LETTER TO THE EDITOR

Validation of the Leprosy Type 1 Reaction Severity Scale in Ethiopia

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Leprosy Type 1 Reactions (T1R) are immune-mediated events leading to nerve damage and preventable disabilities. They manifest clinically with erythema and oedema of skin lesions and tender peripheral nerves with loss of function. Up to 30% of patients with borderline leprosy are affected by T1R.[1] Although T1R can occur at any time, the frequency is higher in the first six months of MDT treatment.[2] T1R are treated with corticosteroids.[3] Clinical trials are needed to assess not only efficacious and safe second line drugs but also to assess the best regimens of prednisolone in terms of dosage, length of treatment and rate of decrease.

A tool which enables clinicians to assess the severity of T1R is useful in defining outcomes in clinical trials. The lack of uniformity surrounding interpretation of data has hindered development of internationally accepted treatment protocols and guidelines, while also making trialling of new therapeutic agents difficult. Using a validated clinical severity scale for leprosy reactions improves research quality and provides a tool to promote uniformity and comparability of research.

A Severity Scale for T1R, based on the INFIR clinical severity scoring system, was developed and prospectively validated in Bangladesh and Brazil.[4] The scale consists of 21 items to assesses three components of T1R.[4] The first section looks at skin involvement using number of affected lesions, the degree of inflammation and the presence of peripheral oedema (Score A). The second section is a measurement of sensory function of the nerves by using graded Semmes-Weinstein monofilaments (SWM) to assess sensation in the hands and feet, and cotton wool for corneal sensation (Score B). The third section uses a standard measure of muscle power (MRC grading) to assess the motor function of the nerves of the face, hands and feet (Score C). The sum of the total for each section (A, B, and C) gives the overall severity scale score with a range of 0–63 (Appendix 1). The maximum score possible for sections A,

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B and C are 9, 24 and 30 respectively. A mild T1R is characterised by a score of 4 or less; a moderate T1R by a score between 4·5 and 8·4 and a severe T1R is a score of 9 or more.

This Severity Scale for T1R has so far been used in clinical trials on intravenous methylprednisolone in Nepal,[5] on azathioprine in India[6] and in the on-going TENLEP studies in India.[7] In order to use such a scale in a trial on ciclosporin efficacy in T1R, we needed to validate it in the population in which the study was to be conducted. The validation exercise in Ethiopian patients is described here.

Methods

Patients presenting with signs and symptoms of T1R at the Leprosy Clinic at ALERT Hospital in Addis Ababa were recruited between February 2010 and August 2010. Ethical approval was granted by the London School of Hygiene and Tropical Medicine (5426/Dec 2008) and ALERT and AHRI Ethical Review Committee (PO22/08).

Inclusion criteria were patients aged 18 or more presenting with T1R. Patients unable or unwilling to give informed consent were excluded. All patients gave informed consent to participate in the assessment. Patients could be presenting with new T1R or be on treatment for T1R. Patients were examined independently, on the same day, by a health worker who was trained to use the scale and by an experienced leprologist who categorised the reaction as mild, moderate or severe. Neither assessor was aware of the result of the others examination. The scoring was done on pre-prepared scoring sheet which listed skin finding and results of voluntary muscle testing and sensory testing.

The results were entered into an Access database and the data was analysed using the Statistical Package for Social Sciences (SPSS version 20).

Results

135 patients with T1R were examined using the T1R severity scale assessment sheet.

The severity of the T1R was categorised by the specialist as mild in 43 (32%), moderate in 34 (25%) and severe in 38 (28%) patients. Another 20 patients (15%) with no signs of active T1R but on prednisolone treatment were assessed. Median scores for each category were none $= 0 \pm 1\cdot69$; mild $= 3\cdot0 \pm 2\cdot55$; moderate $= 6\cdot5 \pm 2\cdot55$ and severe $= 19\cdot0 \pm 9\cdot70$. The box-plot in Figure 1 illustrates the score distribution clearly.

The differences in the scores between the group with no active reaction and the mild group, the mild group and the moderate group and the moderate group and the severe group were all statistically significance ($P < 0\cdot001$, Independent sample t test). The group of patients graded as having severe TIR had the widest confidence interval, and there is an overlap between each category.

Discussion

This is the first report of the use of the T1R Severity Scale in Ethiopia and it shown that it is a valid tool for assessing the severity of T1R in Ethiopian patients and can be used to differentiate between mild, moderate and severe T1R. Some limitations were noted. The
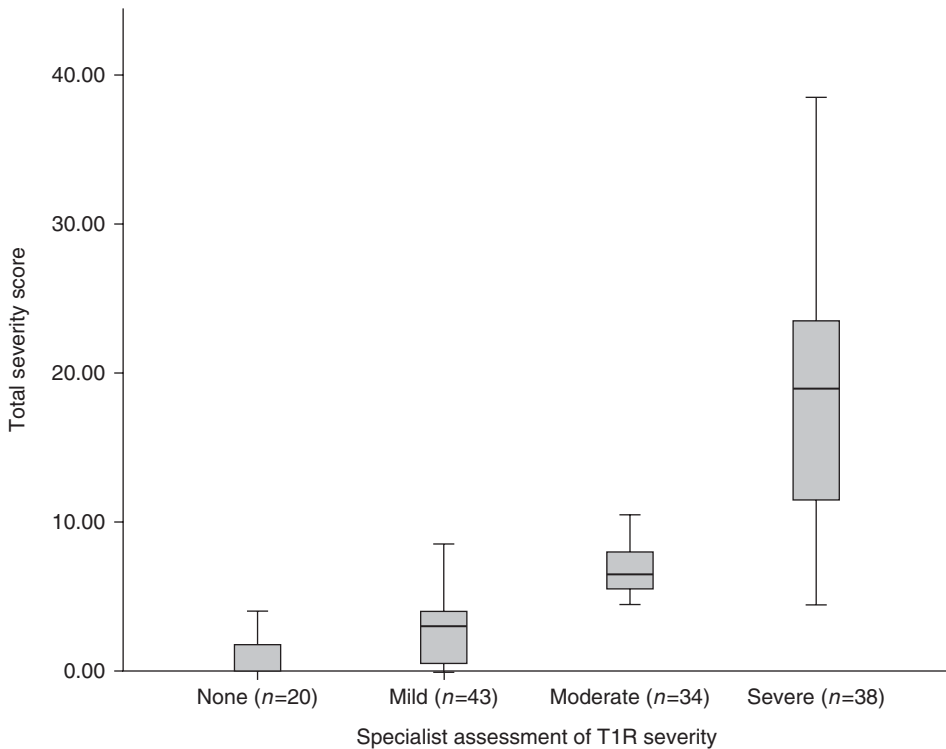
Figure 1. Box plot of Clinical Severity Scores by specialist severity classification showing medians, interquartile ranges and minimum and maximum scores. *Legend: Box-and-whisker plot of Clinical Severity Score. Participants were classified as follows: n = 20 None (CSS median = 0; range:0–4; SD = 1·29); n = 43 Mild (CSS median = 3·0; range:0–8·5; SD = 2,55); n = 34 Moderate (CSS median = 6·5; range 0·5–10·5; SD = 2·55) and n = 38 Severe (CSS = 19; range = 4·5–38·5; SD = 9·70).*

reliability of the tool could have been tested by doing a further inter-observer validation exercise but due to limitations in clinic staff this was not possible in this context. This has been done previously in Bangladesh and Brazil[4] and there is no reason to expect than trained Ethiopian health care workers would score differently. VMT and SWM in the assessment of nerve function impairment (NFI) have been shown to be reliable.[8]

Old NFI can constantly raise the score in the absence of active T1R. A way of adjusting the score to take into account the effect of old NFI needs to be investigated. In the Azalep study patients were asked whether their nerve damage had been present for more than 6 months.[6] Old NFI, i.e. greater than 6 months duration, may not respond to treatment but it is also difficult for patients to accurately time the loss of nerve function, especially when acute NFI occurs in a nerve that already has some pre-existing permanent impairment. A set of questions that define old nerve damage and its importance should be tested. This work needs developing and validating

We also noticed that because the scoring system is not equally weighted, neurological parameters are more heavily represented. This may reflect the importance of nerve function impairment but may not adequately reflect treatment requirements. For example, it is very difficult to associate a value of 7 (which equates to moderate T1R) to a patient who has severe reaction in the skin of the face but nerves are unaffected. Such a patient would clinically be

graded as severe and treatment would be given accordingly despite a moderate score on the severity scale. A study assessing whether adjusting the weighting would be useful could be carried out in conjunction with a study assessing the minimally important difference (MID) from a patient perspective in scores derived from the scale before and after treatment. This is important because it provides a meaningful patient centred outcome measure of change. This study should be performed in a population in which the scale has been validated. Knowing the magnitude of the change in score required to achieve a MID would facilitate power calculations for clinical trials.

Although we have validated the T1R Severity Scale in Ethiopian patients with T1R, further studies are warranted to determine its utility in future clinical studies as well as a consensus on how to report scores in studies to allow easy comparison and pooling of results.

Acknowledgements

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Appendix 1. Clinical Severity Scale for T1Rs

	Criteria	0	1	2	3	Score
A1	Degree of inflammation of skin lesions	None	Erythema	Erythema and raised	Ulceration	
A2	Number of raised and/ or inflamed lesions	0	1–5	6–10	>10	
A3	Peripheral oedema due to reactions	None	Minimal	Visible but not affecting functions	Odema affecting function	
	A SORE					

	HANDS	**Purple 2g Monofilament scores**				**Orange 10g Monofilament score**			**Score**
	Nerves	0	0.5	1	1.5	2	2.5	3	
B1	Rt Trigeminal	Felt						Not felt	
B2	Lt Trigeminal	Felt						Not felt	
B3	Rt Ulnar	All sites felt	1 sites not felt	2 sites not felt	3 sites not felt	1 sites not felt	2 sites not felt	3 sites not felt	
B4	Lt Ulnar	All sites felt	1 sites not felt	2 sites not felt	3 sites not felt	1 sites not felt	2 sites not felt	3 sites not felt	
B5	Rt Median	All sites felt	1 sites not felt	2 sites not felt	3 sites not felt	1 sites not felt	2 sites not felt	3 sites not felt	
B6	Lt Median	All sites felt	1 sites not felt	2 sites not felt	3 sites not felt	1 sites not felt	2 sites not felt	3 sites not felt	
	FEET	Orange 10g Monofilament score				Pink 300g Monofilament score			**Score**
	Nerves	0	0.5	1	1.5	2	2.5	3	
B7	Rt. Post. tibial	All sites felt	1 sites not felt	2 sites not felt	3 sites not felt	1 sites not felt	2 sites not felt	3 sites not felt	
B8	Lt. Post. tibial	All sites felt	1 sites not felt	2 sites not felt	3 sites not felt	1 sites not felt	2 sites not felt	3 sites not felt	
	B SCORE								

	Nerves	0	1	2	3	Score
C1	Rt. Facial	MRC=5	MRC=4	MRC=3	MRC<3	
C2	Lt. Facial	MRC=5	MRC=4	MRC=3	MRC<3	
C3	Rt. Ulnar	MRC=5	MRC=4	MRC=3	MRC<3	
C4	Lt. Ulnar	MRC=5	MRC=4	MRC=3	MRC<3	
C5	Rt. Median	MRC=5	MRC=4	MRC=3	MRC<3	
C6	Lt. Median	MRC=5	MRC=4	MRC=3	MRC<3	
C7	Rt. Radial	MRC=5	MRC=4	MRC=3	MRC<3	
C8	Lt. Radial	MRC=5	MRC=4	MRC=3	MRC<3	
C9	Rt. Lateral Popliteal	MRC=5	MRC=4	MRC=3	MRC<3	
C10	Lt. Lateral Popliteal	MRC=5	MRC=4	MRC=3	MRC<3	
	C SCORE					

Total Score	**Score of A + B + C**	