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FACTORS ASSOCIATED WITH THE INCIDENCE OF TYPE 2 LEPROSY REACTION IN MULTI-BACILLARY (MB) LEPROSY SURVIVORS IN THE WORKING AREA OF THE BIAK CITY COMMUNITY HEALTH CENTER IN BIAK NUMFOR REGENCY

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Abstract

Type 2 leprosy reaction, or Erythema Nodosum Leprosum (ENL), is a serious immunological complication in multibacillary (MB) leprosy survivors that can cause peripheral nerve damage and permanent disability. Papua Province has the highest prevalence in Indonesia, including Biak Numfor Regency, with 35 cases of leprosy reactions. This study aims to analyze factors associated with the incidence of type 2 leprosy reactions in MB leprosy survivors within the Biak City Community Health Center (Puskesmas) of Biak Numfor Regency. This study was a quantitative cross-sectional design using secondary medical record data. The total sample size was 129 MB leprosy survivors registered at the Biak City Community Health Center between 2021 and 2025. Data analysis included univariate (frequency distribution) and bivariate (chi-square/Fisher's Exact Test with prevalence ratio calculation) analyses. The study found that of the 129 respondents, 60.5% experienced type 2 leprosy reactions. The majority of respondents were male (75.2%), and adults (86.0%). Bivariate analysis revealed two variables significantly associated with the incidence of type 2 leprosy reactions: fatigue (RP=2.346; 95% CI=1.564-3.519; p<0.001), stress (RP=2.213; 95% CI=1.571-3.118; p<0.001). Age and gender did not show a statistically significant association (p>0.05).
Keywords: Type 2 Leprosy Reaction, Multibacillary

Introduction

Leprosy, or Hansen's disease, is a chronic infectious disease caused by Mycobacterium leprae and remains a global public health problem, particularly in developing countries. According to the latest data from the World Health Organization (WHO), in 2023, 182,815 new cases of leprosy were recorded worldwide, an increase of approximately 5% compared to the previous year's 174,094 cases. In 2024, this figure decreased slightly to 172,717 new cases reported from 188 countries. Southeast Asia dominated with 131,425 cases, or approximately 79.3% of the global burden, with India, Brazil, and Indonesia as the three largest contributing countries [(1)].

In 2023, 5.3% of all new cases already had Grade 2 Disability (G2D) at the time of diagnosis, indicating that late case detection remains a serious challenge. The proportion of cases in children reached 5.7% of all new global cases in 2023, an important indicator of ongoing active transmission in the community [(1), (2)].

The WHO's Global Leprosy Strategy 2021-2030 embraces the vision of "Towards Zero Leprosy" with three key pillars: zero infection and disease, zero disability, and zero stigma and discrimination. This ambitious target includes a 90% reduction in the rate of new case detection and

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grade 2 disability by 2030. The persistent negative stigma associated with leprosy in many countries, including Indonesia, poses a serious obstacle to achieving this elimination target, leading to delays in case detection and treatment [3].

Leprosy sufferers can experience reactions that are acute episodes during the chronic course of the disease. These reactions are divided into two types: type 1 reactions (Reversal Reaction/RR), which are associated with increased cellular immunity, and type 2 reactions, or Erythema Nodosum Leprosum (ENL), which are type III hypersensitivity reactions involving humoral immune complexes. Erythema Nodosum Leprosum is characterized by painful erythematous nodules, systemic symptoms such as fever, acute neuritis, and involvement of other organs such as the eyes, joints, and testicles. [4],[5].

If treatment is delayed or inadequate, it can result in irreversible peripheral nerve damage and permanent disability. Disability resulting from leprosy reactions has widespread social, economic, and cultural impacts. Disabled leprosy survivors often experience social exclusion, loss of productivity, and various forms of discrimination, placing them at risk of multiple social challenges. This burden is borne not only by the individual but also by the family, the community, and the health system as a whole [2].

Based on a systematic review by Voorend et al. (2013) involving 65 studies, the incidence of Erythema Nodosum Leprosum ranges from 0.7-4.6% of all MB cases at the population level and reaches 13.7-49.4% in lepromatous patients in referral centers. ENL can occur before, during, or years after the completion of MDT treatment, with an average recurrence of 2.6 times per patient [6]. A recent study by Anggraini et al. (2025) identified that age, neuritis, skin ulcers, comorbidities, bacterial index, and sodium and albumin levels were associated with the severity of ENL [7].

In Indonesia, leprosy remains a significant public health problem. The Ministry of Health reported 17,251 new leprosy cases in 2023, up from 14,821 cases in 2022, with 90% being the multibacillary type and 8.2% affecting children. Indonesia still ranks third in the world in the number of leprosy cases after India and Brazil. Although Indonesia has achieved its national elimination target with a prevalence below 1 per 10,000 population, several provinces still have prevalence far above the national average, particularly in Eastern Indonesia. [7].

Papua Province is one of the regions with the highest leprosy burden in Indonesia. According to 2023 Ministry of Health data, Papua Province recorded a prevalence of 10.77 cases per 10,000 people, far exceeding the national average of 0.62 per 10,000. West Papua even recorded the highest national prevalence at 13.6 cases per 10,000 people, approximately 22 times the national average. This condition is compounded by the still high proportion of multibacillary cases, the proportion of child cases, and limited access to health services in remote areas of Papua [7].

Biak Numfor Regency in Papua Province remains one of the areas with a relatively high leprosy rate. According to data from the Biak Numfor Regency Health Office, in 2025, 250 new cases were recorded, with a prevalence of 39 per 10,000 residents and a Case Detection Rate (CDR) of 164 per 100,000 residents. The proportion of MB leprosy reached 80% and the proportion of pediatric cases was 24%, two indicators that cumulatively indicate the continued high level of active community transmission. The discovery of new cases at the Biak City Community Health Center over the past five years shows a fluctuating trend: 2021 (58 cases), 2022 (89 cases), 2023 (76 cases), 2024 (165 cases), and 2025 (70 cases) [8].

The number of leprosy reactions treated at the Biak City Community Health Center during the 2021-2025 period also showed significant numbers: 11 cases in 2021, 17 cases in 2022, 22 cases in 2023, 15 cases in 2024, and 35 cases in 2025. The high number of these reactions, particularly type 2 reactions, is a serious concern given their impact on disability and quality of life for survivors. Several factors thought to be associated with the occurrence of type 2 reactions in the local context of Biak

City include fatigue, stress, lack of rest, poor diet, and comorbidities with infectious and non-infectious diseases [8].

Given the high caseload of type 2 leprosy reactions and the resulting disability, an in-depth analysis of the factors significantly associated with the occurrence of these reactions in the Biak City Community Health Center (Puskesmas) area is needed. Understanding these factors is expected to form the basis for developing a more effective and contextual leprosy reaction control program tailored to local Papuan conditions.

Method

This research is a quantitative study with a cross-sectional design. Cross-sectional design is a type of observational research that collects data at a specific point in time to obtain an overview of a phenomenon or the relationship between variables [9]. The study population was all MB leprosy survivors who had experienced leprosy reactions (both type 1 and type 2) and were recorded in the leprosy program data of the Biak City Health Center in the period 2021-2025, namely 360 people. A sample of 129 people was taken using the purposive sampling technique.

Results

1. Univariate analysis

Table 1. Independent variable distribution

Characteristics	n	%
Age		
Adult	111	86,0
Adolescent/Child	18	14,0
Gender		
Male	97	75,2
Female	32	24,8
Reaction Occurrence		
Before/During MDT	84	65,1
After MDT	45	35,0
Fatigue		
Fatigue	78	60,5
No Fatigue	51	39,5
Stress		
Stress	67	51,9
No Stress	62	48,1
Type 2 Leprosy Reaction Occurrence		
Type 2 Reaction	78	60,5
Not a Type 2 Reaction (Type 1 Reaction)	51	39,5
Total	**129**	**100**

2. Bivariate Analysis

Table 1. Rasio Prevalensi, Chi-Square Analysis Type-2 Leprosy Reaction Occurrence

No	Variable	Type-2Leprosy Reaction Occurrence				P value	RP	Lower-Upper
		Rection Tipe 2		Non Reaction				
		N	%	n	%			
1	Age							
	Adult	63	56,8	48	43,2			
	Younger	15	83,3	3	16,7	0.060	0.681	0.52-0.886
2	Gender							
	Male	57	58,8	40	41,2	0.631	0.895	0.663-1.21
	Female	21	65,6	11	34,4			
3	Fatique							
	Yes	61	78,2	17	21,8	0.001	2.346	1.56-3.51
	No	17	33,3	34	66,7			
4	Stress							
	Yes	55	82,1	12	17,9	0.001	2.213	1.57-3.11
	No	23	37,1	39	62,9			

Based on the table above, it is known that of the 4 independent variables, it is known that the variables that are significantly related to the emergence of type 2 leprosy reactions are fatigue with a p value = 0.001 with RP = 2.346 CI 95% (1.56-3.51) and stress with a p value = 0.001 with RP = 2.13 CI 95% (1.57-3.11). Meanwhile, the age and gender variables have no significant relationship because the p value is > 0.005.

Discussion

1. Age

The majority of respondents were adults (111 people) (86.0%), while only 18 (14.0%) were adolescents or children. This finding is consistent with the general epidemiological pattern of MB leprosy. Leprosy is a disease with a long incubation period, averaging 2-5 years, so full clinical manifestations are more common in adults with long-term exposure [(1)]. An Indonesian national epidemiological study involving 2,461 patients from 13 teaching hospitals showed that patients aged over 14 years old accounted for 95.3% of the total leprosy cases [(10)]. Yosi et al. (2024) at Adam Malik Hospital in Medan also reported that the 18-59 age group dominated leprosy reaction cases, accounting for 95.1%. The high proportion of adults in Biak City indicates that MB leprosy, accompanied by the potential for severe reactions, poses a significant burden on the productive age group, with direct implications for economic productivity and quality of life [(11)].

2. Gender

Male respondents predominated at 97 (75.2%), while female respondents were only 32 (24.8%), with a ratio of 3:1. This finding aligns with global and national literature. Prakoeswa et al. (2022) reported a male predominance of 66.8% among Indonesian leprosy patients [(10)]. Yosi et al. (2024) reported that leprosy reactions were more common in men (70.7%). This male predominance can be explained by several mechanisms: first, men are generally more exposed to endemic environments due to work activities outside the home; second, men tend to seek treatment later, resulting in a greater bacterial load at diagnosis; and third, possible sex-based differences in immune responses. In Papua, socio-cultural norms and work conditions that involve more outdoor activities for men also contribute

to this pattern [11]. Leprosy can affect both men and women. Reports indicate that in most countries worldwide, with the exception of some in Africa, men outnumber women. The relatively low incidence of leprosy in women is likely due to environmental or sociocultural factors. In certain cultures, women's access to health care is very limited. Severity at diagnosis Men are more likely to present with multibacillary disease and with grade 2 disability at diagnosis in several large series, indicating more severe disease or later presentation among men in those settings [12],[13].

The results of this study are similar to those of studies conducted in Africa that males experience worse social reactions or more severe illness, which underscores that local culture, program performance, and research methods result in different sex ratios [14],[15].

3. Reaction Incidence

A total of 84 respondents (65.1%) experienced reactions before or during MDT treatment, while 45 respondents (35.0%) experienced reactions after MDT completion. This distribution is consistent with the literature showing that ENL occurs most frequently during MDT treatment but can also occur long after RFT [6]. Costa et al. emphasized that ENL can occur even years after a patient has completed treatment because persistent M. leprae antigens in tissues can trigger immune complex activation. The significant proportion of post-MDT reactions (35.0%) in this study underscores that clinical surveillance of MB leprosy survivors should not stop upon completion of MDT but should continue periodically to detect and manage reactions as early as possible [16],[6].

4. Fatigue

Seventy-eight respondents (60.5%) experienced fatigue, significantly more than those without fatigue (51; 39.5%). This relatively high proportion reflects the physical burden experienced by MB leprosy survivors in the study area. Fatigue in the context of MB leprosy is not only a common clinical symptom but also a condition that can trigger immune dysregulation through activation of the HPA axis and increased levels of the pro-inflammatory cytokines TNF-alpha, IL-1, and IL-6, which play a central role in the pathogenesis of Erythema Nodosum Leprosum [17]. The high proportion of fatigue in Biak City is likely related to the general physical condition of people living in areas with limited access to adequate nutrition, good rest facilities, and preventive health services.

ENL is often accompanied by systemic symptoms including fever, malaise, joint pain, and decreased energy, leading patients to report significant fatigue on quality-of-life assessments. Cross-sectional studies have shown significantly lower energy/fatigue domain scores on the SF 36 in patients with ENL compared to MB patients without ENL in Bangladesh and Brazil.

Clinically, fatigue appears as part of the constitutional syndrome of ENL and is associated with acute or recurrent episodes of reactivity. Direct quantitative measures of how ENL treatment changes specific fatigue scores are scarce in the available literature, so evidence for interventions targeting fatigue alone is limited [18].

5. Stress

The distribution of stress was almost even, with 67 respondents (51.9%) experiencing stress and 62 respondents (48.1%) not. This nearly equal proportion indicates that psychological stress is widespread among MB leprosy survivors, likely related to the burden of chronic disease, persistent social stigma, economic constraints, and anxiety about disability. Chronic stress activates inflammatory pathways through stimulation of the NLRP3 inflammasome, which produces IL-1beta and promotes the production of TNF-alpha, a key cytokine in the pathogenesis of ENL (17).(11). explicitly mentions stress as a risk factor for type 2 reactions, consistent with the finding of a high distribution of stress in this study.

Conclusion

1. There is a significant relationship between stress and type 2 leprosy reactions in multibacillary (mb) leprosy survivors in the Biak City Community Health Center, Biak Numfor Regency.
2. There is a significant relationship between fatigue and type 2 leprosy reactions in multibacillary (mb) leprosy survivors in the Biak City Community Health Center, Biak Numfor Regency.
3. There is no significant relationship between age and type 2 leprosy reactions in multibacillary (mb) leprosy survivors in the Biak City Community Health Center, Biak Numfor Regency.
4. There is no significant relationship between gender and type 2 leprosy reactions in multibacillary (mb) leprosy survivors in the Biak City Community Health Center, Biak Numfor Regency.

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