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Clinicodemographic and laboratory characteristics of cutaneous tuberculosis at tertiary referral hospital in West Java, Indonesia

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Abstract

Background: Cutaneous tuberculosis (TB) is a chronic infectious disease affecting the skin caused by *Mycobacterium tuberculosis* (*M. tuberculosis*). It constitutes 1–1.5% of extrapulmonary TB, with Indonesia being the third-highest TB burden country worldwide. Cutaneous TB is difficult to diagnose due to its varied presentations. This study aimed to describe the clinicodemographic and laboratory characteristics of cutaneous TB in a tertiary referral hospital in West Java, Indonesia.

Methods: This was a descriptive retrospective cross-sectional study. Data were obtained from the medical record of patients with cutaneous TB in the Tropical Dermatology Clinic of Hasan Sadikin Hospital Bandung, West Java, Indonesia from January 2017 to December 2019 using total sampling method.

Results: Of the 15 data retrieved, tuberculosis verrucosa cutis (n=5) was the most common type of cutaneous TB. Most of patients were males (n=8), between 15–24 years of age (n=6), were students (n=5), with the highest education level of primary school (n=5). Clinically, most of the cases presented as plaques and ulcers (n=6, respectively), had multiple lesions (n=9), located on lower limb (n=6). Acid-fast staining was negative in 8/8 cases, and culture was negative in 4/4 cases. The DNA of *M. tuberculosis* was detected in 2/5 polymerase chain reaction tests, while granuloma with caseous necrosis was found in 3/5 histopathological examinations.

Conclusion: Patients with cutaneous TB have a variety of characteristics. The results of laboratory examinations are often negative, and diagnosis may depend on clinical morphology. Therefore, clinicians should be familiar with the diverse clinical manifestations of cutaneous TB.

Keywords: clinicodemographic, cutaneous tuberculosis, laboratory examination, *Mycobacterium tuberculosis*.

Background

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis* (*M. tuberculosis*), which affects the lungs (pulmonary TB) or other organs (extrapulmonary TB).¹ According to the 2019 Global Tuberculosis Report by the World Health Organization (WHO), ten million people had TB worldwide.² Indonesia is the country with the third-highest burden for TB after India and China, with new cases increasing by 28% from 2017–2018.² According to the 2018

Indonesian Health Profile reported by the Ministry of Health of the Republic of Indonesia, West Java province has the highest incidence of TB, with 99,398 cases.³ According to the WHO, 15% of new TB cases worldwide are extrapulmonary, and can be classified based on infected organs (the meninges, pleura, lymph node, abdomen, urinary tract, bones and joints, and skin).^{1,2} About 1–1.5% of all extrapulmonary TB cases are cutaneous TB.⁴

Cutaneous TB is a chronic infection of *M. tuberculosis* that affects the skin.⁵ It can also be caused by *M. bovis* and the Bacillus Calmette-

Guerin (BCG) vaccine.^{5,6} Based on the transmission of *M. tuberculosis*, cutaneous TB can be classified into exogenous and endogenous cutaneous TB.^{5,6} Exogenous cutaneous TB consists of primary inoculation TB or TB chancre and TB verrucosa cutis (TVC).^{5,6} Endogenous cutaneous TB may occur by continuity, lymphatic, or hematogenic dissemination.^{5,6,7} This category includes lupus vulgaris (LV), scrofuloderma, TB gumma, acute miliary TB, and orificial TB.^{5,6} The clinical appearance of cutaneous TB varied, which include inflammatory papules, verrucous plaques, suppurative nodules, chronic ulcers, and other skin lesions.⁶ Therefore, the culture of *M. tuberculosis* or polymerase chain reaction (PCR) with specimens from skin lesions needs to be performed to diagnose cutaneous TB.^{8,9} In addition, other examinations such as histopathological examination, acid-fast staining, and tuberculin skin test can be performed.^{8,9}

The risk of infection by *M. tuberculosis* is higher in a person that has close contact with infectious TB cases, including household contact and health care workers.¹⁰ Individual factors such as age, gender, immune status, and malnutrition influence a person's susceptibility to infection.^{6,10} Moreover, people with low socioeconomic status are exposed to several factors such as poor ventilation and crowding that increases the risk of infection by *M. tuberculosis*.¹⁰ Subject to global epidemiology, scrofuloderma and LV are the most common cutaneous TB.⁵ Based on a retrospective study in India between October 2012–April 2016, there were 25 cases of cutaneous TB. LV has the highest incidence (44%), followed by TVC (16%) and scrofuloderma (8%), with a male-to-female ratio of 1,5:1.¹¹ To date, publications concerning epidemiological data and characteristics of cutaneous TB remain limited. Therefore, this study aimed to describe the clinicodemographic and

laboratory characteristics of cutaneous TB in the Tropical Dermatology Clinic of Hasan Sadikin Hospital Bandung as a tertiary hospital in West Java, Indonesia, from 2017 to 2019.

Methods

This descriptive retrospective cross-sectional study was approved by the Research Ethics Committee of Universitas Padjadjaran Bandung with approval letter number 940/UN6.KEP/EC/2020 and was also approved by the Medical Research Ethics Committee of Hasan Sadikin General Hospital Bandung through approval letter number LB.02.01/X.2.2.1/23338/2020. Data collection was conducted in the Tropical Dermatology Clinic and Medical Records Unit of Hasan Sadikin Hospital Bandung. The medical record of all cutaneous TB patients registered at the inpatient wards and/or outpatient clinics between January 2017 and December 2019 were collected using a total sampling method. The number of cutaneous TB patients was documented, and patient records were further reviewed for demographic, clinical, and laboratory characteristics. Secondary data were analyzed using descriptive statistics and processed by Microsoft® Excel 2013.

Results

A total of 19 patients with cutaneous TB were registered at the inpatient wards and/or outpatient clinics in Hasan Sadikin General Hospital Bandung. Four patients were excluded due to unavailable medical records; subsequently, only fifteen patients with cutaneous TB were included in this study. The distribution of cutaneous TB cases based on the clinical type was summarized in Table 1. The most common type of cutaneous TB was TVC, and the least common was TB

Table 1. Distribution of Clinical Type of Cutaneous Tuberculosis (TB)

Clinical type	Total patient (n = 15)	
	n	%
Exogenous Cutaneous TB	TB chancre	0
	TB verrucosa cutis	5
Endogenous Cutaneous TB	Lupus vulgaris	4
	Scrofuloderma	4
	TB gumma	2
	Orificial TB	0
	Acute miliary TB	0

gumma, with no cases found for TB chancre, acute miliary TB, and orificial TB.

Cutaneous TB showed a slightly higher incidence in males compared to females, with a ratio of 1.14:1. Out of five patients of TVC, four were male. The distribution of gender and types of cutaneous TB was presented in Figure 1. The highest prevalence of cutaneous TB occurred in the 15–24 years' age group. Based on the educational level, patients who graduated from primary school were the predominant cases of cutaneous TB. According to occupation, most cutaneous TB patients were students. One patient had a history of trauma, one patient had malnutrition, and the rest of the cases had unknown risk factors. Demographic characteristics of cutaneous TB patients were summarized in Table 2.

Cutaneous TB lesions were mostly located on the lower extremities, followed by the upper extremities. Multiple skin lesions were found in 9 out of 15 cases of cutaneous TB, with plaques and ulcers found in most cases. Clinical characteristics of cutaneous TB patients were summarized in Table 3. The histopathological features showed the presence of granuloma with caseous necrosis in three patients and well-formed granuloma without caseous necrosis in two patients. Acid-fast or Ziehl-Neelsen staining was performed in eight patients, but AFB were not found in all cases. *M. tuberculosis* cultures were performed on four patients without any positive results. In addition, two out of five patients on whom PCR examinations

were performed showed positive results. The laboratory characteristics of cutaneous TB patients were summarized in Table 4.

Discussion

A total of 15 cutaneous TB cases were analyzed in this study. TVC was the most common type of cutaneous TB, followed by LV and scrofuloderma. This was similar to retrospective studies conducted in Hong Kong published 1968 that found TVC as the most prevalent type of cutaneous TB, accounting for 46% of cases¹² and in 2006 found 6/16 cases of cutaneous TB to be TVC.¹³ In tropical zones, TVC is seen more often in barefooted patients who walked on soil contaminated with tuberculous sputum.⁶ This finding was in contrast with studies conducted in India published 2017 that showed LV as the most common type of cutaneous TB, accounting for 44% of cases, in 1999 reported 55% prevalence, and in coastal Karnataka, India reported 35.48% prevalence, followed by scrofuloderma.^{11,14,15} Meanwhile, TVC was the third most common cutaneous TB found in India.^{14,15} A similar study in Barcelona, Spain published 2013 also showed LV as the most common type of cutaneous TB with 22/36 cases of cutaneous TB.¹⁶ The difference in the results may be due to the difference in the study population characteristics, including the source of infection. LV occurs primarily in the previously-sensitized individual, endogenously via lymphohematogenous route, and occasionally via exogenous route.⁴

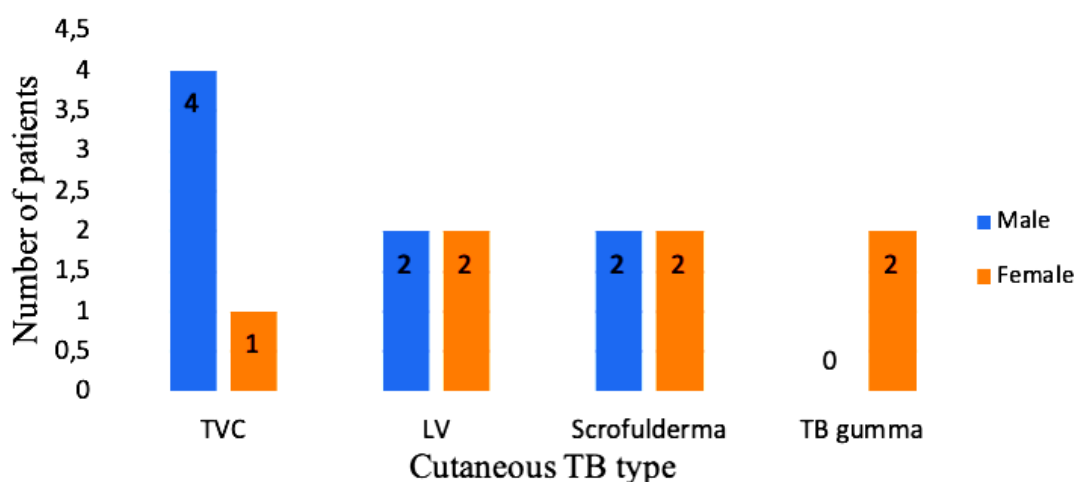


Figure 1. Distribution of Gender and Clinical Type of Cutaneous Tuberculosis (TB)
TVC: TB verrucosa cutis; LV: lupus vulgaris

Table 2. Demographic Characteristic of Cutaneous Tuberculosis (TB)

Characteristics		TB verrucosa cutis (n=5)	Lupus vulgaris (n=4)	Scrofuloderma (n=4)	TB gumma (n=2)	Total (n=15)
Gender	Male	4	2	2	0	8
	Female	1	2	2	2	7
Age	0–4 years old	0	0	1	0	1
	5–14 years old	2	1	0	2	5
	15–24 years old	1	2	3	0	6
	25–44 years old	2	1	0	0	3
	45–64 years old	0	0	0	0	0
	≥ 65 years old	0	0	0	0	0
	No data	0	0	0	0	0
Education	Primary school	2	2	0	1	5
	Junior high school	0	1	0	0	1
	Senior high school	1	1	0	0	2
	University graduates	0	0	0	0	0
	No data	2	0	4	1	7
Occupation	Student	3	2	0	0	5
	Housewife	0	0	1	1	2
	Laborer	0	0	0	0	0
	Farmer	0	0	0	0	0
	Fisherman	0	0	0	0	0
	No data	2	2	3	1	8
	No data	2	2	3	1	8
Risk Factor	Minor trauma	1	0	0	0	1
	Malnutrition	0	1	0	0	1
	Diabetes	0	0	0	0	0
	HIV infection	0	0	0	0	0
	No data	4	3	4	2	13

HIV: *human immunodeficiency virus*

Table 3. Clinical Characteristic of Cutaneous Tuberculosis (TB)

Characteristics		TB verrucosa cutis (n=5)	Lupus vulgaris (n=4)	Scrofuloderma (n=4)	TB gumma (n=2)	Total (n=15)
Type of lesions	Plaques	5	1	0	0	6
	Ulcers	0	3	2	1	6
	Nodules	0	0	0	1	1
	Vesicles	0	0	0	0	0
	Erythematous papules	0	0	0	0	0
	Erythematous pustules	0	0	0	0	0
	No data	0	0	2	0	2
Number of lesion	Solitary	2	2	0	0	4
	Multiple	3	2	2	2	9
	No data	0	0	2	0	2
Location of lesions	Head	0	2	0	0	2
	Neck	0	0	0	0	1
	Trunk	0	0	0	0	1
	Arm, hand	3	0	2	1	4
	Leg, foot	2	2	1	1	6
	No data	0	0	1	0	1

Table 4. Laboratory Characteristic of Cutaneous Tuberculosis (TB)

Characteristics		TB verrucosa cutis (n=5)	Lupus vulgaris (n=4)	Scrofuloderma (n=4)	TB gumma (n=2)	Total (n=15)
Acid-fast staining	Negative	2	4	1	1	8
	Positive	0	0	0	0	0
	No data	3	0	3	1	7
Histopathology examination	Granuloma with caseous necrosis	0	2	0	1	3
	Well-formed granuloma without caseous necrosis	2	0	0	0	2
	Poorly formed granuloma with intense caseous necrosis	0	0	0	0	0
	No data	3	2	4	1	10
<i>M. tuberculosis</i> culture	Negative	2	2	0	0	4
	Positive	0	0	0	0	0
	No data	3	2	4	2	11
PCR	Negative	1	2	0	0	3
	Positive	1	0	0	1	2
	No data	3	2	4	1	10

Scrofuloderma was also found to be the most common type of cutaneous TB in Morocco and Brazil, where a 72% prevalence was reported in a study published 2007 and 50.7% prevalence was reported in a study published 2019.^{17,18} Scrofuloderma represents direct extension into the skin from an underlying tubercular focus, most commonly tubercular lymphadenitis or skeletal TB.¹⁹ Additionally, consumption of unpasteurized milk leads to infection by *M. bovis* in cervical lymph nodes via tonsils and subsequent development of scrofuloderma.¹⁹

Male to female ratio for cutaneous TB in this study was 1.14:1. This result was similar to studies conducted in India published 1999 and in 2017 that showed cutaneous TB to be more often in males compared to females with a ratio of 1.2:1.^{14,15} In this study, TVC was seen more often in male. This was consistent with a study conducted in India published 1999.¹⁴ These results may be attributed to a higher risk of sustaining an injury since males spend more time outdoors than females.¹¹

In this study, the highest percentage of cutaneous TB was among students and between the ages of 15 and 24. It was consistent with a study conducted in India published 2006 which reported the most common age group to be 16–25 years (30.76%).²⁰ Cutaneous TB is commonly seen in young adults

because of their propensity to sustain injuries at work, leading to inoculation of tubercle bacilli.²¹

Tuberculosis verrucosa cutis usually presents as hyperkeratotic plaques (verrucous) lesions on exposed sites.¹⁹ It starts as erythematous papules surrounded by a purplish inflammatory halo that evolves into asymptomatic verrucous plaques, which are 1 to 5 cm in diameter. It may rarely ulcerate.⁶ Moreover, the most common skin lesions in the current study were plaques and ulcers, and most of the cases had multiple lesions. This result was in accordance with a study conducted in India published 2017 that found most of the cases to be of plaque lesions (46.77%), followed by sinus lesions (22.58%), and ulcerative lesions (16.13%).¹⁵

The most common site of infection in the current study was the lower extremities, which explained the findings of TVC as the most common type of cutaneous TB. This was similar to a study in India published 2017 which reports that cutaneous TB lesions commonly affects the lower limb (37.10%), followed by the face and neck (24.19%).¹⁵ It also corresponded to a study in Hong Kong published 2006 that showed lower limbs were affected in all TVC cases.¹³ Studies conducted in India published 2017 and in 2010 also found the lower limb to be the most commonly involved site of cutaneous TB.^{11,19}

TVC is mainly acquired by inoculation.¹⁴ Re-inoculation of tuberculosis bacilli often occurs through minor trauma, especially during squatting.^{11,19} The current study found that one TVC case had a history of minor trauma as the risk factor.

In addition to clinical features, the diagnosis of cutaneous TB is based on culture and PCR examinations, acid-fast staining, and histopathological findings.^{9,13,22} In the current study, *M. tuberculosis* DNA was detected in two out of five cases using PCR examinations. A study published 1999 showed that PCR performed in 23 TVC cases and 3 LV cases had all negative results.²³ The yield from PCR has been low in paucibacillary cases due to low bacterial load, including LV and TVC.²³ Culture was performed in four cases in this study, and all showed negative results. At the same time, acid-fast staining was performed in eight cases, and all showed negative results. A study conducted in Hong Kong published 2006 showed that the yield from culture was only 38%,¹³ and the study conducted in India published 2017 showed that acid-fast staining was positive in 20.96%, and culture was only positive in two cases.¹⁵ The sensitivity of *M. tuberculosis* culture is much lower than its specificity, at 80-85% and 98.5%, respectively, for pulmonary TB.²⁴ In a cutaneous presentation, positivity is even lower, at around 23% in traditional media.²⁴ A low number of viable bacilli in the specimen may cause a low yield from acid-fast staining, PCR, and culture.¹³ Most diagnostic methods have lower sensitivity and specificity rates for cutaneous TB than the pulmonary form.²⁴ Therefore, physicians must resort to every possible test and broad clinical consideration; as the sum of positive elements would be auxiliary in a precise diagnosis.²⁴

All cutaneous TB have a similar histopathological basis, composed of lymphocytes, epithelioid histiocytes, and giant cells.⁸ In this study, histopathological examinations were performed on five cases. Two cases had well-formed granulomas without caseous necrosis, and three cases had granulomas with caseous necrosis. A study conducted in Brazil published 2016 found chronic granulomatous inflammation and caseous necrosis in 51.4% of patients.²² The histological differences observed for each type of cutaneous TB result from the variation in the host's ability to organize the granulomatous process.⁸

The limitation of this study lies in the fact that study data were obtained from a paper-based medical record. Therefore, not all medical records were available during data collection as they might be

incomplete or missing. The sample size should be increased to present clearer data evidence as a suggestion for further studies.

Conclusion

In conclusion, the current study found TVC to be the most common type of cutaneous TB, with most patients being male and 15–25 years of age. Skin lesions are commonly located on the lower limb, with multiple plaques and ulcers as the most common type of skin lesions. The results of laboratory examinations are often negative, and diagnosis may depend on clinical morphology. Therefore, clinicians should be familiar with the diverse clinical manifestations of cutaneous TB.

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