Abdomen: Including TB of the intestines, peritoneum, or abdominal lymph nodes.

D. Genitourinary Tract: Involving the kidneys, bladder, or reproductive organs.

E. Skin: Manifesting as cutaneous TB.

F. Joints and Bones: Causing osteoarticular TB, which can lead to severe complications if not treated promptly.

G. Meninges: Leading to tuberculous meningitis, a severe form that can result in significant neurological impairment.

In the context of TB, late-stage HIV infection is characterized as a CD4 cell count less than 200 cells/mm³ or the presence of WHO clinical stage 3 symptoms. Because of their seriously impaired immune system, people at this stage are more susceptible to opportunistic infections including extrapulmonary TB. Improving health outcomes and stopping further disease spread depend on accurate identification and treatment of TB in those living with late-stage HIV. Particularly in communities with a high HIV prevalence, this categorization emphasizes the need of realizing both pulmonary and extrapulmonary types of TB in order to apply appropriate public health policies and clinical treatments(Sm et al., 2024).

RESULTS AND DISCUSSION

With notable variation in case distribution across districts, the Osh area documented 1,553 HIV-infected individuals between 2012 and 2023 (Figure No. 1). This diversity emphasizes the requirement of customized public health plans to handle the particular socioeconomic situations, healthcare availability, and cultural attitudes within every area. Moreover, the interdependence of HIV and tuberculosis (TB) co-infection emphasizes the need of integrated healthcare strategies as, especially in late-stage HIV infection, persons with HIV are more likely to develop tuberculosis. Improving health outcomes and reducing the incidence of HIV and TB in the Osh area will depend on developing thorough public health projects aiming at both illnesses.

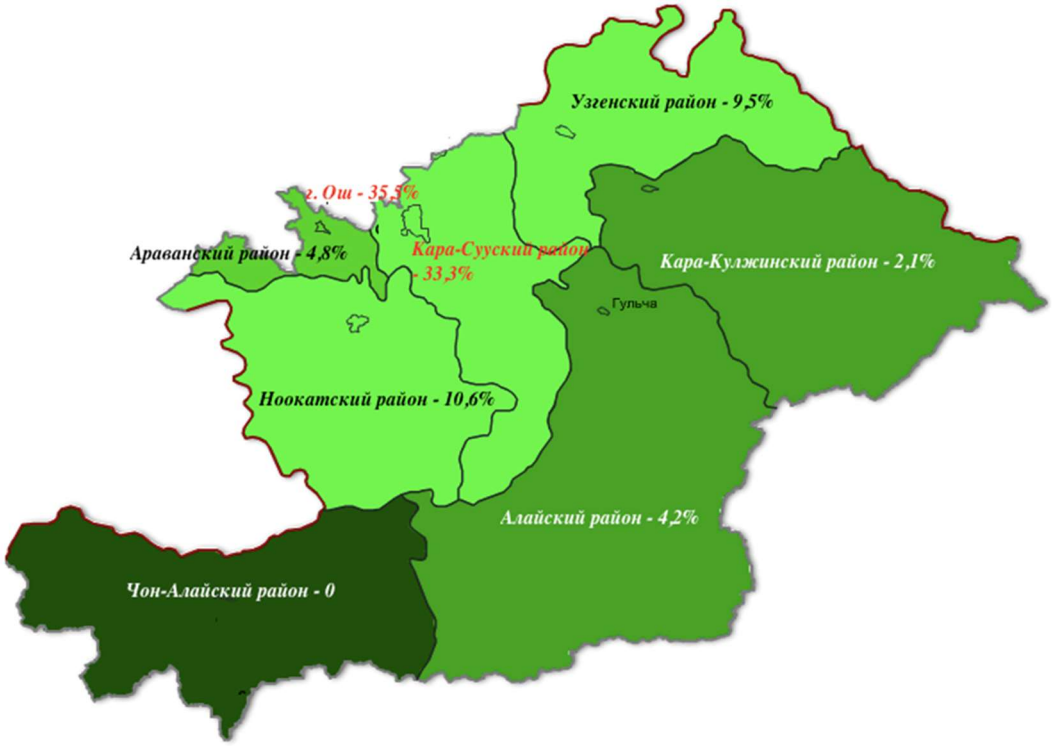


Figure 1: *Distribution of patients by districts of Osh region n=1557*

Examining patients under the age of 29 recently, HIV testing was mostly carried out in response to disease signs seen in those over 30 years of age, therefore exposing a significant age-related discrepancy in HIV diagnosis and treatment. Although age affected the dynamics of monitoring for HIV symptoms, both age groups showed clearly comparable patterns of disease development and symptomatology independent of age. Of the documented instances of HIV infection, a notable number—187 people—were shown to have coexisting HIV and TB diseases. As shown in Table 1, the age distribution of these individuals highlights the degree of comorbidity between HIV and TB, therefore stressing the requirement of focused treatments and all-encompassing healthcare plans to handle this double load. Given the rising sensitivity of younger populations to opportunistic infections, this connection is especially alarming and emphasizes the need of early identification and combined treatment of HIV and TB in both younger and older groups.

Table 1: Age category of HIV+tuberculosis n=187

Age group	абс.ч	%
10-19 y	31	16,4
20-29 y	9	4,8
30-39 y	33	17,5
40-49 y	70	37,0
50+	46	24,3

Figure 2: Clinical stages of HIV infection

Among the observed patients, a significant number exhibited advanced forms of tuberculosis, classified as clinical stages 3 or 4 according to WHO standards, highlighting the urgent need for targeted interventions in high-risk populations, particularly those co-infected with HIV (n=50). Patients in clinical stage 3 presented with severe symptoms, including substantial weight loss, oral mucosa lesions, and prolonged diarrhea, which indicated a weakened immune system and increased susceptibility to opportunistic infections. In contrast, those classified as clinical stage 4 faced even more severe manifestations, such as cachexia syndrome, opportunistic infections like Pneumocystis pneumonia, and extrapulmonary tuberculosis, complicating their overall health. These findings emphasize the necessity for early detection, integrated treatment plans, nutritional support, and multidisciplinary care to improve health outcomes and address the complex needs of patients with advanced tuberculosis and HIV co-infection (Deeks et al., 2013).

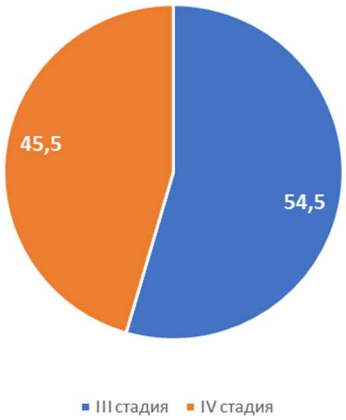
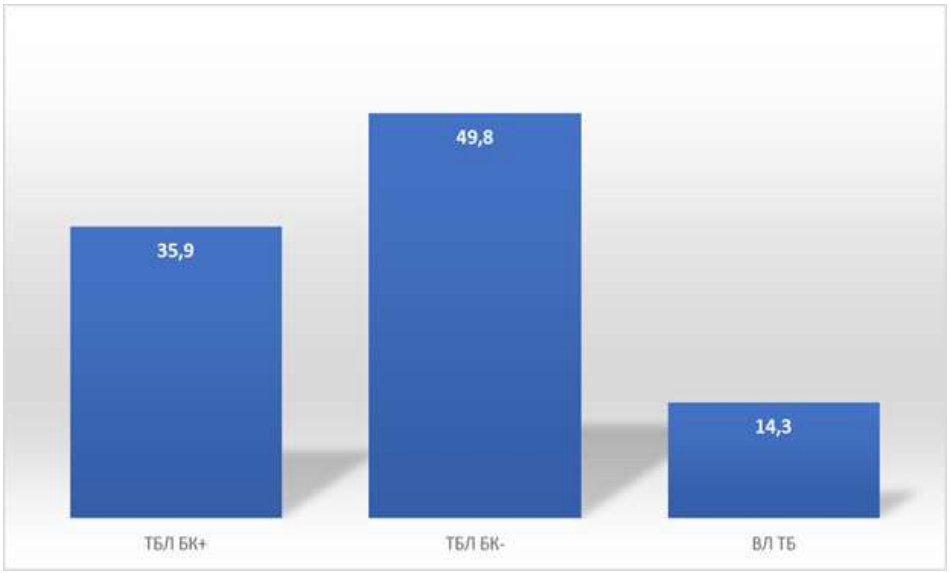


Figure 3: Clinical forms of tuberculosis n=187

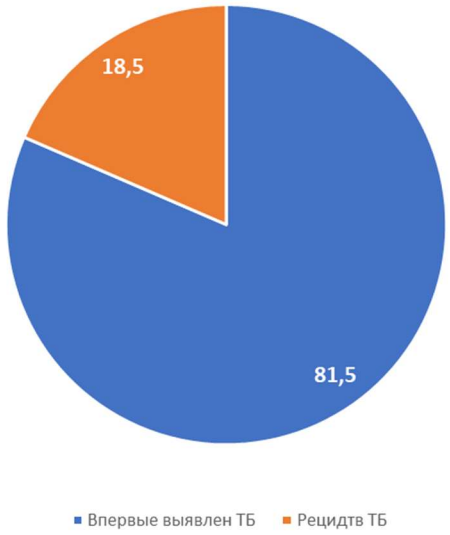


(TBLBC (Tuberculosis and Lung Diseases+ pulmonary tuberculosis with bacterial excretion, TBLBC pulmonary tuberculosis without bacterial excretion ,PTB (Pulmonary Tuberculosis) extrapulmonary tuberculosis)

Among the examined patients, 49.8% had pulmonary TB, with a notable prevalence of pulmonary

tuberculosis without bacterial excretion ($p < 0.001$). Extrapulmonary forms were seen four times less often. The progression of TB in individuals infected with HIV may be linked to the emergence of primary active disease types as well as the reactivation of a latent tuberculosis infection. Among HIV-positive TB patients, 152 were newly diagnosed with tuberculosis, whereas 35 had recurrent tuberculosis.

Figure 4: Frequency of newly diagnosed tuberculosis and relapse n=187



Of the newly discovered patients, 32.5% exhibited pulmonary TB with bacterial excretion, 50.6% presented pulmonary tuberculosis without bacterial excretion, and 16.9% showed extrapulmonary tuberculosis.

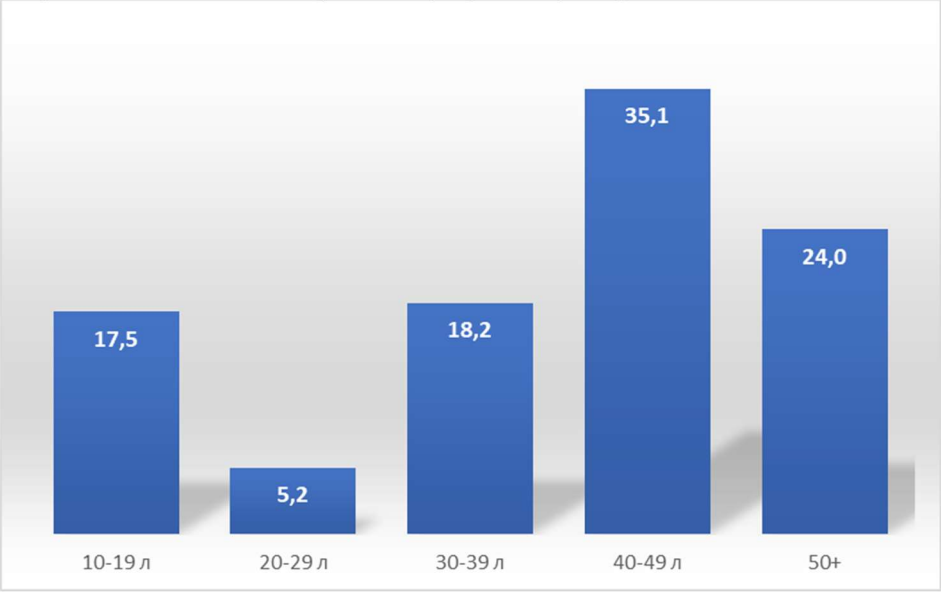
Figure 5: Forms of tuberculosis among the first detected cases n=152

Among the cases of recurrent tuberculosis, a notable distinction was observed in the forms of pulmonary tuberculosis present in the patients. Specifically, 45.6% of the recurrent cases were characterized by pulmonary tuberculosis with bacterial excretion, while 51.4% were classified as pulmonary tuberculosis without bacterial excretion.

Figure 6: Forms of tuberculosis during relapse n=35

The age category of patients newly diagnosed with tuberculosis is shown in Figure 7

Figure 7: Distribution of patients by age newly diagnosed tuberculosis n=152



New cases of tuberculosis were detected in all age groups

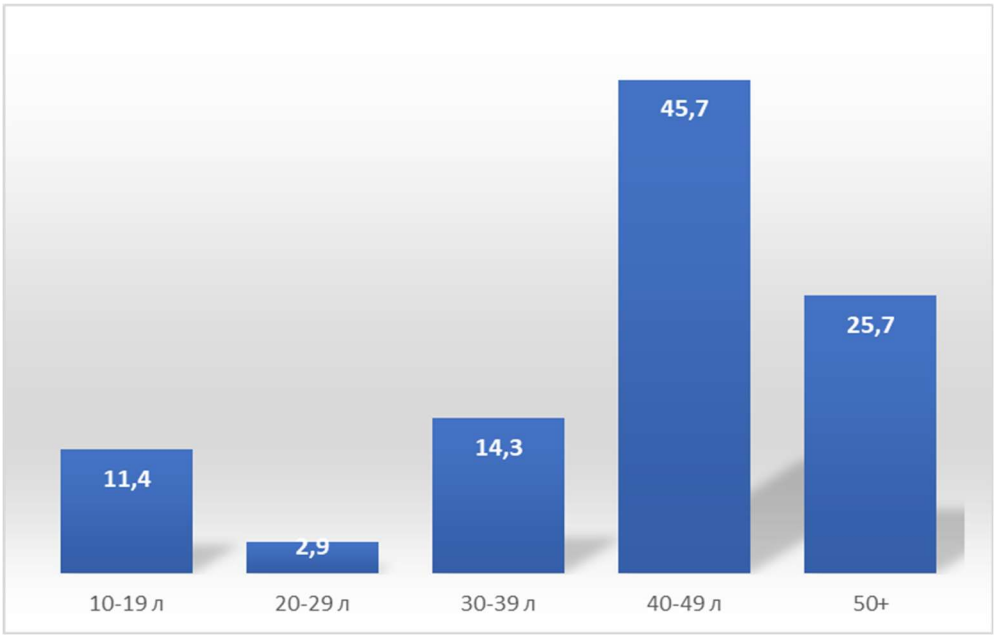
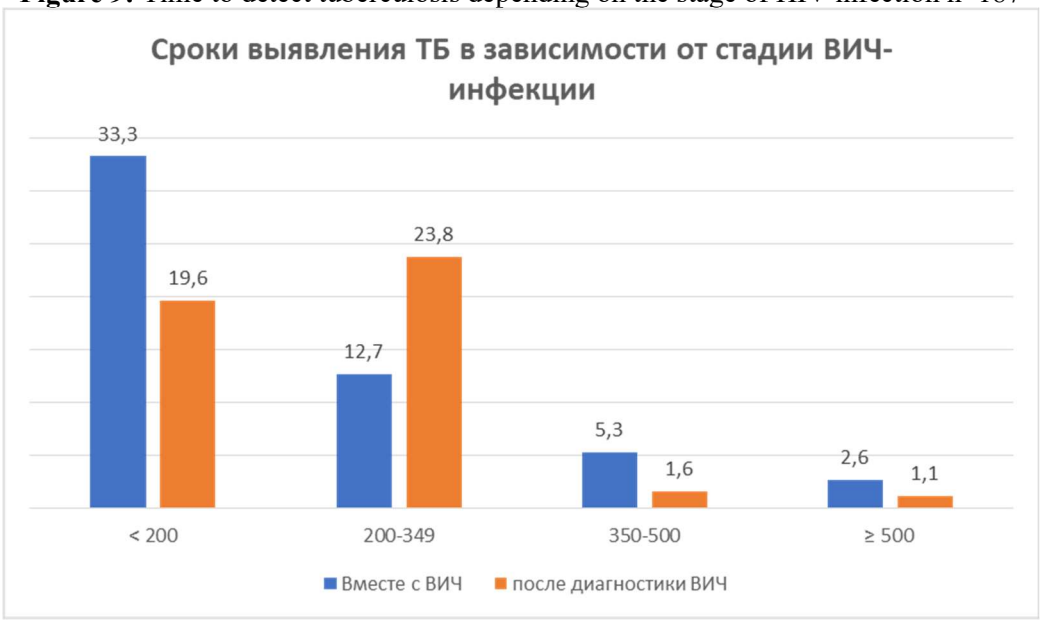


Figure 8: Relapses of tuberculosis were more common among people over 40 years of age n=35

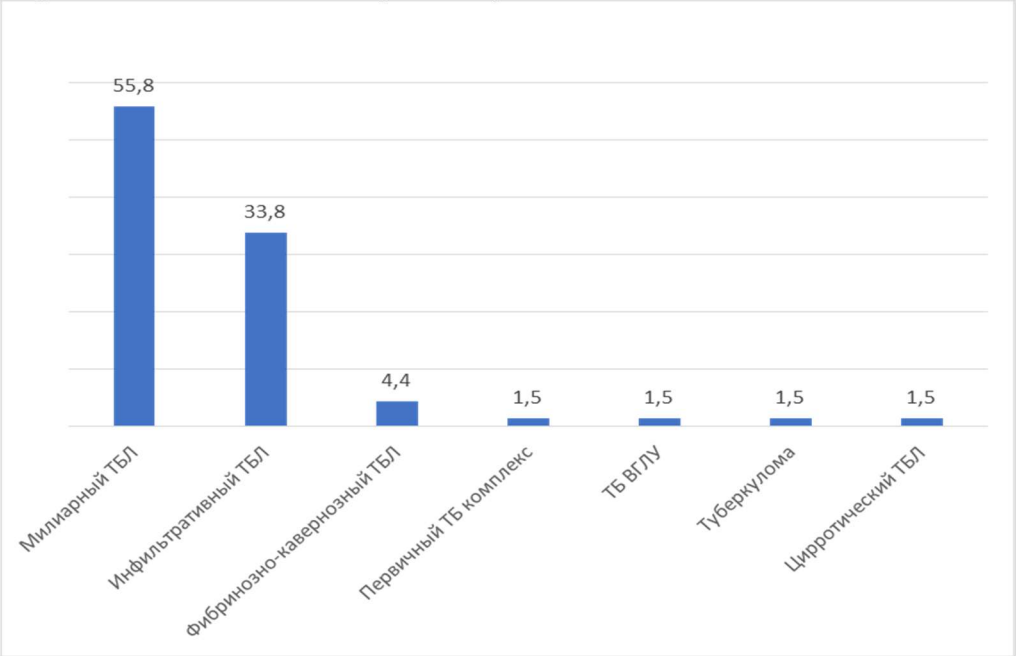
Figure 9: Time to detect tuberculosis depending on the stage of HIV infection n=187



In the initial stage of HIV infection, the simultaneous detection of tuberculosis (TB) and HIV was a prominent finding, indicating a close association between the two diseases at this critical juncture. As the HIV infection progresses into moderate immunodeficiency, characterized by CD4+ counts between 200 and 349 cells/µl, the likelihood of detecting tuberculosis increases significantly, occurring two times more frequently after the diagnosis of HIV. This trend underscores the heightened vulnerability of individuals with compromised immune systems, where latent TB infections may reactivate due to the weakening immune response. In cases of severe immunodeficiency, defined by CD4+ counts below 200 cells/µl, the simultaneous detection of both infections is 1.7 times higher, further emphasizing the interplay between HIV and TB as the immune system becomes increasingly compromised. This relationship illustrates the critical need for proactive screening and management strategies in HIV-positive individuals, particularly as their immune status declines, to mitigate

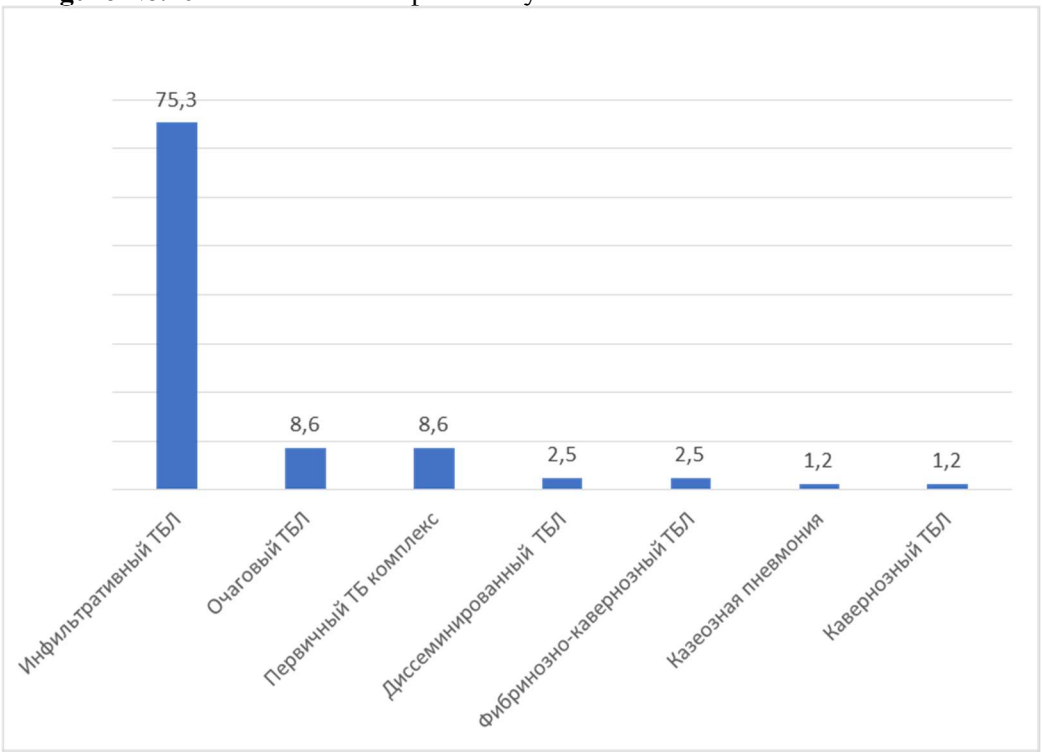
the risk of developing active tuberculosis and improve overall health outcomes (Xh et al., 2015).

Figure No. 9 Clinical forms of pulmonary tuberculosis with bacterial excretion n=61



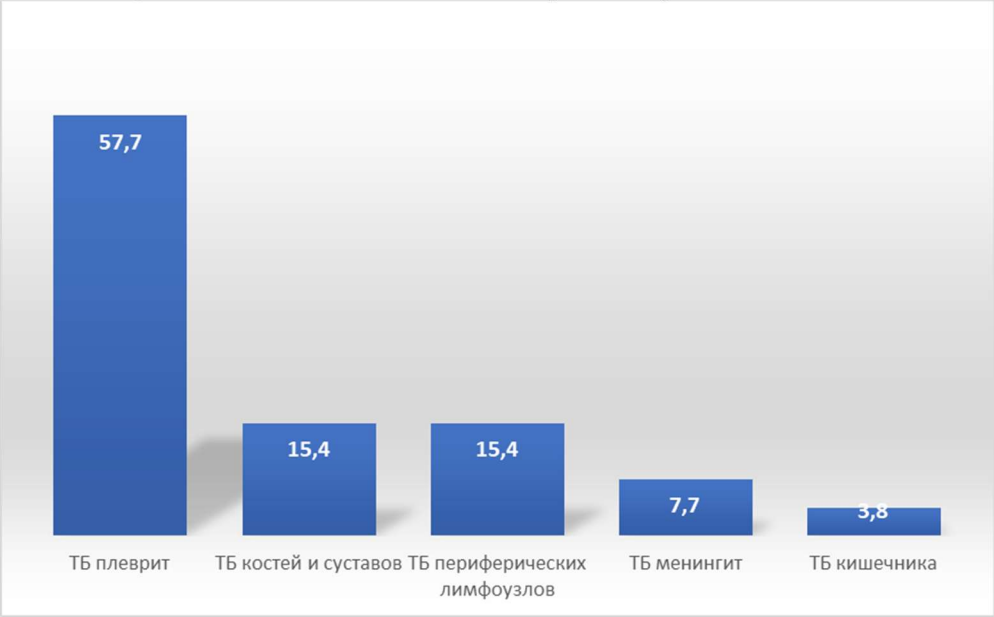
In the cohort of patients diagnosed with pulmonary tuberculosis characterized by bacterial excretion, there is a notable predominance of infiltrative and disseminated forms of the disease. Infiltrative pulmonary tuberculosis typically manifests with the formation of infiltrates in the lung parenchyma, indicating an active inflammatory response and significant tissue involvement.

Figure No.10 Clinical forms of pulmonary tuberculosis without bacterial excretion



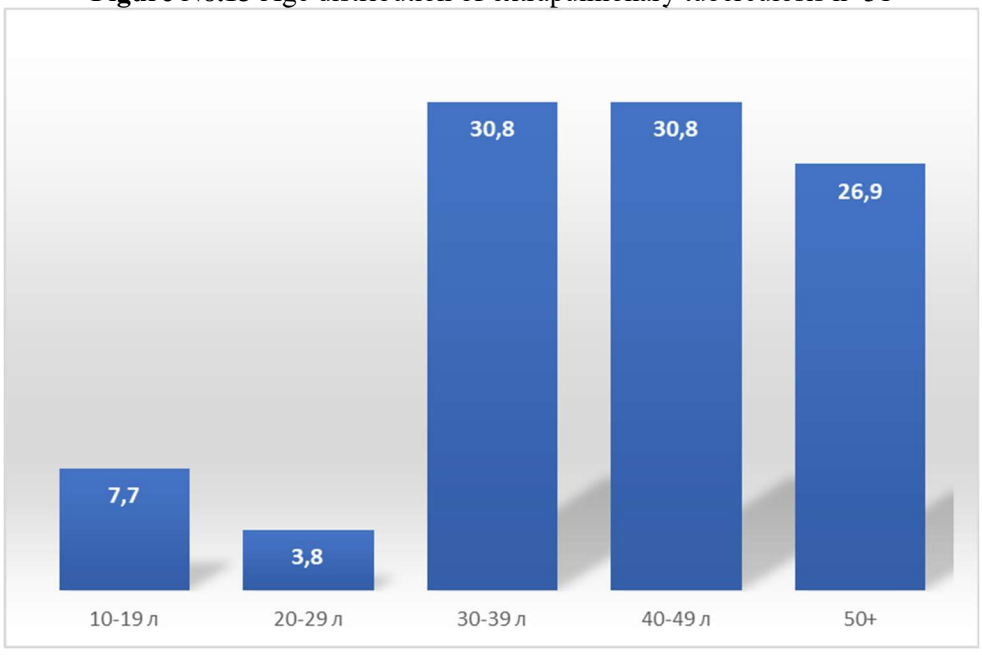
In the group of patients with pulmonary tuberculosis without bacterial excretion, the infiltrative form is predominantly found n=95

Figure No. 11 Clinical forms of extrapulmonary tuberculosis n=31



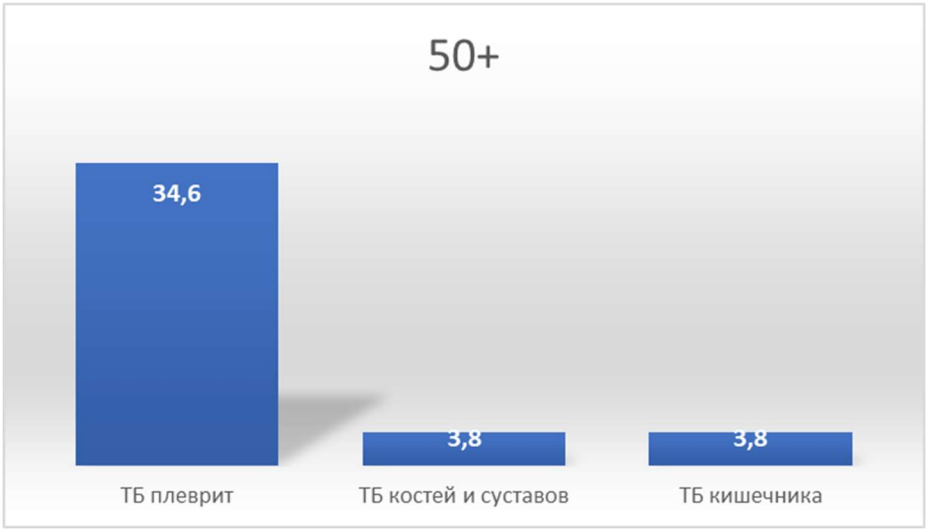
Among the extrapulmonary forms of tuberculosis, pleurisy emerged as the most prevalent manifestation, highlighting its significant association with the disease. The incidence of tuberculosis affecting the bones and peripheral lymph nodes was noted to occur with equal frequency, indicating a noteworthy pattern of extrapulmonary involvement in these sites. Conversely, the occurrence of tuberculous meningitis and intestinal tuberculosis was relatively rare, suggesting that while extrapulmonary tuberculosis can affect various organs, these particular forms may be less common in the studied population (VanderWeele & Ding, 2017).

Figure No.13 Age distribution of extrapulmonary tuberculosis n=31

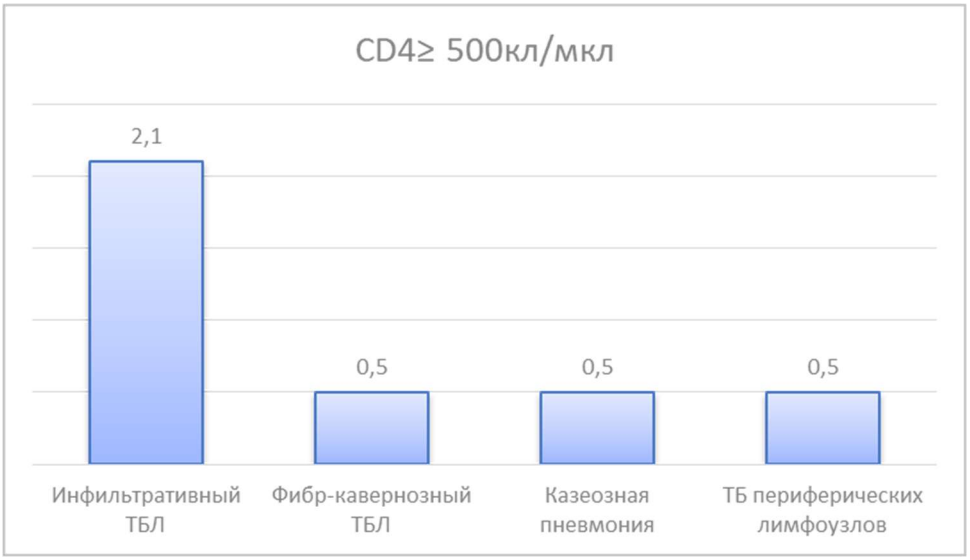


Extrapulmonary forms among young people occurred in rare cases; their prevalence was noted among people over 30 years of age.

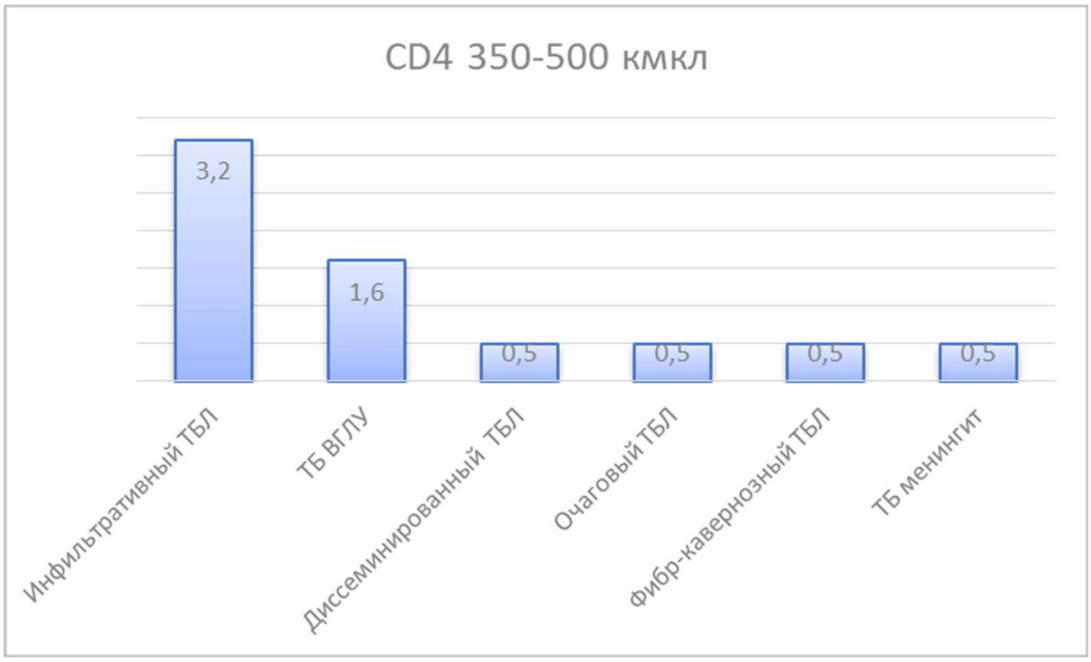
Figure No. 14 Clinical forms of extrapulmonary tuberculosis depending on age n=31



Reported in isolated instances among patients under 29 years of age, extrapulmonary forms of TB were indicated as somewhat rare in this younger population. This implies that younger people may have less extrapulmonary TB, maybe because of a greater immune response or less exposure to risk factors linked with the illness. On the other hand, among those over thirty years of age, extrapulmonary TB appeared with a wider spectrum of clinical symptoms over many anatomical locations. These localizations included the pleura, lymph nodes, belly, genitourinary tract, and skeletal system but were not restricted to these (An et al., 2024).

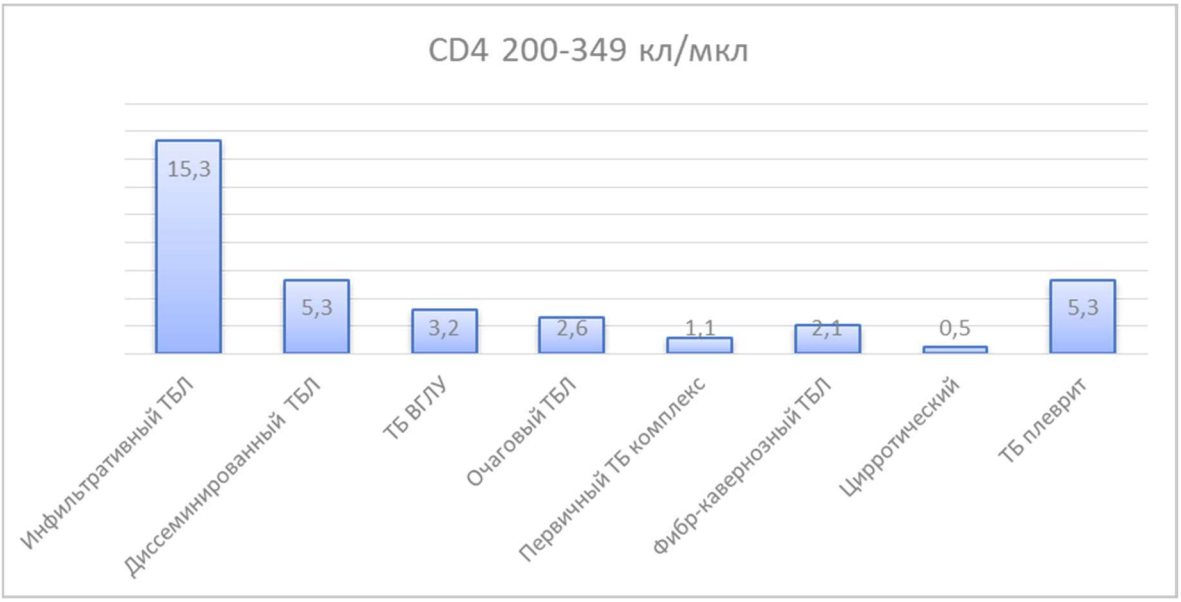


Mostly detected in individuals with CD4 counts more than 500 cells/µl, infiltrative pulmonary tuberculosis indicates a strong immunological response that enables the diagnosis of active TB even at this quite high degree of immune competence. Of these patients, 71.4% had preventative therapy with isoniazid (INH), a common method meant to lower the incidence of active tuberculosis in persons with latent TB infection. Given HIV, where immunosuppression may cause latent infections become reactivated, this preventive step is very crucial. Furthermore, the combination of anti-tuberculosis drugs with antiretroviral treatment (ART) showed significant immune system enhancement, which was shown by higher CD4 cell counts and general immunological recovery. This combined therapy not only addresses the opportunistic character of TB in HIV-positive individuals but also improves the immunological response of the host, thus improving clinical results and lowering the morbidity related with both diseases (An et al., 2024).

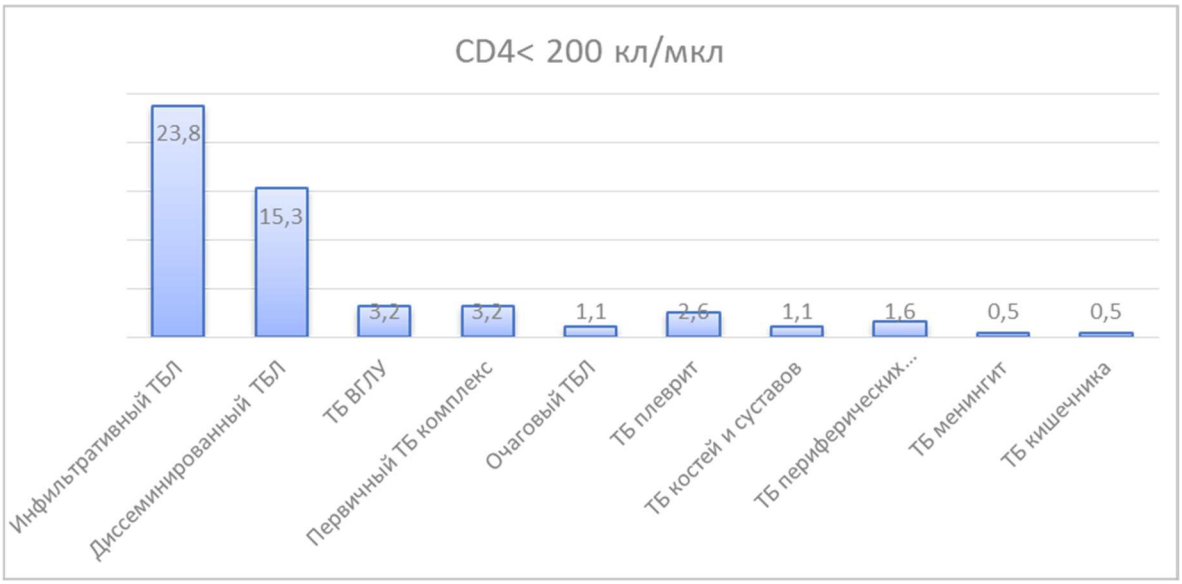


The most common clinical presentation seen in patients presenting with a CD4 count between 350 and 500 cells/µl was pulmonary TB, which emphasizes the higher vulnerability to this infection even in people with somewhat maintained immune system. Only one instance of meningitis was reported in this cohort, indicating

that while they may develop, extrapulmonary forms of TB are less common than pulmonary types. Especially, 65% of cases included isoniazid (INH) prophylactic treatment, suggesting a proactive strategy to stop the starting of TB in this high-risk population. Combining antiretroviral treatment (ART) with anti-tubercular drugs showed significant changes in immune system parameters, especially in terms of raising CD4 counts and hence strengthening general immunological resistance (Y et al., 2024).



In patients with CD4 levels ranging from 200 to 349 cells/µl, pulmonary tuberculosis presented in various forms, with a predominant occurrence of the infiltrative form. Among extrapulmonary cases, pleurisy was observed in 5% of patients. Additionally, isoniazid (INH) prophylaxis was administered to 46.2% of cases. The implementation of combination therapy involving antiretroviral treatment (ART) and anti-tuberculosis medications resulted in significant improvements in immune system function.



Reflecting extreme immunological deficits, pulmonary TB typically appeared in infiltrative and disseminated forms in individuals with CD4 levels less than 200 cells/µL. Observation of extrapulmonary TB in many

localities emphasizes the systematic character of the illness in immunocompromised people. In 38% of instances, isoniazid (INH) prophylaxis was given to stop active TB starting. Moreover, the mix of anti-tuberculosis drugs and antiretroviral treatment (ART) greatly strengthened immune system performance, shown by higher CD4 cell counts and greater immunological responsiveness. These results highlight the need of integrated management methods for co-infected patients to enhance health outcomes via early detection, efficient prophylactic action, and complete treatment approaches (Vidya Vijayan et al., 2017).

CONCLUSION

For the Kyrgyz population especially among males over 40 years of age, co-infection of HIV and tuberculosis (TB) is a major public health issue. According to recent research, 54% of cases in this population show simultaneous diagnosis of HIV and TB; nevertheless, tuberculosis usually develops in around 46% of patients roughly six years following an HIV diagnosis. Among persons living with HIV in Kyrgyzstan, newly diagnosed pulmonary tuberculosis without bacterial excretion is more common, which begs questions regarding undetectable TB cases fueling current transmission. Higher frequency of both pulmonary tuberculosis with bacterial excretion and extrapulmonary forms is linked to severe immunodeficiency (CD4 count under 350 cells/µl). TB is typically found concurrently in the early phases of HIV infection, however as immunodeficiency advances the prevalence of TB diagnosed after HIV rises. Those with intermediate immunodeficiency (CD4 count of 200–349 cells/µl) show especially this tendency; the identification of TB after HIV diagnosis is two times more prevalent in these patients. Severe immunodeficiency (CD4 count <200 cells/µl) increases the chance of simultaneous infection detection by quite a margin. Furthermore, while being somewhat uncommon among younger people in Kyrgyzstan, extrapulmonary TB is more common in those over 30 years of age. The most often occurring extrapulmonary type is still pleurisy; occurrences affecting bone and peripheral lymph nodes are less prevalent. Even less prevalent are meningeal and intestinal tuberculosis, which highlight the many clinical manifestations connected with HIV and tuberculosis co-infection. Improving health outcomes and creating focused treatments within the Kyrgyz healthcare system—especially in underprivileged groups—depend on addressing this co-infection.

Conflict of Interest: The authors declare that they have no conflicts of interest.

Data Availability: The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

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