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Profile of Clinical, Radiological and Laboratory Pattern in TB-HIV Coinfection in National Infection Centre of Indonesia

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Abstract

Background: The study aims to map TB (Tuberculosis) – HIV (Human Immunodeficiency Virus) patients based on clinical, radiological, and laboratory patterns. **Objective**: This study is expected to provide previous research investigating radiologic and laboratory examinations in TB-HIV patients. **Method:** We conducted a cross-sectional study based on medical records of TB-HIV patients at RSPI Sulianti Saroso from January 2004 - March 2017. Samples were 240 TB-HIV patients from a population of 1014 People Living with HIV/AIDS (PLWHA). Inclusion criteria were PLWHA, aged over 18 years, diagnosed with TB with completed medical record status. **Result:** Characteristics of the majority of patients were in the productive age group (99.2%) with an average age of 33 years and male sex (78%). The main symptom is cough (91.7%) and cough with phlegm (59.1%). Most patients (83.37%) have not received ART (Anti-Retroviral Therapy). Pulmonary physical examination showed that most patients had Ronchi (95.8%) while others got wheezing (5%). Laboratory tests revealed an initial CD4 cell count of 71.6 cells/ml and a negative Acid-Fast Bacillus (AFB) smear (59.2%). The patient's radiology was mainly with an infiltrate (82.5%); most infiltrate was presented in apex (52.4%). **Conclusion:** The majority of TB-HIV coinfected patients are young males, presenting with common TB symptoms, low CD4 counts, and negative AFB smears, complicating diagnosis. Radiological findings frequently show infiltrates, particularly in the apex. These findings emphasize the importance of early diagnosis and ART initiation to improve outcomes in TB-HIV coinfected patients.

Keywords: Co-infection, TB-HIV, PLWHA

Original Research Article

INTRODUCTION

Tuberculosis (TB) is a highly infectious disease that remains a leading cause of death worldwide (World Health Organization, 2015). According to the World Health Organization (WHO), in 2014, approximately 9.6 million people were affected by TB globally. In Indonesia, a prevalence survey conducted in 2013-2014 found that the rate of pulmonary TB diagnosed with a positive smear test was 257 cases per 100,000 people. This number was much lower than the prevalence of TB cases confirmed through bacteriological testing, which stood at 759 cases per 100,000 people. Furthermore, it is essential to note that many provinces in Indonesia witnessed an uptick in TB cases and also

experienced an increase in HIV-AIDS cases (Kemenkes RI, 2015). This indicates that the HIV epidemic is contributing to the growing incidence of TB (Kemenkes RI, 2012).

Tuberculosis is a contagious infection that can rapidly affect individuals with weakened immune systems, such as HIV. The symptoms of HIV-associated TB are different from those of TB without HIV. When comparing the clinical progression of HIV-associated TB to TB in general, common symptoms include fever and weight loss, particularly in the advanced AIDS stage. Additionally, there are notable differences in lung characteristics between TB in HIV-infected individuals and TB in those without HIV (Cain et al., 2010).

Culture is a recommended diagnostic method for tuberculosis, but it takes 6-8 weeks, causing delays in treatment. General sputum examinations are limited, especially in terms of sensitivity for childhood TB and TB in HIV cases. Chest X-ray exams are most effective when conducted early after HIV diagnosis; later on, it becomes challenging to detect distinct TB signs, usually indicating advanced lung involvement. One solution is to develop an early diagnosis method based on clinical and laboratory findings (Armedi, 2016; Swaminathan et al., 2010). This can be achieved by creating an early diagnostic algorithm using established TB diagnosis criteria for People Living with HIV/AIDS (PLWHA) in healthcare facilities. This study is expected to provide previous research investigating radiologic and laboratory examinations in TB-HIV patients.

MATERIALS AND METHODS

This study follows a descriptive observational design and focuses on TB-HIV. Study in Sulianti Saroso Infectious Disease Hospital Ministry of Health in North Jakarta. The source of secondary data was taken from medical records. It includes patients with the ICD X diagnostic codes B20.0 and B20.7 from the Medical Record Report spanning January 2004 to March 2017, totalling 1,014 patients. Sample size determination employed the estimated population proportion formula with a specified absolute precision (the Lemeshow formula). The calculation yielded a minimum sample size of 138.84. The calculated sample size was 138.84, and to account for potential dropouts, a 10% increase was applied, resulting in a minimum sample size of 153 individuals. We used consecutive sampling. Inclusion criteria encompassed patients diagnosed with TB-HIV at Sulianti Saroso Hospital between January 2004 and March 2017, adult patients (aged > 18 years), and those with comprehensive medical records, including laboratory data, clinical symptoms, physical examinations, and radiological reports. Exclusion criteria were applied to PLWHA with a prior history of TB (relapse). Analysis was done using IBM SPSS Statistics 23.0. Univariate data analysis was done by serving frequency distribution. The study was approved by the ethical reviewer from the Health Research Ethics Committee of Sulianti Saroso Hospital (Approval number: 21a /VII.10 /VII /2017)

Variables

Data were taken from medical records (MR). Demographic data included gender and age. Symptoms were taken from anamnesis at the admission date. TB history described both treated and untreated TB infection in the past. Glasgow Coma Scale was used to define the level of consciousness, then categorized into compos mentis, somnolence, apathy, delirium, sopor, or coma. Lung sound and respiratory rate were identified by pulmonologist at the hospital admission and recorded in the MR. Chest X-ray description was taken from radiologist expertise. Laboratory results (CD4 counts, sputum AFB, and Molecular Rapid Test for *Mycobacterium tuberculosis*) included were recorded not older than six months before the admission date.

RESULTS

Title of table Demographic data, Clinical signs, Symptoms, and Laboratory results of the study participants are shown in Table 1.

Table 1. Demographic, Profile Clinical Signs, Symptoms for TB and HIV Patients

Demographic, Clinical Signs and Symptoms (N=240)	Number (%)
Male	187 (77,9)
Female	53 (22,1)
Mean of Age (Years)	33,31 (20-72)
Anamnesis	
Cough	220 (91,7)
Fever	189 (78,8)
Night Sweat	113 (47,1)
Weight Loss	201 (83,8)
Dyspnea	118 (49,2)
Chest Pain	50 (20,8)
TB History	60 (25.0)
Number of Symptoms	
One	16 (6,7)
Two	37 (15,4)
Three	99 (41,3)
Four	84 (35.0)
Not Specific	4 (1,7)
General Condition	
Compos Mentis	230 (95,8)
Somnolence	7 (2,9)
Apathy	3 (1,3)
Rhonchi	74 (30,8)
Wheezing	12 (5.0)
Respiration Rate (x/minute)	
>20	129 (53,8)
≤20	111 (46,3)

Table 2. Profile Laboratory Finding for TB and HIV Patients

Laboratory (N=240)	**Number (%)**
CD4 Counts (Cells/mL)	
≤200	219 (91.3)
> 200	21 (8.7)
Sputum AFB	
Positive	34 (14,2)
Negative	142 (59,2)
ND*	64 (26,7)
Molecular Rapid Test for Mycobacterium Tuberculosis	
Positive	5 (2,1)
Negative	17 (7,1)
ND*	218 (90,8)

Based on the table 3, 240 respondents were mostly men; the average age of respondents was 33.31 years. Clinical symptoms of TB in PLWHA, such as TB in general, where symptoms often appear, are coughing, weight loss and fever.

Of the 240 TB-HIV patients, based on the signs and symptoms in screening, most of the three symptoms were 99 respondents (41.3%), but there were four respondents (1.7%) with non-typical symptoms (extrapulmonary patients). The results of laboratory tests were the majority of CD4 <200

cells/mL, negative sputum AFB, Onl 2.1% Molecular rapid test for Mycobacterium tuberculosis positive. Based on chest radiographs, most of them are infiltrates and non-apexes. The final diagnosis of most pulmonary tuberculosis is 99 patients diagnosed with pulmonary ecstasy and a combination of both, most of which are lymphadenitis tuberculosis.

Table 3. Profile Radiology Finding for TB and HIV Patients

Radiology (N=240)	Number (%)
Chest X-Ray	
Infiltrates	202 (84,2)
None Infiltrates	20 (8,3)
Hilum Enlargement	13 (5,4)
Infiltrates and Hilum Enlargement	5 (2,1)
Infiltrates Location	
Apex	67 (32,4)
Non-Apex	140 (67,6)
Final Diagnosis TB	
Lung TB	141 (58,8)
Extra Pulmonary TB	71 (29,6)
Combination	28 (11,7)
Extra Pulmonary TB and Combination (N=99)	
Tuberculosis Lymphadenitis	27 (27,27)
Tuberculosis Peritonitis	1 (1,01)
Miliary Tuberculosis	2 (2,02)
Tuberculosis Meningitis	1 (1,01)
ND	68 (68,68)

DISCUSSION

Coughing, phlegm, fever, weight loss, shortness of breath, and chest pain are clinical signs strongly associated with TB in PLWHA. This study's findings reveal that the majority of TB-HIV patients experience some form of cough, with or without phlegm. On the other hand, night sweats and shortness of breath are symptoms that are not usually specific to TB, but they become noteworthy in TB patients with HIV. The occurrence of cough and its variations can also be influenced by other factors, including viral infections. Importantly, some HIV TB patients show no signs of cough (18.3%) or phlegm cough (45.8%). This highlights that relying solely on the presence of clinical cough or its variations may not be sensitive or specific enough to diagnose TB.

However, the presence of cough with phlegm appears to be a stronger predictor of TB. Armedi's 2016 research indicated that symptoms like coughing for more than 24 hours and coughing with phlegm had high sensitivity but low specificity in predicting TB (Armedi, 2016). On the other hand, night sweats, while a clinical manifestation, are more commonly observed in people with HIV who don't have TB. The analysis revealed that 113 (47.1%) TB-HIV patients experienced night sweats, which often disrupt their sleep patterns. Other studies suggest that approximately 59.3% of people with HIV experience sleep disturbances (Oshinaike et al., 2014).

In this study, shortness of breath was a common complaint among patients. Shortness of breath is typically associated with chronic cases, including TB with complications. The study's findings also show that fever is a common symptom experienced by TB-HIV patients. Weight loss, another clinical sign, is believed to be linked to diarrhoea resulting from HIV-related enteropathy, which was observed in 76 (31.7%) patients. This aligns with findings from the Sharma et al. study, where weight loss was prevalent in TB-HIV patients, a condition often referred to as 'slim disease (Sharma et al., 2005).

Most of the patients (n=200; 83.37%) had not received ART (Antiretroviral Therapy). Out of the 40 individuals who received ART, the majority, 23 (57.5%), had been on ART for less than 6 months. It was observed that previously dormant TB infections became apparent approximately 2-3 weeks after initiating ART, primarily because of an amplified inflammatory response. Symptoms included fever, swollen lymph nodes, abscesses, deteriorating lung conditions, and widespread lesions affecting the central nervous system and joints. It's crucial to administer antituberculosis drugs promptly to prevent the worsening of TB in people with HIV (Mao et al., 2014). ART can only be initiated after a certain period of Antituberculosis Treatment. It's important to avoid using rifampicin in patients who are also receiving ART, as this can lead to interactions that increase rifampicin resistance and decrease the effectiveness of ART. To start the medication, CD4 levels are required as a guideline (Avihingsanon et al., 2010; Swaminathan et al., 2010). Given these findings, it is evident that careful management of TB and HIV co-infection is crucial to improving patient outcomes. The unmasking of dormant TB following ART initiation underscores the need for clinicians to be vigilant during this critical period. The avoidance of rifampicin in ART regimens, while necessary to prevent resistance, also highlights the complexity of treating co-infections.

CD4 levels provide insight into the immune system's status in individuals with HIV. The analysis revealed an initial CD4 level of 67.20, which is consistent with findings from previous studies, such as Rosamarlina's research, which noted CD4 cell counts were often low in TB-HIV coinfected patients, with 73.7% having CD4 counts below 100 cells/mm3 (Rosamarlina et al., 2017). This result is in line with research in Zimbabwe where results of 72% of CD4 counts of TB-HIV patients were below 200 cells / mm3 with an average of 104.5 cells / mm3 (Nzou et al., 2010). The presence of TB will increase the progression of HIV infection through a mechanism for increasing viral replication, thus accelerating the decrease in immunity (Albrecht et al., 2007). Generally, TB cases occur when CD4 levels are low. This event can be related to TB events that had happened sometime before and were detected at the time of treatment.

Laboratory test results in TB-HIV patients showed that the majority, 142 (59.2%), had negative smear tests, and 220 (91.7%) had positive results. This aligns with a study by Amin et al., which also found that sputum examinations in TB-HIV patients were mostly negative (Amin et al., 2013). Another study conducted by Dikromo noted that the majority of AFB (Acid-Fast Bacilli) examination results were negative due to the declining immune status of PLWHA. A weakened immune system impact the bacteriological features, leading to negative smear sputum results (Dikromo et al., 2011). The sensitivity of AFB examination in PLWHA is around 50%, and it becomes less accurate as the immune system is severely compromised (Affusim et al., 2012). Some TB-HIV coinfected patients turns out to be negative AFB, possibly due to experiencing dry cough, making it difficult to produce phlegm for testing. Additionally, the decreased immunity in PLWHA leads to nonspecific symptoms and clinical signs of TB resulting in delayed TB diagnosis (Desikan, 2013).

The accuracy of the AFB depends greatly on the quality of sputum samples and the amount of smear present in infected individuals. This limitation can significantly affect the test's reliability, especially when assessing sputum with less than 10,000 bacteria per milliliter. Despite its limitations, the AFB test remains a cost-effective option which is particularly suitable for resource-limited and remote areas where obtaining GenExpert or Xpert MTB/RIF® may be challenging (Padmapriyadarsini et al., 2011). The World Health Organization (WHO) recommends GenExpert for TB-HIV patients, as it simultaneously diagnose TB and Rifampicin resistance. GenExpert employs nucleic acid amplification technology and automatically processes samples, amplifies DNA, and performs PCR analysis within approximately 100 minutes. The ability of Xpert MTB/RIF has shown consistent performance in TB-HIV cases, with sensitivity reaching 92.2% in various countries worldwide (Padmapriyadarsini et al., 2011). However, in this study, 220 (91.7%) of the cases were not tested with GenExpert or Xpert MTB / RIF Machine® as RSPI Prof. Dr. Sulianti Saroso only acquired this technology in 2016, whereas the data for this study spans from 2004 to 2017.

According to Padmapriyadarsini et al., the introduction of Xpert MTB/RIF testing in three provincial hospitals in Indonesia led to a remarkable 47% increase in TB detection rates. This surge in demand for sputum examination for TB indicates that the higher TB detection rate is not solely attributed to the improved sensitivity of Xpert MTB/RIF compared to traditional smear examination or M. tuberculosis culture (Padmapriyadarsini et al., 2011). However, the availability of Xpert MTB/RIF has encouraged doctors to order these tests more frequently, even if they were previously hesitant due to concerns about the complexity or duration of the testing process, as they now recognize its value in helping them provide better care for their patients.

In PLWHA, the concentration of Mycobacterium tuberculosis (MTb) in sputum is often too low to be visually detected under a microscope. Attempts can be made to grow these low concentrations through culture. However, conducting MTb culture is a complex process requiring specialized reference laboratories due to biological safety standards, technical expertise, and the need for skilled human resources. Another challenge with MTb culture is the lengthy testing process. It takes several weeks or even months to obtain results. Solid MTb culture media requires 6-8 weeks, while liquid culture media takes 2-3 weeks for identification. Some alternative techniques, such as recombinant mycobacteriophage and a colorimetric culture system provide results in a shorter timeframe, typically 9-10 days.Due to the(Badie et al., 2012) time-consuming nature of these methods, the study conducted at RSPI Prof. Dr. Suliani Saroso found that 220 (91.7%) of the cases were not cultured using AFB.

The most common radiological findings in TB cases among HIV patients include intestinal infiltrates and infiltrates in the lung lobes. These findings are more prevalent in TB-HIV cases compared to HIV cases without TB. The presence of upper and intestinal lobe infiltrates is a characteristic feature of TB. Upon analyzing radiological results in TB-HIV patients, it was observed that the majority, 201 (83.8%), had infiltrates, while a smaller number, 5 (2.1%) patients, displayed infiltrates along with an enlarged hilum. These findings align with research conducted in Nigeria, where the majority of TB-HIV coinfected patients (81.8%) exhibited atypical chest X-ray results (Padyana et al., 2012). Another study by Mahesha noted that diffuse infiltrates in the latter half of the lung were more frequently seen in TB-HIV coinfected patients (Badie et al., 2012).

Chest X-ray examination plays an essential role in helping diagnose pulmonary tuberculosis in PLWHA especially when bacteriological tests are negative or when individuals cannot produce sputum. However, it's important to note that chest X-ray results may not always provide a specific indication of pulmonary TB in PLWHA. This can lead to both over-diagnosis and under-diagnosis. Therefore, it's not advisable to solely rely on chest X-ray results for diagnosing pulmonary TB. In general TB cases, including early-stage PLWHA patients with normal immune function, chest X-rays typically show characteristic infiltrate patterns in the upper lobe apex, often with cavities or unilateral pleural effusions. In advanced TB among PLWHA, particularly when their immune system is severely compromised, X-ray results often reveal infiltrates in the middle and lower lung lobes. These infiltrates can manifest as miliary patterns, diffuse infiltrates, or enlarged lymph nodes (Hoy & Lewin, 2003).

Around 70% of PLWHA often experience respiratory issues during the course of their disease. Chest X-rays are essential for assessing respiratory symptoms in HIV patients. In TB-HIV co-infections, the appearance of non-cavity infiltrates and intrathoracic adenopathy becomes more pronounced as CD4 cell counts decline. In mild immunosuppression, a typical TB pattern on chest X-rays is characterized by infiltrations at the lung apex and cavities. Conversely, those with severe immunosuppression tend to exhibit diffuse infiltrates, particularly in the lower lungs, without cavities. demonstrated that chest X-ray images often showed infiltrates and consolidation, primarily in TB-HIV patients with CD4 counts below 200 cells/mm3. These X-rays also indicated that TB patterns were often atypical, with most infiltrates found in the middle and lower lung lobes. In a study by Maniar, infiltrates were observed in the superior lobe in only 3.7% of cases, the middle lobe in 62.5%, and the inferior lobe in 33.8% (McAdam & Sharpe, 2005).

The predominant diagnosis among TB-HIV patients was primarily pulmonary tuberculosis, accounting for 58.8% of cases. Among the 32 lung specimens examined, the majority (84.38%)

exhibited signs of lymphadenitis. This finding aligns with earlier research conducted by Rosamarlina in 2016, which reported that the majority of TB-HIV patients had pulmonary TB, at 44.7% (Klatt et al., 2010).

Enlarged lymph nodes are the most frequently observed symptoms in individuals with TB-HIV co-infection. These symptoms may manifest early in the course of the infection or emerge at any stage of HIV infection. Lymphadenopathy is detectable in a significant proportion of PLWHA, with at least 25% of them exhibiting this condition during physical examinations (Klatt et al., 2010).

Limitation

This study has several limitations that should be acknowledged. First, the data utilized for analysis were derived from medical records spanning a long period (2004 to 2017). Given the advancements in diagnostic techniques and treatment options, the data may not fully reflect the current state of TB-HIV coinfection management, especially with the introduction of newer diagnostic tools like GenExpert, which was only available toward the end of the study period. Second, the study relied on secondary data from medical records, which may have led to missing or incomplete information. For example, not all patients were tested using the Molecular Rapid Test for Mycobacterium Tuberculosis, and many records lacked complete laboratory data for TB diagnosis, including smear results and CD4 counts. Lastly, the cross-sectional design of the study precludes any conclusions regarding causality between the clinical, radiological, and laboratory findings and patient outcomes. A prospective study design might be more effective in tracking disease progression and the effects of different treatments over time.

CONCLUSION

We found that most of the TB-HIV patients in Sulianti Saroso Hospital were male, with an average of 33,31 years old. They mainly experienced cough, fever and weight loss. Most of the patients had CD4 ≤200 cells and tested negative in SFB sputum. Chest X-ray showed most of them had infiltrated in the non-apical part. The results could be used as baseline data to conduct further research on existing diagnostics and treatments.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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