

## Health-related quality of life associated with erythema nodosum leprosum in Purulia, West Bengal, India

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### Summary

**Objectives:** To determine the impact of erythema nodosum leprosum (ENL) on health-related quality of life (HRQoL) of persons affected by leprosy compared to individuals without ENL using the Medical Outcomes Study: 36-Item Short Form Survey (SF-36).

**Methods:** Individuals with a diagnosis of leprosy completed the Bengali version of the SF-36. The responses to the items of the surveys were coded, summed and transformed into a score for each of the eight domains. A lower score reflects a worse HRQoL.

**Results:** 290 individuals with a median age of 32 years (Range 14–82) participated. Individuals with ENL and those with isolated neuritis had significantly lower mean scores in all domains compared with individuals without reaction or neuritis except the domain of physical functioning in those with ENL.

**Conclusions:** This study demonstrates an association of reduced HRQoL with ENL compared to individuals without reaction or neuritis.

**Keywords:** Erythema nodosum leprosum, health related quality of life, leprosy, nerve function impairment, Purulia

## Introduction

Leprosy is a disabling disease that may lead to stigma and discrimination. The World Health Organization (WHO) multi-drug therapy (MDT) has been successful in treating the infection. However individuals still experience disability secondary to nerve function impairment. Over 200,000 new cases of leprosy were reported to WHO in 2017 and 63% of these cases were from India.<sup>2</sup> In India 4.6% of individuals had Grade 2 disability at the time of diagnosis.<sup>3</sup> Leprosy patients continue to develop disability during or after MDT.<sup>4</sup> Disability is associated with worse health related quality of life (HRQoL).<sup>5</sup>

HRQoL is defined as a person's perception of his or her physical and mental health and covers broad domains including physical, psychological, economic, spiritual and social wellbeing.<sup>6</sup> HRQoL in leprosy is hampered in the areas of prejudice, marginalization, stigma and illness.<sup>7,8</sup> Leprosy has been shown to be associated with considerable reduction in the quality of life compared to other dermatological conditions.<sup>8</sup> Erythema nodosum leprosum (ENL) is associated with worse HRQoL in individuals in Bangladesh and Brazil.<sup>9,10</sup>

ENL affects approximately 50% of individuals with lepromatous leprosy (LL) and 5–10% of borderline lepromatous (BL) leprosy patients.<sup>11</sup> ENL is characterized by multiple tender, crops of erythematous cutaneous nodules, with inflammation of nerves and other organs. Neuritis during ENL episodes results in nerve function impairment. ENL is often chronic and may lead to impaired organ function.<sup>11</sup> ENL is often treated with prolonged courses of high-dose oral corticosteroids which are associated with severe adverse effects and death.<sup>12</sup> ENL is associated with more hospital visits and hospital admissions than other leprosy patients.<sup>13</sup>

ENL characteristically affects patients in their thirties<sup>12</sup> which has consequences on the wider community as productivity is hampered and the family suffers. A previous study conducted in Purulia by us showed that families with ENL are affected by both out of pocket expenditure of treatment-seeking and loss of income household members.<sup>13</sup> ENL therefore exacerbates the financial situation of individuals who are already economically insecure. ENL affects HRQoL in physical and psychological health domains.<sup>14</sup>

We aimed to measure HRQoL associated with ENL and compare it to individuals without ENL.

## Methods

A cross-sectional study was conducted of individuals attending the Purulia Leprosy Mission Home and Hospital outpatient department between January and March 2015. The hospital is located in district of Purulia in the state of West Bengal in Eastern India. Purulia district is endemic for leprosy.<sup>15</sup>

Patients with leprosy including individuals newly diagnosed, those on MDT or those who had completed MDT were eligible to participate. Participants were classified as having ENL, Type 1 reaction (T1R), neuritis only and “no reaction or neuritis”.

Ethical approval was obtained from the ethics committee of The Leprosy Mission (TLM) Trust India. Written informed consent was provided by all adult participants or the guardian for those under the age of 18 years.

### CASE DEFINITIONS

**Leprosy** was diagnosed in individuals who had hypopigmented, anaesthetic skin patches and/or thickened nerves and/or acid-fast bacilli on slit skin smears.

**ENL** was diagnosed if participants with BL leprosy or LL had crops of tender cutaneous or subcutaneous lesions.

**Type 1 Reaction (T1R)** was defined as the development of erythema and oedema of pre-existing leprosy skin lesions. There may be accompanying neuritis and oedema of the hands, feet and face.

**Neuritis was diagnosed if there was spontaneous nerve pain or tenderness; paraesthesia; new sensory or motor nerve impairment.**

The Bengali version of the SF-36 was administered to assess HRQoL.<sup>16</sup> A lower score reflects a worse HRQoL compared to a higher one. The SF-36 consists of 36 items and it generates subscale scores for Physical Functioning (PH), Role Limitations due to Physical problems (RP), Bodily Pain (BP), General Health perceptions (GH), Vitality (VT), Social Functioning (SF), Role-limitations due to Emotional Problems (RE), and Emotional Well-Being (MH). Two summary scores can also be derived from the SF-36: the Physical Component Summary (Physical Health) and the Mental Component Summary (Mental Health) which leads to an Overall Quality Score (HRQoL score).

The eight domains of SF-36 may be combined to derive physical health component (PHC) and mental health component (MHC) scores. The PHC includes domains of physical functioning (PF), role - physical (RP), bodily pain (BP) and general health (GH). The MHC includes domains of vitality (VT), social functioning (SF), role-emotional (RE) and mental health (MH).

Clinical and demographic data were collected using a standard form. A trained investigator recruited participants and conducted the interview in a private setting. Literate patients who were willing completed the questionnaire themselves.

Raw scale scores were summated and linearly transformed into a 0–100 scale assigned for each sub-domain, domain and overall HRQoL. A score ranging from 0 (indicating the worse health status) to 100 (indicating the best health status) and the higher scores indicating better health.

The data were entered in to Microsoft Excel database and analyzed using SPSS statistics programme. Simple frequencies and distribution measures were calculated for demographic and disease profile and compared using Chi-square test. The differences between groups were analyzed with independent 't' test. The threshold for accepting statistical significance was  $p < 0.05$ .

## Results

Two hundred and ninety individuals with a median age of 32 years (Range 14–82) were recruited. Among the 290 participants, 44 (15.2%) had ENL, 39 (13.4%) T1R, 94 (32.4%) neuritis and 113 (39.0%) had no reaction/neuritis. One hundred and sixty-six (57.2%) participants were literate, of this 94 (32.4% in total patient) of them the questionnaire was self-administered. Of the 290 participants, 184 were male and 106 (36.6%) were female (Table 1).

The median time since leprosy diagnosis for the ENL group was 10 months. Among ENL patients, 9 (23.1%) had completed MDT, 14 (31.8%) patients with T1R and 39 (41.5%) patients with neuritis had completed MDT. The disease profile was showed in Table 2.

### RELIABILITY ANALYSIS

Internal consistency was assessed using Cronbach's alpha coefficients and corrected item-scale correlations. Corrected correlations between the items and their hypothesized scales ranged

**Table 1.** Demographic profile of study participant (n =290)

Variables	ENL n = 44	T1 R n = 39	Neuritis n = 94	No Reaction/ Neuritis n = 113	Total n = 290	X <sup>2</sup> (P)
Gender						
Male	28 (15%)	24 (13%)	61 (33%)	71 (39%)	184 (63%)	0.17
Female	16 (15%)	15 (14%)	33 (32%)	42 (40%)	106 (37%)	(0.98)
Literate						
Yes	29 (17%)	19 (11%)	49 (30%)	69 (42%)	166 (57%)	4.19
No	15 (12%)	20 (16%)	45 (36%)	44 (35%)	124 (43%)	(0.24)
Mean age (years)	37.8	31.2	37.3	32.7	34.7	
Occupation						
Farmer	16 (16%)	14 (14%)	29 (29%)	42 (42%)	101 (35%)	8.37
House wife	14 (15%)	13 (14%)	33 (34%)	36 (38%)	96 (33%)	(0.76)
Labor	6 (13%)	5 (11%)	16 (36%)	18 (40%)	45 (16%)	
Student	4 (16%)	3 (12%)	5 (20%)	13 (52%)	25 (9%)	
Business	4 (17%)	4 (17%)	11 (48%)	4 (17%)	23 (8%)	

Note. Parenthesis indicates row percentages.

**Table 2.** Disease profile of study participant (n =290)

Variables	ENL n = 44	T1 R n = 39	Neuritis n = 94	No R/Neuritis n = 113	Total n = 290	X <sup>2</sup> (P)
Median time since leprosy diagnosis						
In months	8	10	7.5	8	8	
RJ Classification						
TT	0 (0%)	0 (0%)	0 (0%)	3 (3%)	3 (1%)	
BT	0 (0%)	26 (67%)	80 (85%)	85 (75%)	191 (66%)	134.29
BB	0 (0%)	1 (3%)	0 (0%)	0 (0%)	1 (0%)	(0.000)
BL	25 (57%)	8 (21%)	4 (4%)	14 (12%)	51 (18%)	
LL	19 (43%)	4 (10%)	7 (7%)	11 (10%)	41 (14%)	
PNL	0 (0%)	0 (0%)	3 (3%)	0 (0%)	3 (1%)	
MDT Status						
Naïve	1 (2%)	8 (21%)	20 (21%)	34 (30%)	63 (22%)	22.14
Current	29 (66%)	22 (56%)	35 (37%)	47 (42%)	133 (46%)	(0.001)
Completed	14 (32%)	9 (23%)	39 (41%)	32 (28%)	94 (32%)	
WHO Disability grade						
Grade 0	24 (55%)	16 (41%)	15 (16%)	101 (89%)	156 (54%)	117.21
Grade 1	6 (14%)	9 (23%)	19 (20%)	3 (3%)	37 (13%)	(0.000)
Grade 2	14 (32%)	14 (36%)	60 (64%)	9 (8%)	97 (33%)	
Relapse						
Yes	1 (2%)	4 (10%)	0 (0%)	1 (1%)	6 (2%)	15.68
No	43 (98%)	35 (90%)	94 (100%)	112 (99%)	284 (98%)	(0.001)

from 0.36 to 0.76 and were 0.4 or above for all items except for two items from the GH scale. Cronbach’s alpha ranged from 0.924 (SF) to 0.937 (GH and MH) and exceeded the 0.70 standard for all scales.

Furthermore, in patients with leprosy reaction, ENL affected patients had lower mean scores in all domains of SF-36 than the patients with T1R.

**Table 3.** One-way ANOVA test between Disability Grade and domains of SF-36

Disability Grade	<i>n</i>	Mean Score							
		PF	RP	RE	VT	MH	SF	BP	GH
Grade 0	156	80.9	74.5	75.2	78.9	81	82.9	72.8	55.7
Grade 1	37	80.1	60.1	58.6	76.2	76.4	75.3	63.2	50.8
Grade 2	97	65.2	41	39.5	71.1	73.7	62.5	52.8	49.1
<i>p</i> -value		0.000**	0.000**	0.000**	0.009*	0.007*	0.000**	0.000**	0.014*

**Table 4.** Independent ‘*t*’ test between No Reaction/neuritis vs ENL, T1R and Neuritis

Domain	Mean score ± Standard deviation				p-value		
	ENL ( <i>n</i> = 44)	T1R ( <i>n</i> = 39)	Neuritis ( <i>n</i> = 94)	No reaction/ neuritis ( <i>n</i> = 113)	No reaction/neuritis vs		
					ENL	T1R	Neuritis
PF	73.07 ±23.482	76.41 ±27.790	71.60 ±23.557	79.47 ±25.906	0.156	0.534	0.024
RP	52.84 ±47.070	66.03 ±47.464	47.07 ±47.215	76.70 ±41.280	0.001	0.246	<0.001
RE	50.76 ±49.015	67.52 ±45.555	44.68 ±48.281	75.22 ±41.792	0.004	0.255	<0.001
VT	70.45 ±20.398	73.59 ±21.550	73.94 ±19.301	80.62 ±18.116	0.003	0.049	0.011
MH	71.27 ±19.525	78.67 ±16.061	75.91 ±19.250	82.09 ±16.588	0.001	0.265	0.014
SF	67.57 ±35.857	74.79 ±35.044	68.13 ±36.196	83.99 ±29.613	0.004	0.113	0.001
BP	59.77 ±35.372	69.74 ±36.457	55.38 ±38.082	73.14 ±32.708	0.026	0.588	<0.001
GH	49.66 ±15.863	55.15 ±19.129	48.26 ±18.269	57.09 ±17.249	0.014	0.558	<0.001
PHC	58.8 ±25.7	66.8 ±27.8	55.6 ±26.0	71.2 ±23.5	0.031	0.784	0.000
MHC	65.0 ±27.4	73.6 ±25.4	65.7 ±25.1	80.8 ±21.8	0.002	0.381	0.000

#### COMPARISON OF PARTICIPANT GENDER, OCCUPATION, RJ CLASSIFICATION AND DISABILITY GRADE WITH DOMAINS OF SF-36

There was no significant difference between gender, occupation and RJ classification in all the domains of SF-36. For Disability Grade, there was a significant difference observed in all the domains of SF-36 (Table 3).

#### COMPARISON OF PARTICIPANTS WITH ENL OR T1R OR NEURITIS AND PARTICIPANTS WITH NO REACTION OR NEURITIS

The “no reaction or neuritis” group had higher scores in all domains of SF-36 than the ENL group. There is a significant difference between the two groups in all domains except in PF (Table 4).

The “no reaction or neuritis” group had higher scores in all domains of SF-36 than the neuritis group. The differences were statistical significant in all domains (Table 4).

The “no reaction or neuritis” group had higher scores in all domains of SF-36 than T1R group. However, there is a significant difference seen only in VT domain (Table 4).

#### PHYSICAL COMPONENT AND MENTAL COMPONENT

Individuals with ENL had significantly worse HRQoL than patients with “no reaction or neuritis” in both the PHC and MHC. This was also the case for individuals with neuritis who had significantly worse HRQoL compared with those without reaction or neuritis. There was no significant difference found in HRQoL between individuals with T1R and those without reaction or neuritis in both the PHC (Figure 1) and MHC (Figure 2).

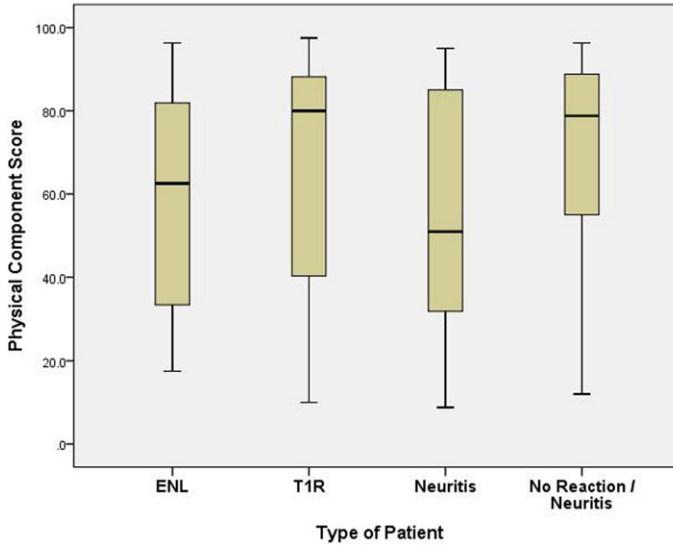


Figure 1. Physical Component Score for the study participants.

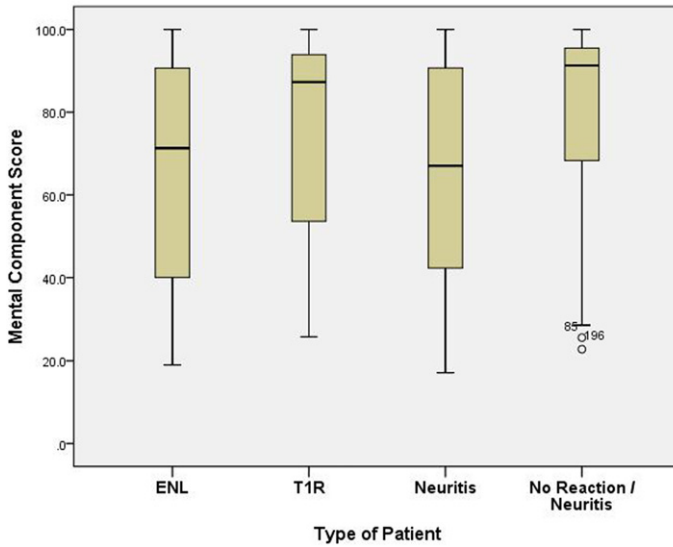


Figure 2. Mental Component Score for the study participants.

**Discussion**

This is the first study from India to examine HRQoL of individuals with ENL, T1R and those with isolated neuritis. Studies from India, using the WHOQOL-bref questionnaire found that leprosy affected people had lower QoL scores than the non-leprosy affected general population especially in the physical and psychological domains.<sup>17</sup>

Studies from Bangladesh and Brazil reported that ENL is associated with a severe impact on HRQoL.<sup>9,10</sup> In this study, a significant difference was found between individuals with ENL or those with isolated neuritis and participants without reaction or neuritis. ENL affected patients had lower HRQoL in all domains except in physical functioning than patients without reaction or neuritis. In Bangladesh, Bowers *et al.*<sup>9</sup> using the Bengali version of the SF-36 found that patients with ENL had lower HRQoL in the domains than individuals without ENL.<sup>9</sup> A similar study by Sales *et al.*<sup>10</sup> in Brazil found that people with ENL had impaired HRQoL compared to those without ENL, however the difference was only significant in the bodily pain domain.<sup>10</sup>

Studies from Brazil using the WHOQOL-bref questionnaire showed that participants with “leprosy reactions” tend to have more severe impairment in the physical domain.<sup>18</sup> Lustosa *et al.* measured HRQoL by SF-36, found that individuals with leprosy reactions in Brazil had significantly lower HRQoL than those with no reaction.<sup>19</sup> Participants with T1R had a significant lower HRQoL score than those without reaction or neuritis, however this only statistically significant in the VT domain. The impact of neuritis on HRQoL may be due to NFI, neuropathic pain and disability and the contribution of such factors need to be further clarified.<sup>20</sup> In this study, patient with neuritis had a significant lower HRQoL score in all domains than the patients without reaction/neuritis.

Our study has limitations. The study was cross-sectional and did not have matched controls. The SF-36 is a general tool and may not reflect specific aspects of ENL and leprosy which may have an important bearing on HRQoL.

In conclusion, this is the first study from India to show that ENL and neuritis is associated with reduced HRQoL. Further prospective, adequately powered longitudinal studies should be conducted which control for potential confounders including reactions with concomitant neuritis. We suggest that HRQoL should be measured try and better understand the impact of the disease on well-being, especially for patients with ENL and neuritis.

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### **Author's Contribution**

Joydeepa Darlong, was involved in study conceptualization and design, implementation of the study, monitoring the study and manuscript writing.

Pitchaimani Govindharaj, was involved in monitoring the study, conducted the interview, data analysis, and manuscript writing.

Babananda Mahato, involved in identifying the study participants and conducted the interview.

Diana N. Lockwood, was involved in study conceptualization and design and co-ordinated the study.

Stephen L Walker, was involved in study conceptualization, design, data analysis, co-ordinated the study and commented on the manuscript.

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