

Serum Brain-derived Neurotrophic Factor, Stress Levels, and Quality of Life Among Leprosy Patients: A Cross-sectional Study

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This study aimed to evaluate serum brain-derived neurotrophic factor levels, stress, and quality of life in leprosy patients, and to explore their interrelations. A cross-sectional study was conducted from September 2024 to May 2025 at 3 hospitals in Medan, Indonesia, involving 45 leprosy patients aged ≥ 18 years who met inclusion criteria. Serum brain-derived neurotrophic factor levels were measured using ELISA, stress was assessed using the Perceived Stress Scale-10, and quality of life was evaluated through the WHOQOL-BREF questionnaire. Descriptive statistics, Shapiro-Wilk normality test, and Spearman's rank correlation were used for analysis. The mean serum brain-derived neurotrophic factor level was 7.38 ± 3.37 ng/mL. Patients with multibacillary leprosy without reaction had higher brain-derived neurotrophic factor levels than those with type 1 or type 2 reactions. Stress levels were mild in 42.22% and severe in 28.89% of patients. Quality of life scores varied widely. A strong negative correlation was found between brain-derived neurotrophic factor and stress ($r = -0.953$, $p < 0.0001$), and a strong positive correlation between brain-derived neurotrophic factor and quality of life ($r = 0.962$, $p < 0.0001$). These findings suggest that serum brain-derived neurotrophic factor levels are associated with psychological well-being in leprosy patients and may serve as a potential biomarker for mental health monitoring in this population.

Key words: leprosy; brain-derived neurotrophic factor; stress; quality of life; multibacillary; paucibacillary.

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Leprosy is a chronic granulomatous infectious disease caused by *Mycobacterium leprae*, with a primary affinity for peripheral nerves, but it does not infect the central nervous system. The brain itself is generally not infected by *M. leprae*, due to the absence of Schwann cells in the central nervous system. Other commonly involved sites include the skin, eyes, upper respiratory tract mucosa, muscles, bones, and testes (1–3). Despite significant reductions in prevalence due to global eradica-

SIGNIFICANCE

Leprosy is not only a physical disease but also affects mental well-being and quality of life. This study highlights the role of a brain-related protein, brain-derived neurotrophic factor, in reflecting stress and life satisfaction in people with leprosy. Higher BDNF levels were linked to lower stress and better quality of life. These findings suggest that BDNF could be used as a biological marker to help doctors better understand and support the mental health of leprosy patients, leading to more holistic and compassionate care.

tion programmes, leprosy remains a major public health concern, particularly in endemic countries such as India, Brazil, and Indonesia, which together accounted for 74% of new global cases in 2021 (4). In Indonesia, the 2023 data reported 5.2 new cases per 100,000 population, with 90% being multibacillary (MB) (1).

Beyond its physical manifestations, leprosy is heavily burdened by social stigma and discrimination, contributing to psychological distress, social isolation, and decreased quality of life (4, 5). Chronic stress is particularly concerning, as it negatively affects both mental health and immune function. However, mental health in leprosy patients often remains under-addressed in clinical management (6–8).

Recent research highlights the potential role of brain-derived neurotrophic factor (BDNF) as a biomarker linking psychological stress with neurobiological changes. Physiological serum BDNF concentrations in healthy individuals typically range between 15 and 20 ng/ml (9), which are considered sufficient to support neuronal survival, growth, and plasticity. BDNF supports neuronal survival, growth, and plasticity, and is found in both the central nervous system and peripheral tissues, with approximately 90% stored in platelets (5, 6, 10). Physiological serum BDNF levels of approximately 15–20 ng/mL have been reported in healthy populations, and such levels are considered supportive of neuronal survival, growth, and plasticity. Chronic stress can alter BDNF expression through activation of the hypothalamic–pituitary–adrenal (HPA) axis and the release of pro-inflammatory cytokines, contributing to anxiety, depression, and cognitive dysfunction (6, 8, 11, 12).

The Perceived Stress Scale (PSS) is a validated tool used to assess subjective stress levels, while the WHO

Quality of Life-BREF (WHOQOL-BREF) questionnaire measures physical, psychological, social, and environmental dimensions of quality of life (13, 14). Previous studies, including Nogueira et al. (15), reported lower BDNF levels in leprosy patients compared with healthy individuals, suggesting a link between *M. leprae* infection and disrupted neurotrophic signalling (15).

However, the relationship between BDNF levels, stress, and quality of life in leprosy remains poorly understood. No studies to date have comprehensively explored these parameters together. Understanding these interactions may provide a more holistic perspective on leprosy and inform more integrated patient care approaches. Therefore, this study aims to investigate the correlation between serum BDNF levels, stress levels, and quality of life in individuals affected by leprosy.

MATERIALS AND METHODS

Methodology

An analytical observational study with a cross-sectional design was conducted between September 2024 and May 2025 at the Dermatology and Venereology Outpatient Clinics of Dr. Pirngadi General Hospital Medan, Prof. Dr. Chairuddin P. Lubis Universitas Sumatera Utara Hospital, and Adam Malik Hospital. Blood samples were processed at the Integrated Laboratory, Faculty of Medicine, Universitas Sumatera Utara. The study population comprised all individuals diagnosed with leprosy who attended the aforementioned clinics during the study period. Participants were enrolled using a non-probability consecutive sampling method, resulting in a final sample of 45 patients who met the inclusion criteria. Classification strictly followed the WHO criteria based on both lesion count and slit-skin smear status to minimize diagnostic errors.

Inclusion criteria

Inclusion criteria were: patients diagnosed with leprosy (either paucibacillary [PB] or multibacillary [MB]), aged 18 years or older, and willing to participate as indicated by signing an informed consent form.

Exclusion criteria

Exclusion criteria included patients who were uncooperative, had physical disabilities, or had a history of psychiatric disorders such as schizophrenia, depression, or mood disorders. Patients with chronic systemic or dermatological diseases (e.g., diabetes mellitus, psoriasis), those who had taken specific medications in the past 6 months (such as statins, corticosteroids, antidepressants, psychotropic drugs, or beta-blockers), and pregnant or breastfeeding women were also excluded from the study.

Clinical evaluation and classification

Patients were classified into PB or MB based on WHO criteria (≤ 5 skin lesions and negative slit-skin smear for PB; > 5 lesions or positive smear for MB). Reactions were categorized as type 1 or type 2. One PB patient with type 2 reaction was re-evaluated and likely represented a borderline case misclassified as PB.

Procedure

After obtaining informed consent, each participant underwent clinical evaluation to determine disease classification and duration. Demographic and clinical characteristics were recorded, followed by venous blood collection. A total of 5 mL of blood was drawn from the median cubital vein using standard sterile techniques. The blood sample was allowed to clot at room temperature for 30 min and then centrifuged at 3,000 rpm for 15 min. The serum was separated and stored at -20°C until further analysis. Serum BDNF levels were measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (R&D Systems, Minneapolis, MN, USA), and all procedures followed the manufacturer's instructions. Optical density was measured at 450 nm using a microplate reader. The majority of participants were receiving multi-drug therapy (MDT) at the time of sampling; no post-treatment samples were collected. Blood was obtained once, at baseline.

Stress levels were assessed using the Perceived Stress Scale-10 (PSS-10), which was administered through direct interviews. Based on the total score, stress levels were categorized as mild (0–13), moderate (14–26), or severe (27–40). Quality of life was evaluated using the WHOQOL-BREF questionnaire, also conducted through interviews, covering 4 domains: physical, psychological, social relationships, and environmental aspects.

A total of 48 eligible patients were screened, of whom 3 (6.25%) declined participation due to time constraints or reluctance to undergo venipuncture. Consequently, 45 patients were enrolled and included in the final analysis. None were excluded due to mental health conditions.

Statistical analysis

All data underwent statistical analysis. Univariate analysis was performed to summarize demographic and clinical characteristics. The Shapiro–Wilk test was applied to assess the normality of the data distribution. As the data were not normally distributed, Spearman's rank correlation test was employed to examine the relationship between serum BDNF levels, stress levels, and quality of life. A p -value of < 0.05 was considered statistically significant. All analyses were conducted using appropriate statistical software.

Table I. Demographic and clinical characteristics of leprosy patients (n=45)

Variable	Category	n	%
Age (years)	18–25	8	17.78%
	26–35	14	31.11%
	36–45	12	26.67%
	46–55	9	20.00%
	56–65	2	4.44%
Sex	Male	27	60.00%
	Female	18	40.00%
Leprosy type	Multibacillary (MB)	23	51.11%
Without reaction	—	18	—
	Type 1 reaction	2	—
	Type 2 reaction	3	—
Paucibacillary (PB)	—	22	48.89%
	Type 1 reaction	4	—
	Type 2 reaction	1	—
Duration of disease	≤6 months	15	33.33%
	7–12 months	14	31.11%
	>12 months	16	35.56%

RESULTS

A total of 45 patients diagnosed with leprosy were included in this study. All participants underwent a comprehensive evaluation consisting of anamnesis, physical and dermatological examinations, serum brain-derived neurotrophic factor (BDNF) measurement, assessment of stress levels using the Perceived Stress Scale-10 (PSS-10), and quality of life evaluation.

The demographic and clinical characteristics of the patients are summarized in **Table I**. The age distribution showed that the majority of patients were between 26 and 35 years old (31.11%), followed by 36–45 years (26.67%), 46–55 years (20.00%), 18–25 years (17.78%), and 56–65 years (4.44%). Regarding sex distribution, 60.00% were male and 40.00% female.

Based on leprosy classification, 51.11% of patients were diagnosed with MB leprosy, and 48.89% with PB leprosy. Among MB patients, 18 (40.00%) had no reaction, 2 (4.44%) presented with type 1 reaction, and 3 (6.67%) with type 2 reaction. In the PB group, 17 (37.78%) were without reaction, 4 (8.89%) had type 1 reaction, and 1 (2.22%) had type 2 reaction. The duration of disease was relatively evenly distributed, with 35.56% having leprosy for more than 12 months, 33.33% for 6 months or less, and 31.11% for 7 to 12 months.

The overall mean serum BDNF level among all participants was 7.38 ± 3.37 ng/mL, with a median of 8.02 ng/

Table II. Psychological profile and serum brain-derived neurotrophic factor (BDNF) levels

Variable	Category	n (%)	Mean±SD	Median (range)
Serum BDNF (ng/mL)	—	45	7.38 ± 3.37	8.02 (2–12)
Stress level	Mild	19 (42.22%)	18.47 ± 13.16	16 (0–40)
	Moderate	13 (28.89%)		
	Severe	13 (28.89%)		
Quality of life	Very Poor	13 (28.89%)	2.67 ± 1.28	3 (1–5)
	Poor	6 (13.33%)		
	Fair	10 (22.22%)		
	Good	15 (33.33%)		
	Very Good	1 (2.22%)		

Table III. Serum brain-derived neurotrophic factor (BDNF) levels by leprosy type and reaction status

Leprosy type	Reaction status	n (%)	Mean BDNF±SD (ng/mL)
MB	Without reaction	18 (40.00%)	8.14 ± 3.54
	Type 1 reaction	2 (4.44%)	10.94 ± 0.46
	Type 2 reaction	3 (6.67%)	5.38 ± 4.26
PB	Without reaction	17 (37.78%)	7.34 ± 3.05
	Type 1 reaction	4 (8.89%)	4.82 ± 2.11
	Type 2 reaction	1 (2.22%)	3.51

MB: multibacillary; PB: paucibacillary; SD: standard deviation.

mL and a range from 2 to 12 ng/mL (**Table II**). When analysed by leprosy type and reaction status (**Table III**), MB patients without reaction showed a mean BDNF level of 8.14 ± 3.54 ng/mL, those with type 1 reaction had a higher mean level of 10.94 ± 0.46 ng/mL, and those with type 2 reaction had a lower mean level of 5.38 ± 4.26 ng/mL. In PB patients, the mean BDNF level was 7.34 ± 3.05 ng/mL without reaction, 4.82 ± 2.11 ng/mL with type 1 reaction, and 3.51 ng/mL in the single patient with type 2 reaction.

Stress assessment revealed that 42.22% of participants experienced mild stress, 28.89% moderate stress (mean score 18.47 ± 13.16), and 28.89% severe stress. Quality of life assessment showed that 33.33% reported good quality of life, 28.89% very poor, 22.22% fair (mean score 2.67 ± 1.28), 13.33% poor, and 2.22% very good (see **Table II**).

Correlation analysis demonstrated a strong and statistically significant negative correlation between serum BDNF levels and stress scores ($r = -0.953$, $p < 0.0001$), indicating that higher BDNF levels were associated with lower perceived stress. Conversely, serum BDNF levels showed a strong positive correlation with quality of life ($r = 0.962$, $p < 0.0001$), suggesting that higher BDNF concentrations corresponded with better quality of life among leprosy patients (**Table IV**).

DISCUSSION

This study involved 45 leprosy patients who underwent a series of evaluations, including medical history taking, physical and dermatological examination, as well as serum BDNF level measurements, stress assessment, and quality of life evaluation. The collected data were processed and analysed using appropriate statistical methods.

The age classification in this study adhered to the categories defined by the Indonesian Ministry of Health: late adolescence (18–25 years), early adulthood (26–35 years), middle adulthood (36–45 years), early elderly (46–55 years), late elderly (56–65 years), and senior (>65

Table IV. Correlation between serum brain-derived neurotrophic factor (BDNF) levels, stress, and quality of life in leprosy patients

Variable	p-value	Correlation coefficient (r)
BDNF vs stress	<0.0001	-0.953
BDNF vs quality of life	<0.0001	0.962

years (16, 17). The most prevalent age group among participants was early adulthood (26–35 years), accounting for 31.11%, followed by middle adulthood (36–45 years) at 26.67%, and early elderly (46–55 years) at 20%. Participants' ages ranged from 18 to 59 years. No paediatric patients were included in this study. According to the Indonesian Ministry of Health, approximately 8.5% of new leprosy cases nationwide occur among individuals under 15 years of age, indicating ongoing transmission in the community.

This finding aligns with literature suggesting that individuals in their productive years are more vulnerable to *M. leprae* exposure due to increased mobility and social interaction (18–20). Additionally, delayed diagnosis and declining immune efficiency in older adults may contribute to higher incidence in this group (18, 21).

Although leprosy can affect all age groups, it is most prevalent among individuals aged 15–44 and tends to decline in older populations, possibly due to reduced mobility and the potential reactivation of latent infection (22, 23).

The majority of patients in this study were male (60%), while females comprised 40%. This result is consistent with previous findings and WHO reports (2022), indicating that men are at greater risk due to more frequent outdoor activity and delays in seeking medical care. Hormonal and behavioural differences may also influence immune responses to *M. leprae* infection (24, 25).

The distribution of leprosy types was relatively balanced, with MB cases accounting for 51.1% and PB for 48.89%. According to WHO, the MB type is more common in endemic areas due to frequent late-stage diagnoses (26).

Among MB patients, most did not experience leprosy reactions (18 individuals), while type 1 and type 2 reactions were found in 2 and 3 patients, respectively. Type 2 reactions are more common in MB cases due to high bacterial load and more complex immune responses (27).

In PB patients, 17 did not develop reactions, 4 had type 1 reactions, and 1 had a type 2 reaction. Type 1 reactions are more prevalent in PB cases due to stronger cellular immune responses (28).

The duration of disease varied from 2 to 20 months, with the majority (35.56%) experiencing illness for more than 12 months. This indicates that delayed diagnosis remains a significant problem, increasing the risk of complications and immune reactions (26).

Longer disease duration is associated with higher risk of disability and chronic immune reactions. Casotti et al. reported that chronic antigen accumulation and prolonged immune stress aggravate leprosy reactions (27).

The mean serum BDNF level in this study was 7.38 ± 3.37 ng/mL, lower than the average in healthy populations (16.3 ± 7.3 ng/mL according to Karege et al. (9)). This suggests possible neuroimmune dysfunction or impaired nerve regeneration due to *M. leprae* infection (30).

BDNF plays an essential role in neuronal maintenance, regeneration, and immune modulation. Reduced BDNF levels may indicate peripheral nerve damage and chronic inflammation (31).

BDNF levels varied by leprosy type and reaction. MB cases without reactions had higher BDNF levels (8.14 ± 3.54) compared with PB without reactions (7.34 ± 3.05). In MB with reactions, type 1 showed higher levels (10.94 ± 0.46) than type 2 (5.38 ± 4.26). In PB, BDNF levels were also higher in type 1 (4.82 ± 2.11) than in type 2 reactions (3.51). This suggests neuroprotective compensation or differing pathophysiological mechanisms between reaction types.

Nogueira et al. reported that *M. leprae* reduces BDNF expression in Schwann cells and mouse nerves, contributing to peripheral neuropathy. Decreased BDNF is also thought to reflect the severity of nerve damage and inflammation, making it a potential clinical biomarker (15, 32).

The mean stress score was 18.47 (median 16), ranging from 0 to 40. Most patients experienced mild stress (42.2%), indicating varying degrees of psychological distress among leprosy patients.

High stress levels may be due to emotional burdens from stigma, fear of disability, and social exclusion, as previously noted by Reis et al. (33). Depression, as a mood disorder, may also be precipitated by the psychosocial stigma and inflammatory consequences of leprosy, contributing to overall stress and reduced quality of life.

Patients reported diverse quality of life experiences: 33.3% rated their quality of life as good, while 28.9% reported it as very poor. This demonstrates a wide spectrum of lived experiences, influenced by medical, psychological, and social factors.

Patients with good quality of life often receive sufficient medical treatment and social support. In contrast, those with very poor quality of life frequently suffer from physical deformities, social stigma, and low self-esteem, as reported by Sinambela et al. (34).

Subjects with severe systemic illness, psychiatric disorders, or other medical conditions that could interfere with quality-of-life assessment were excluded from this study. Therefore, the data reflect the actual quality-of-life conditions of leprosy patients with relatively homogeneous medical backgrounds.

The Shapiro–Wilk normality test indicated that data for BDNF, PSS, and quality of life were not normally distributed ($p < 0.05$); thus, Spearman correlation was used. The results showed a very strong negative correlation between BDNF and stress levels ($r = -0.953$, $p < 0.001$), and a very strong positive correlation between BDNF and quality of life ($r = 0.962$, $p < 0.001$). These associations may also be influenced by individual differences in psychological resilience, social support, and life circumstances, which could not be fully accounted for in this cross-sectional design.

Progressive demyelination of nerves infected by *M. leprae* has been verified both *in vivo* and *in vitro*, along with glial pathology similar to that seen in other peripheral neuropathies (15). The peripheral nerve tropism of *M. leprae* involves binding to Schwann cells via a complex formed by alpha-dystroglycan receptors and the extracellular matrix protein laminin- α 2 (15, 35). The observed reduction in cytoplasmic expression and secretion of BDNF in human Schwann cells treated with *M. leprae* is associated with diminished neurotrophic and immunomodulatory function, leading to impaired tissue integrity. Conversely, Schwann cells rich in BDNF exhibit enhanced proliferative and secretory capacity *in vitro* (15, 36).

BDNF (Brain-Derived Neurotrophic Factor) is a major neurotrophin predominantly expressed in the postnatal brain, though it is also found in peripheral tissues such as the heart, lungs, and platelets. Besides neurons, BDNF is also secreted by astrocytes and microglia, with its release regulated by stimuli such as neuronal depolarization, neuropeptides, and compounds like glutamate and ATP.

BDNF plays a vital role in neuroinflammation, neuroplasticity, and cognitive and emotional function. Numerous studies have demonstrated its involvement in neuropsychiatric disorders, including schizophrenia, Alzheimer's disease, mood disorders, and Parkinsonism (15, 35).

Miao et al. (2018) found that both physical and psychological stress can reduce BDNF expression, impacting synaptic plasticity, neurogenesis, and overall quality of life. The current study's findings are consistent, showing negative correlations between BDNF and stress, and positive correlations between BDNF and quality of life (37). Buselli et al. (38) reported increased plasma BDNF in workers under chronic stress, possibly reflecting a neuroprotective compensatory response. Puhlmann et al. (39) observed elevated BDNF after acute psychosocial stress, with an antagonistic relationship to cortisol levels. Li et al. (40) found higher BDNF levels correlated negatively with depression scores in haemodialysis patients, suggesting its potential as a psychological well-being marker. Abd El Raheem et al. (41) also linked elevated BDNF to acne vulgaris severity, indicating a role in inflammation and skin cell proliferation, beyond its established neural functions. This study had several limitations. Only baseline sampling was performed; longitudinal changes in BDNF were not assessed. Patients with neuritis or silent neuropathy were not analysed separately. Paediatric patients were not included. One case classified as PB with type 2 reaction likely represented borderline misclassification. These issues should be addressed in future studies. Additionally, serum BDNF was not re-evaluated after treatment or reaction resolution; thus, dynamic changes over time could not be assessed. Longitudinal follow-up comparing patients with high and low baseline BDNF levels is warranted to determine predictive value.

This study demonstrates that serum BDNF levels are strongly negatively correlated with stress levels and positively correlated with quality of life among patients with leprosy. These findings highlight the potential of BDNF as a sensitive biomarker for assessing psychological condition and well-being in this population. Thus, measuring BDNF levels may be an important component of the comprehensive evaluation of leprosy patients, particularly in the early detection of chronic stress and declining quality of life. While alterations in BDNF are not specific to leprosy neuropathy, their consistent relationship with stress and neuroinflammatory responses underscores their potential utility as a general neuroimmune biomarker within this disease context.

The practical implication of this study is the urgent need to integrate mental health services and psychosocial rehabilitation into leprosy control programmes. Interventions aimed at reducing stress and improving quality of life are expected to enhance clinical outcomes and accelerate holistic recovery in patients affected by leprosy.

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The authors have no conflicts of interest to declare.

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