# Reversal Reaction in Leprosy Patients: Study on Prevalence, Sociodemographic Characteristics, and Precipitating Factors at a Tertiary Referral Hospital in West Java, Indonesia

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## Abstract

**Background:** Heretofore, leprosy remains one of the most stigmatizing diseases with serious social consequences. Patients with leprosy might develop inflammatory reactions that interrupt with stable and chronic disease which are called leprosy reactions. Type 1 leprosy reactions, also known as reversal reactions (RR), are caused by immune responses that initially decreases, then "reverses" to become more intense, leading to considerable disability. The aim of this study was to identify the prevalence, sociodemographic characteristics, and precipitating factors of reversal reaction in leprosy patients.

**Methods:** This was a retrospective study with a cross-sectional design, with an approach to collecting data from the medical records of the Leprosy Clinic, Department of Dermatology and Venereology Dr. Hasan Sadikin General Hospital Bandung West Java, during January 2015–December 2019.

**Results:** The results showed that 53 patients (24.7%) of the total 214 leprosy patients experienced a reversal reaction. The most frequent type of leprosy with reversal reaction was borderline lepromatous (BL) (56.5%). Most of the patients were male (68%), aged between 25–44 years (47.2%), unemployed patients (35.8%), and the last education was senior high school (71.7%). Physical stress was suspected as the most precipitating factor in reversal reaction patients (50.9%).

**Conclusions:** The prevalence of leprosy patients with reversal reaction in a Tertiary Referral Hospital West Java, Indonesia is 24.7%, with various characteristics based on sociodemographic. Physical stress is suspected as the most precipitating factor of RR in leprosy patients. Early diagnosis of reversal reaction is important to prevent nerve damage and disability.

**Keywords:** Leprosy, patient's sociodemographic, prevalence, reversal reaction

## Introduction

Leprosy is a chronic granulomatous disease caused by *Mycobacterium leprae* (*M. leprae*), which mainly affects the skin and peripheral nerve, and the other organs, such as nose and testis.[1] This disease occurs mainly in developing countries in tropical and subtropical regions.[2] Globally, 208,619 new cases of leprosy were reported in 2018. The majority of cases occurred in the South-East Asia Region with 71% of all new cases.[3] Indonesia is the country with the third largest leprosy case in the world after India and Brazil, with 15,107 new cases in 2017. Based on the provinces in Indonesia, West Java ranks second with the largest new leprosy cases after East Java, with a total of 1,813 new cases.[3,4]

Leprosy is often characterized by an immune reaction, which is caused by the body's immune response to the infectious organism, M. leprae.[5] Based on clinical, histopathologic, and immunological criteria, leprosy is classified into two polar forms, tuberculoid leprosy (TT) and lepromatous leprosy (LL). There are borderline groups between the two polar forms, for example borderline tuberculoid (BT), mid-borderline (BB), and borderline lepromatous (BL).[6] Sudden changes in the immune-mediated response to *M. leprae* antigen are called leprosy reactions.[7] Although multidrug

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therapy (MDT) is effective, the morbidity from the reaction remains high. There remains an unmet need for effective therapy to prevent or mitigate nerve damage due to the reactions.[8] There are two types of leprosy reaction, type 1 leprosy reaction, also known as reversal reaction (RR), and type 2 leprosy reaction or erythema nodosum leprosum (ENL).[9] RR is a type IV hypersensitivity immune response caused by a specific increase in cell-mediated immunity against *M. leprae*. This reaction usually occurs during the first months of treatment to several years after the first symptoms of peripheral neuropathy.[2] RR manifests as pre-existing hypopigmented or slightly erythematous macules that become red and swollen, induration of existing plaque, ulceration formation, and the progressive neuritis that often leading to sensory and motor neuropathy.[9,10] There are several factors that trigger RR, such as focal infections, psychological and physical stresses, vaccination, chemotherapy, puerperium, and use of oral contraceptives.[11] Systemic symptoms are uncommon, but acute inflammation of the peripheral nerves occurs, leading to neurological impairment, which if not treated promptly and appropriately will lead to permanent loss of neurological function, usually due to the development of deformities of varying degrees.[12]

Studies on leprosy reactions in West Java, Indonesia are still limited and incomplete. The purpose of this study was to identify the prevalence, sociodemographic characteristics, and precipitating factors for reversal reaction in leprosy patients at a Tertiary Referral Hospital in West Java, Indonesia.

## Methods

This research was a retrospective study with a cross-sectional design, approved by the Research Ethics Committee of the Universitas Padjadjaran no. 893/UN6.KEP/EC/2020 and by the Medical Research Ethics Committee Dr. Hasan Sadikin General Hospital Bandung no. LB.02.01/X.2.2.1/22551/2020.

Data were collected using medical records from the Leprosy Clinic at the Department of Dermatology and Venereology Dr. Hasan Sadikin General Hospital Bandung West Java. The target population in this study used a total sampling of outpatient and inpatient diagnosed with leprosy patients with RR during January 2015–December 2019. Data collected were anamnesis, physical and laboratory examinations. The number of reversal reaction patients was conducted and reviewed based on sociodemographic, including age, gender, occupation, last education, and precipitating factors. Incomplete data were excluded. The data were further processed with Microsoft® Excel 2013, and presented in tables.

## Results

From January 2015–December 2019, 230 leprosy patients were enrolled in this study. Sixteen patients were excluded due

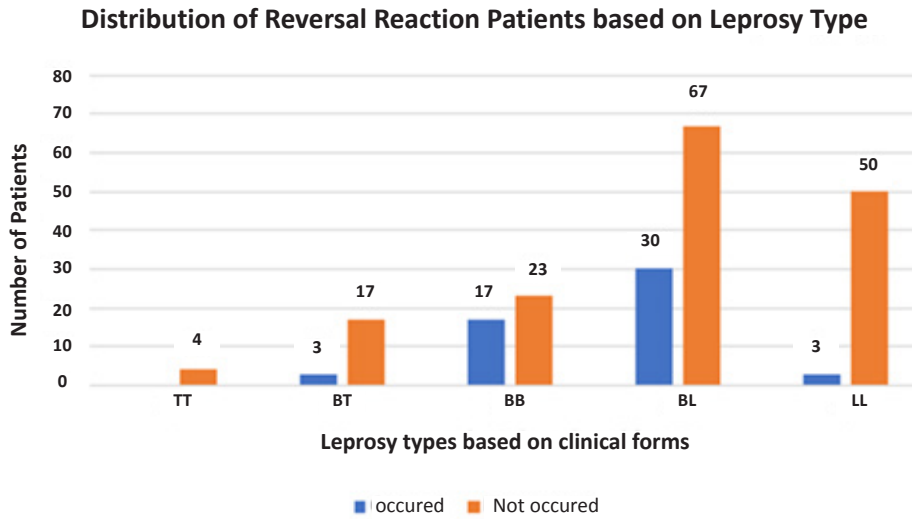


**Figure Distribution of Reversal Reaction Patients based on Leprosy Type**

**Table 1 Distribution of New Leprosy Cases Based on Leprosy Types**

| Leprosy Type | New Leprosy Cases (n=214) | |
|---|---|---|
| | n | % |
| PB | 24 | 11.2 |
| TT | 4 | 1.9 |
| BT | 20 | 9.3 |
| MB | 190 | 88.8 |
| BB | 40 | 18.6 |
| BL | 97 | 45.3 |
| LL | 53 | 24.7 |

Note: BB= Mid-borderline leprosy; BL= Borderline lepromatous leprosy; BT= Borderline tuberculoid leprosy; LL= Lepromatous leprosy; MB=Multibacillary leprosy; PB= Aucibacillary; TT= Tuberculoid leprosy

to inaccessible and incomplete data. The remaining two hundred and fourteen patients were eligible and had been identified in this study. The distribution of leprosy cases based on the classification of the World Health Organization (WHO) and Ridley Jopling was summarized in Table 1. MB was the most prevalent type with 190 cases (88.8%), whereas PB with 24 cases (11.2%). Based on the clinical form of leprosy, BL leprosy was the most frequent type (45.3%) (Table 1).

From a total of 214 leprosy patients, reversal reaction was documented in 53 patients (24.7%). BL leprosy was the clinical form that most commonly developed leprosy reactions with the number of 30 patients (56.6%). Figure showed the distribution of reversal reaction patients based on leprosy type.

Of the 53 patients with a reversal reaction, the results showed that male had the highest frequency with 36 patients (68%). Reversal reaction most occurred in the age range of 25–44 years (47%). In this study, it was found that unemployed patients had the highest frequency of 19 patients (36%). The data

**Table 2 Distribution of Reversal Reaction Patients based on Sociodemographic Characteristics**

| Patient Characteristics | | Total RR Patients (n=53) | |
|---|---|---|---|
| | | n | % |
| Gender | Male | 36 | 68 |
| | Female | 17 | 32 |
| Aged (years) | 0–4 | 0 | 0 |
| | 5–14 | 0 | 0 |
| | 15–24 | 11 | 21 |
| | 25–44 | 25 | 47 |
| | 45–64 | 15 | 28 |
| | ≥ 65 | 2 | 4 |
| Occupation | Unemployment | 19 | 36 |
| | Housewife | 12 | 23 |
| | Entrepreneur | 10 | 19 |
| | Labor | 8 | 15 |
| | Government employees | 3 | 6 |
| | Farmer | 1 | 2 |
| Last education | Not finished primary school | 0 | 0 |
| | Primary school | 4 | 8 |
| | Junior high school | 8 | 15 |
| | Senior high school | 38 | 72 |
| | Bachelor | 3 | 6 |

Note: RR= Reversal reaction

**Table 3 Distribution of Reversal Reaction Precipitating Factors**

| Precipitating Factors | RR Patients (n=53) | |
|---|---|---|
| | Frequency (n) | Percentage (%) |
| Physical stress | 27 | 51 |
| Infection | 19 | 36 |
| Psychological stress | 10 | 19 |
| Menstruation | 1 | 2 |
| Unknown | 6 | 11 |

Note: RR= Reversal reaction

showed that the most common education of patients was senior high school (72%). Physical stress was suspected as the most frequent precipitating factor in leprosy patients with reversal reaction (51%). There were six cases with undetected precipitating factors. Sociodemographic characteristics and precipitating factor of reversal reaction in leprosy patients were summarized in Table 2 and Table 3.

## Discussions

Leprosy reactions can cause poor quality of life in leprosy patients.[8] Early diagnosis of the reaction is important to detect the risk of developing leprosy disease and prevent complications, such as nerve damage and disability.

The total leprosy patients in this study were 214 patients, of which 24.7% of these leprosy patients experienced a reversal reaction. The most prevalent type of leprosy in these patients is MB, conform the WHO classification. This number is similar to the previous study in Denpasar.[13] Leprosy patients with MB type have more visible symptoms compared to Paucibacillary (PB) type, therefore, many patients with MB type come to medical health care and seek the treatment.[14] Interestingly, according to Ridley and Jopling's classification, BL is the most frequent type of clinical form in leprosy patients (45.3%). This is in contrast to study from Thailand[16] that found Borderline Tuberculoid Leprosy (BT) was the most common clinical form of all leprosy patients (32.4%).

Leprosy has five different types based on clinical, histopathologic, and immunological criteria.[1] Each country and region has a different result in the highest number of leprosy type, depending on the patient education about leprosy disease, health care facilities in the region, and the patients condition who come to the hospital and do an examination.

Fifty-three patients have developed a reversal reaction from overall leprosy patients (24.7%). This data can be interpreted as the prevalence of leprosy with reversal reaction of patients treated at the Leprosy Clinic in Dr. Hasan Sadikin General Hospital. This study found that the most reactions occurred in leprosy patients with BL type (56.6%). This is in contrast with the study in Surabaya[14] which found BB as the most frequent type among all reversal reaction patients. Reversal reaction mainly occurs in borderline forms of leprosy, such as BT, BB, and BL forms.[11] Multivariate analysis showed that borderline forms of leprosy and the MB treatment regimen were known to be major risk factor for the development of leprosy reactions.[15,18] The reversal reaction was observed in the presence of inflammatory infiltration by predominance CD4+ T lymphocytes, differentiated macrophages, human leukocyte antigen expression, giant cell formation, and epidermal thickening.[6] This inequality in this study might be due to the highest prevalence of leprosy patients with BL type.

Leprosy reactions are more commonly found in males than females with a ratio of 2:1.[14] Male has increased mobility and frequent interactions with the community, leading to increased access to contact with the disease more than female.[15] Self-report rates are also higher among men. The age group most affected (47.2%) by leprosy reaction was 25–44 years, comparable to study in other site in Indonesia.[13] Based on sociodemographic characteristics, unemployed people were found to be the highest in reversal reaction patients (35.8%). Unemployment has been studied as a high-risk factor from leprosy studies in a high-risk community setting in Sri Lanka.[17] Most of the patients had senior high school as their last education (71.7%). This is similar to a previous study conducted in eight out of the 20 countries with a high burden of leprosy, such as Brazil, India, Myanmar, Sri Lanka, Bangladesh, Indonesia, Egypt, and Philippines which reported that undergraduate

of education had an association with a higher leprosy incidence among neighbors.[18]

Moreover, physical stress is suspected as the highest precipitating factor causing RR in leprosy patients (50.9%). Stress is a state of the physical, psychological, and emotional tension in a person which can reduce half of his immunity in certain situations.[19] Stress is also an immunostimulator. These both pathways play an important role that may lead to lymphoid tissue, spleen, and other organ through the nervous system and humoral connections. A considerable number of common chemical transmitters (for example endorphins, substance P) can act both directions, indicating the immune system as a "mobile brain". This impairment of the immune balance can precipitate a leprosy reaction.[20]

This study has limitations that the study was a retrospective study using secondary data from medical records. Collecting medical records in the last 5 years might be challenging as there are missing or incomplete data.

In conclusion, the prevalence of RR is 24.7% among all leprosy patients in our study. The most frequent type of leprosy with RR is BL leprosy type and have various sociodemographic characteristics. The most of the patients are male, aged between 25–44 years, unemployed, and the last education is senior high school. Physical stress is suspected as the most precipitating factor for RR in leprosy patients.

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