International Journal of Dermatology, Venereology and Leprosy Sciences

E-ISSN: 2664-942X
P-ISSN: 2664-9411
www.dermatologypaper.com
Derma 2021; 4(1): 08-13
Received: 04-11-2020
Accepted: 09-12-2020

Vannia Christianto Teng
Department of Dermatovenereology, RSUP Dr. Sitanala, Tangerang, Indonesia

Prima Kartika Esti
Department of Dermatovenereology, RSUP Dr. Sitanala, Tangerang, Indonesia

Eka Komarasari
Department of Dermatovenereology, RSUP Dr. Sitanala, Tangerang, Indonesia

Corresponding Author:
Vannia Christianto Teng
Department of Dermatovenereology, RSUP Dr. Sitanala, Tangerang, Indonesia

Prediction of leprosy patient's quality of life from clinical characteristics

Vannia Christianto Teng, Prima Kartika Esti and Eka Komarasari

DOI: https://doi.org/10.33545/26649411.2021.v4.i1a.55

Abstract
Background: Leprosy is one of the chronic skin infection which shares long term impact. It might cause permanent disability, and treatment might take longer before the patient completely recovered. These possibilities highly affect the quality of life (QoL).
Methods: A retrospective cohort study was conducted in the outpatient department of leprosy, in Sitanala Hospital, Tangerang, Indonesia. A total of 102 patients' QoL were assessed by Indonesian version of WHOQOL-BREF and sociodemographic and clinical course data were collected from medical records. P-value smaller than 0.05 is appraised as statistically significant.
Results: Low income was related to worse leprosy form (lepromatous leprosy type) and immune reaction (erythema nodosum leprosum). QoL scores could be predicted by form of leprosy, immune reaction, impairment grade, and duration of illness.
Conclusions: QoL scores in patients with leprosy could be predicted by illness characteristics and duration of illness, whereas forms of leprosy predicted all domains of QoL.

Keywords: Leprosy, quality of life, physical domain, prediction, socioeconomic

1. Introduction
Leprosy is a chronic bacterial infection, caused by *Mycobacterium leprae*. This bacteria targets skin cells and neurons, with Schwann cells in the peripheral nerves as its primary site of infection [1]. The diagnosis was based on clinical characteristics, represented by one or more cardinal sign, namely hypopigmented or erythematous skin patches accompanied with definite sensory loss, thickened peripheral nerves, and/or acid-fast bacilli detected on skin smears [2].
The Ridley-Jopling classification divides leprosy into 5 spectrums based on disease's clinical features, histopathology and immunological criteria, namely tuberculoid leprosy (TT), borderline tuberculoid (BT), borderline borderline (BB), borderline lepromatous (BL), and lepromatous leprosy (LL). Additional morbidity from leprosy-associated pathologic immune reactions was classified to reversal reaction (RR) and erythema nodosum leprosum (ENL). This immune reaction occurs in 1 of 3 people with leprosy, even with effective treatment of *M. leprae* [3] A study by de Paula *et al.* [4] stated that forms of leprosy-affected patients' immunologic reactions due to humoral immune response, with LL form have the greater odds of disability concordant with severe immune responses in this form, in concordant to the immune responses. LL form was characterized by vast production of interleukin-4, interleukin-10, and activation of regulatory T cells, yet failed to restrict *M. leprae* infecting Schwann cells [5] These immunologic reactions affect the clinical course as nerve injuries and impairment [6].
Nerve injury caused by leprosy may result in permanent damage leading to impairment, in which World Health Organization (WHO) classified into three grades: Grade 0 – no impairment, Grade 1 – loss of sensation in the hand or foot, and Grade 2 – visible impairment [7]. These impairments significantly affect patients' quality of life [8], therefore impacting patients' mental wellbeing. Along with physical limitations, patients might feel restricted to conduct daily activities and performance, leading to the sad feeling, fear, shame [9], as well as perceived stigma, contributing to deterioration in the quality of life (QoL) [10]. QoL in disease studies is referred to as health-related QoL (HRQoL), and WHOQOL-BREF assessment was used in this study.

The scoring includes 4 domains, namely Physical Health, Psychological, Social Relationships, and Environment [11]. HRQoL is now recognized as one of the important measures that need to be taken to achieve holistic wellness in patients, especially those suffering chronic and debilitating diseases [12]. However, there are only a few studies analyzing studies of QoL concerning patients' disease courses and basic demographic data, specifically in leprosy.

This study aims to assess the quality of life in patients with leprosy in this national referral hospital, and further assessed which factors associated with the respective Quality of Life (QoL) measured with WHOQOL-BREF, according to sociodemographic profile and disease course.

2. Materials and Methods

2.1. Samples

This retrospective cohort study was conducted in the outpatient department of leprosy, in RSUP dr. Sitanala, Tangerang, Indonesia, from October until November 2020, with informed consent. This study was approved by Health Research Ethical Committee, Faculty of Medicine, Ciputra University number 085/EC/KEPK-FKUC/X/2020. Total sampling was done during the period of the study based on inclusion and exclusion criteria. Patients aged 18 years or older who are diagnosed with leprosy, currently undergoing multi-drug treatment (MDT) were included in this study, while patients diagnosed with other diseases (including other psychiatric conditions) and patients whose medical records and/or self-filled questionnaire were found incomplete were excluded from the study. Demographic data (sex, age, educational background, occupation, monthly income), Indonesian version of WHOQOL-BREF questionnaire, and informed consents were obtained from patients upon their visits to the outpatient department. Patients' information regarding leprosy diagnosis, classification, and leprosy-related immune reactions previously diagnosed by dermatologists, were obtained from the medical records, along with any recorded impairment, duration of disease course and/or other comorbidities.

The sample size was calculated using the following formula: [13].

$$\left[\frac{Z\alpha \times s}{d}\right]^2$$

In which

Z: confidence interval, determined at 95%, with a value of 1.96

P: expected prevalence, with a value of 0.33 [14].

D: desired absolute precision, with a value of 0.1

According to the formula, the minimum required sample was 85 patients.

2.2. Statistical analysis

Statistical analysis was performed using statistical analysis. Demographic data were compared to forms of leprosy and immune reactions using one-way ANOVA and Chi-square tests. If chi-square assumptions were not met, fisher-exact probability test will be used. Mean scores gained from the questionnaire (General QoL, HRQoL, Physical Health Domain, Psychological Domain, Social Relationships Domain, and Environment Domain) were compared to forms of leprosy and immune reactions in one-way ANOVA and Tukey's test as post-hoc analysis was also conducted if significant differences were found. Multiple linear regression analysis was conducted between variables. P-value smaller than 0.05 is appraised as statistically significant.

3. Results and Discussions

3.1. Demographic Characteristics

This study was conducted on 102 patients visiting the outpatient department of leprosy in Sitanala Hospital, with mean age of 37.9 years. Most patients were male (63.73%), graduated from secondary school or any lower degree (64.71%), and living with monthly income less than PMW (60.78%). Regarding their illnesses, they have spent averagely 1.64 years living with leprosy and averagely have received MDT as leprosy treatment for 0.77 years. Most of the samples suffered borderline (50.00%) form of leprosy, with impairment grade 1 (47.06%). Most of their cases were not due to immune reaction (47.06%). Number of samples in this study has reached central limit theorem, thus the distribution of the sample means would be considered normally distributed. Demographic data of the samples were compared according to forms of leprosy and immune reactions [Table 1] is found that lower economic status, higher grade of impairment, and duration of illness share significant difference to forms and immune reactions of leprosy.

Table 1: Demographic- form and immune reaction of leprosy

	Form					p-value
	TT	BT	BB	BL	LL	
Age	38.00 (5.65)	39.06 (15.89)	41.67 (11.85)	35.92 (15.59)	37.11 (16.46)	0.743
Sex						
Male	1 (1.5%)	9 (13.8%)	11 (16.9%)	37 (46.9%)	7 (10.8%)	0.174
Female	1 (2.7%)	7 (18.9%)	13 (35.1%)	14 (37.8%)	2 (5.4%)	
Education						
≤ Secondary School	0 (0%)	9 (13.6%)	16 (24.2%)	35 (53.0%)	6 (9.1%)	0.335
> Secondary School	2 (5.6%)	7 (19.4%)	8 (22.2%)	16 (44.4%)	3 (8.3%)	
Income						
< PMW	0 (0%)	4 (6.5%)	13 (21%)	39 (62.9%)	6 (9.7%)	0.001^
≥ PMW	2 (5%)	12 (30%)	11 (27.5%)	12 (30%)	3 (7.5%)	
Reaction						
Nonreactive	2 (4.2%)	15 (31.3%)	16 (33.3%)	15 (31.3%)	0 (0%)	0.000^
RR	0 (0%)	0 (0%)	1 (6.3%)	12 (75%)	3 (18.8%)	
ENL	0 (0%)	1 (2.6%)	7 (18.4%)	24 (63.2%)	6 (15.8%)	
Impairment						0.000^

Grade 0	2 (12.5%)	5 (31.3%)	6 (37.5%)	3 (18.8%)	0 (0%)	
Grade 1	0 (0%)	10 (20.8%)	14 (29.2%)	22 (45.8%)	2 (4.2%)	
Grade 2	0 (0%)	1 (2.6%)	4 (10.5%)	26 (68.4%)	7 (18.4%)	
Duration of illness, years (Mean±SD)	0.46 (0.41)	0.80 (0.43)	0.96 (0.49)	2.01 (1.04)	3.02 (1.80)	0.000
Duration of treatment, years (Mean±SD)	0.25 (0.35)	0.46 (0.37)	0.88 (0.75)	0.83 (0.54)	0.77 (0.53)	0.504

	Reactions			p-value
	Non-reactive	RR	ENL	
Age, years [Mean (SD)]	40.17 (15.13)	42.25 (18.02)	33.24 (11.54)	0.656
Sex				
Male	25 (38.5%)	11 (16.9%)	29 (44.6%)	0.061
Female	23 (62.2%)	5 (13.5%)	9 (24.3%)	
Education				
≤ Secondary School	32 (48.5%)	12 (18.2%)	32 (48.5%)	0.450
> Secondary School	16 (44.4%)	4 (11.1%)	32 (48.5%)	
Income				
< PMW	17 (27.4%)	11 (17.7%)	34 (54.8%)	0.000^
≥ PMW	31 (77.5%)	5 (12.5%)	4 (10.0%)	
Form				
TT	2 (100%)	0 (0%)	0 (0%)	0.000^
BT	15 (93.8%)	0 (0%)	1 (6.3%)	
BB	16 (66.7%)	1 (4.2%)	7 (29.2%)	
BL	15 (29.4%)	12 (23.5%)	24 (47.1%)	
LL	0 (0%)	3 (33.3%)	6 (66.7%)	
Impairment				
Grade 0	13 (81.3%)	0 (0%)	3 (18.8%)	0.000^
Grade 1	29 (60.4%)	6 (12.5%)	13 (27.1%)	
Grade 2	6 (15.8%)	10 (26.3%)	22 (57.9%)	
Duration of illness, years [Mean (SD)]	0.99 (0.68)	2.37 (1.40)	2.13 (1.14)	0.002
Duration of treatment, years [Mean (SD)]	0.68 (0.62)	0.61 (0.41)	0.93 (0.57)	0.252

^Fisher-Exact Test

3.2. QoL in patients with leprosy

There were significant differences in general QoL, health-related QoL, Physical Domain QoL, etc in forms of leprosy (P<0.001) and immunological reaction (P<0.001) [Table 2].

Table 2: Association between QoL scores and forms and immune reaction of Leprosy

	Form					**p-value**
	TT	**BT**	**BB**	**BL**	**LL**	
QoL General [Mean (SD)]	5.00 (0.00)	4.31 (0.47)	3.71 (0.62)	3.33 (0.55)	2.78 (0.67)	0.000
HRQoL	5.00 (0.00)	3.94 (0.77)	3.08 (0.58)	2.73 (0.77)	1.89 (0.92)	0.000
Physical Health Domain (Transformed Score)	97.00 (4.24)	80.88 (6.34)	66.63 (5.77)	51.59 (12.87)	35.56 (11.28)	0.000
Psychological Domain (Transformed Score)	94.00 (0.00)	75.88 (8.59)	67.04 (9.36)	57.57 (11.99)	48.11 (13.61)	0.000
Social Relationships Domain (Transformed Score)	94.00 (0.00)	71.12 (7.16)	68.29 (7.86)	54.31 (11.41)	55.56 (10.10)	0.000
Environment Domain (Transformed Score)	90.50 (13.43)	70.06 (9.71)	63.92 (10.96)	54.22 (7.92)	52.78 (7.68)	0.000
	Reaction					
	Nonreactive	**RR**	**ENL**			**p-value**
QoL General	4.00 (0.62)	3.25 (0.58)	3.13 (0.58)			0.000
HRQoL	3.52 (0.77)	2.69 (0.60)	2.39 (0.82)			0.000
Physical Health Domain (Transformed Score)	71.6 (12.14)	47.00 (13.90)	48.66 (13.31)			0.000
Psychological Domain (Transformed Score)	70.27 (13.25)	52.44 (8.78)	57.05 (11.85)			0.001
Social Relationships Domain (Transformed Score)	67.79 (12.29)	54.69 (10.04)	55.42 (11.04)			0.000
Environment Domain (Transformed Score)	65.77 (11.54)	54.44 (9.34)	53.89 (8.87)			0.000

Post-hoc analyses from forms of leprosy were summarized in [Table 3].

Table 3: Post-hoc Analysis of Forms of Leprosy.

General QoL	**TT**	**BT**	**BB**	**BL**	**LL**
TT	General QoL	0.492	0.021	0.001	0.000
BT	TT		0.012	0.000	0.000
BB	BT			0.066	0.001
BL	BB				0.060
LL	BL				
HRQoL	TT	BT	BB	BL	LL
TT		0.285	0.004	0.000	0.000
BT			0.003	0.000	0.000
BB				0.266	0.000
BL					0.014

LL					
Physical Health Domain	TT	BT	BB	BL	LL
TT		0.251	0.001	0.000	0.000
BT			0.001	0.000	0.000
BB				0.000	0.000
BL					0.001
LL					
Psychological Domain	TT	BT	BB	BL	LL
TT		0.192	0.011	0.000	0.000
BT			0.103	0.000	0.000
BB				0.007	0.000
BL					0.132
LL					
Social Relationships Domain	TT	BT	BB	BL	LL
TT		0.022	0.006	0.000	0.000
BT			0.901	0.000	0.003
BB				0.000	0.012
BL					0.997
LL					
Environment Domain	TT	BT	BB	BL	LL
TT		0.027	0.001	0.000	0.000
BT			0.228	0.000	0.000
BB				0.000	0.018
BL					0.992
LL					

In post-hoc analyses of immunological reaction, there were significantly higher QoL in all domains between Non-reactive to RR reaction and ENL reaction (P<0.001 and P<0.001, respectively), but there were no significant differences between RR reaction and ENL reaction in General QoL (P = 0.784), HRQoL (P = 0.411), Physical Health Domain (P = 0.902), Psychological Domain (P = 0.413), Social Relationships Domain (P = 0.975) and Environment Domain (P = 0.983).

3.3. Prediction of QoL in patients with leprosy

Prediction analyses were summarized below [Table 4].

Table 4: Multiple linear regression analysis of QoL scores in patients with leprosy

Score	Formula
QoL	5.15 - 0.31(Form*)
HRQoL	6.38 - 0.40(Form*) - 0.28(Reaction**)
Physical Health Domain (TS)	111.23 - 7.90(Form*) - 2.77(Reaction**) - 3.78(Impairment Grade$^{\Delta}$) - 5.8(Duration of illness$^{\square}$)
Psychological Domain (TS)	113.17-6.96(Form*)
Social Relationships Domain (TS)	106.28-6.43(Form*)
Environment Domain (TS)	82.27-4.81(Form*)

Note:
*Forms of leprosy: (1) TT; (2) BT; (3) BB; (4) BL, (5) LL
**Reaction: (1) Non-reactive; (2) RR; (3) ENL
$^{\Delta}$Impairment grade: (1) Grade 0; (2) Grade 1; (3) Grade 2
$^{\square}$Duration of illness (in years)

Form could predict all domains of QoL, while reaction could only predict HRQOL and Physical domain. Physical domain could be predicted by the form of leprosy, immunological reaction, impairment grade, and duration of illness.

3.4. Discussion

This study found male predominance which is concordant to Britton[15] who stated male predominance of 2:1 among patients with leprosy. In this study, most of the subjects graduated from secondary school or any degree lower (6.71%) and live with monthly income below PMW. Socioeconomic background might matter to patients' knowledge, attitude, and behaviour related to illness and their willingness to consult to professionals, as shown by a study by Singh *et al.* [16] This is concordant to the finding in our study. This finding is supported by a study published by Pescarini *et al*, [17] which identified socioeconomic as a risk marker of leprosy in high-burden countries, in which Indonesia was included [18]. The mean duration of illness and clinical characteristics might be related to patients' knowledge, attitude, and behaviour related to leprosy, and their willingness to consult to professionals [19]. Leprosy itself was not easily recognized by patients at early stage, moreover when patients have not had any complaint related to nerve injuries [5].

This study compared demographic data and clinical characteristics of patients regarding their forms and immune reactions of leprosy. Lower income, higher impairment grade, and longer duration of illness were seen in the forms of lepromatous and also ENL, while form of lepromatous was associated with ENL reaction. Lower income would result in prioritizing satiety over nutrition when choosing food, resulting in inadequate nutritional intake. It may affect the immune system and its failure to protect against leprosy infection [20].

Previous studies found that forms [4, 21]. and immune reactions [22, 23]. of leprosy largely affected patients' QoL. As these complications targeting motoric and sensory system, it inevitably leads to deteriorations in QoL—as found in this study. Forms of leprosy could predict general QoL score, HRQoL, and all respective domains under WHOQOL-BREF, while specifically Physical Domain score could be predicted by data supplied regarding immune reactions, impairment grade, and duration of illness. This finding is supported by a previous study by Reis *et al*, [24] stating that some of the factors that potentially contribute to the deteriorated QoL in leprosy are late diagnosis, multibacillary forms, reactions, disability, and visible impairments.

Overall, the results showed forms of leprosy share significant impact on their quality of life. Leprosy-related immune reaction was also found to matter in HRQoL score and specifically in Physical domain, along with impairment grade and duration of illness. This finding is concordant to a study by An *et al*. [21] which found that severe leprosy form affects QoL adversely. This finding is also concordant to a study by Govindharaj *et al*, [25] stating duration of illness affected physical domain of QoL thus reducing QoL adversely. Non-reaction had higher QoL in all domains compared to reaction, regardless in the form of RR or ENL, and there were no significant differences between RR and ENL regarding QoL in all domains. In 2016, the WHO launched a new global strategy for leprosy, aiming to disease transmission and end associated discrimination and stigma,[26f] striving in committed accelerated efforts. This study found that QoL was unable to be predicted directly from patients' income. However, results from this study illustrated how low income affected worse forms and immune reactions of leprosy, as per found in this study. Therefore, intervention of raising the income for populations at risk might bring larger impact to diminish leprosy cases, more in high burden countries. Such approach might be observed to achieve common good for patients, health professionals, as well as policymakers and related stakeholders. The study was conducted with sufficient sample size and measured the QoL with validated tools. However, due to limitations of time and resources, the study was conducted as a cohort retrospective study in a tertiary leprosy referral center in the period of two months, which treats and rehabilitates the persons affected within a short period. Cultural and environmental aspects might play important role in QoL but were not taken into account in this study. Since this study was conducted at an urban area, the findings might not be applicable in different settings.

5. Conclusion

QoL scores in patients with leprosy could be predicted by illness characteristics and duration of illness, whereas forms of leprosy could predict all domains of QoL.

6. Ethical Matters

Health Research Ethical Committee, Faculty of Medicine, Ciputra University number 085/EC/KEPK-FKUC/X/2020

7. References

1. Bhat RM, Prakash C. Leprosy: an overview of pathophysiology. Interdiscip Perspect Infect Dis 2012;2012:1-6.
2. World Health Organization. Leprosy elimination: diagnosis of leprosy. Available at https://www.who.int/lep/diagnosis/en/. Accessed 10 December 2020.
3. Amorim FM, Nobre M, Nascimento LS, Miranda AM, Monteiro GR, Freire-Neto FP *et al*. Differential immunoglobulin and complement levels in leprosy prior to development of reversal reaction and erythema nodosum leprosum. PLoS Negl Trop Dis 2019;13:e0007089.
4. de Paula HL, de Souza CD, Silva SR, Martins-Filho PR, Barreto JG, Gurgel RQ *et al*. Risk factors for physical disability in patients with leprosy: a systematic review and meta-analysis. JAMA Dermatol 2019;155:1120-8
5. Pinheiro RO, Schmitz V, Silva BJ, Dias AA, De Souza BJ, de Mattos Barbosa MG *et al*. Innate immune responses in leprosy. Front Immunol 2018;9:518.
6. Maymone MB, Venkatesh S, Laughter M, Abdat R, Hugh J, Dacso MM *et al*. Leprosy: treatment and management of complications. J Am Acad Dermatol. 2020;83:17-30.
7. Brandsma JW, Brakel WV. WHO disability grading: Operational definitions. Leprosy review 2003;74(4):366-73.
8. Joseph GA, Rao PS. Impact of leprosy on the quality of life. Bulletin of the World Health Organization 1999;77(6):515.
9. Somar PM, Waltz MM, van Brakel WH. The impact of leprosy on the mental wellbeing of leprosy-affected persons and their family members–a systematic review. Global Mental Health 2020, 7.
10. Tsutsumi A, Izutsu T, Islam AM, Maksuda AN, Kato H, Wakai S *et al*. The quality of life, mental health, and perceived stigma of leprosy patients in Bangladesh. Soc Sci Med 2007;64:2443-53.
11. World Health Organization. WHOQoL-BREF. Available at https://www.who.int/mental_health/media/en/76.pdf. Accessed 17 December 2020.
12. Megari K. Quality of life in chronic disease patients. Health Psychol 2013;1:e27.
13. Pourhoseingholi MA, Vahedi M, Rahimzadeh M. Sample size calculation in medical studies. Gastroenterol Hepatol Bed Bench 2013;6:14.
14. Blok DJ, De Vlas SJ, Richardus JH. Global elimination of leprosy by 2020: are we on track?. Parasites Vectors 2015;8:548.
15. Britton, WJ. Leprosy, In: Cohen J, Powderly WG, and Opal SM, eds. Infectious Diseases. 4th ed. Elsevier 2017, 954-60.
16. Singh R, Singh B, Mahato S. Community knowledge, attitude, and perceived stigma of leprosy amongst community members living in Dhanusha and Parsa districts of Southern Central Nepal. PLoS Negl Trop Dis 2019;13:e0007075.
17. Pescarini JM, Strina A, Nery JS, Skalinski LM, de Andrade KV, Penna ML *et al*. Socioeconomic risk markers of leprosy in high-burden countries: a systematic review and meta-analysis. PLoS Negl Trop Dis 2018;12:e0006622.
18. World Health Organization. Leprosy: new data show steady decline in new cases. 2019. Available at https://www.who.int/neglected_diseases/news/Leprosy-new-data-show-steady-decline-in-new-cases/en/.

Accessed 15 December 2020.
19. Stephen T, Selvaraj I, Parameswari PJ. Assessment of knowledge, attitude and practice about leprosy among patients and their families in a rural community in Tamil Nadu. Indian J Lepr 2014;86(1):7-14
20. Wagenaar I, van Muiden L, Alam K, Bowers R, Hossain MA, Kispotta K *et al*. Richardus JH. Diet-related risk factors for leprosy: a case-control study. PLoS Negl Trop Dis 2015;12;9(5):e0003766.
21. An JG, Ma JH, Xiao SX, Xiao SB, Yang F. Quality of life in patients with lepromatous leprosy in China. J Eur Acad Dermatol Venereol 2010;24:827-32.
22. Yap FB, Kiung ST, Yap JB. Quality of life in patients with erythema nodosum leprosum in Kuala Lumpur, Malaysia. Indian Dermatol Online J 2016;7:255.
23. Sales AM, Illarramendi X, Walker SL, Lockwood D, Sarno EN, Da Costa Nery JA *et al*. The impact of erythema nodosum leprosum on health related quality of life in Rio de Janeiro. Lepr Rev 2017;88:499-509.
24. Reis FJ, Cunha AJ, Gosling AP, Fontana AP, Gomes MK. Quality of life and its domains in leprosy patients after neurolysis: a study using WHOQOL-BREF. Lepr Rev 2013;84:119-23.
25. Govindharaj P, Srinivasan S, Darlong J. Quality of life of persons affected by leprosy in an endemic district, West Bengal, India. Indian Journal of Dermatology 2018;63(6):459.
26. World Health Organization. Global leprosy strategy 2016-2020: accelerating towards a leprosy-free world.