Evaluation of the integrity of the facial muscles in leprosy patients using surface electromyography: a cross-sectional study

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Summary

Objective This study sought to evaluate facial muscle integrity in clinical forms of leprosy through surface electromyography.

Methods For evaluation of facial muscle integrity, 19 healthy subjects and 71 patients diagnosed with leprosy and under treatment in a National leprosy reference center were recruited. The muscles investigated, through surface electromyography, were the frontalis, orbicularis oculi, zygomaticus, masseter, and orbicularis oris. The evaluated features were Root Mean Square (RMS) and Mean frequency (Fmean). The facial muscles were analyzed jointly and separately for each leprosy clinical form and healthy individuals.

Results Regarding the Fmean, there was a difference noted between the values of healthy subjects and patients of all clinical forms, except for the LL form ($p = 0.986$). The highest frequency values were seen in TT and BL forms, which did not present a significant difference between each other ($p = 0.757$). Asymmetry of the facial muscles was detected in TT (RMS) and TT, BB, and LL forms from the Fmean. RMS and Fmean indicated motor neurogenic impairment in facial muscles of all leprosy patients, except the LL form.

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Conclusions  Surface electromyography is shown to be an auxiliary tool for the
diagnosis of facial motor disorders imperceptible to clinical examination, helping
to prevent impairments, which is fundamental for the social inclusion of leprosy
patients.

Keywords: Leprosy, facial nerve, electromyography

Introduction
Leprosy is a disease with a long incubation period, making treatment difficult and lead-
ing to impairments and deformities, with sensory-motor impairment in several parts of
the body. The face that is the most evident part of the human body, also being dynamic
and expressive, essential for communication, transmitting emotions and for social relations.
Consequences often associated with leprosy are mutilation and distress along with sig-
nificant suffering, which limit social inclusion, often pushing the patient to isolation and
depression.¹

The clinical forms of leprosy occur on a spectrum, and are defined according to clinical,
bacteriological, histopathological and immunological analyses.²⁻⁴

Facial impairment frequently occurs in leprosy patients, especially in multibacillary forms.
Most facial deformities and disabilities derive from the direct action of the bacillus on the
structures of this region, except for lagophthalmos and corneal sensory impairment that usually
result from reactional episodes.⁵

Clinically, leprosy neuropathy is a mixed neuropathy that affects sensory, motor and
autonomic nerve fibers. The most frequently affected peripheral nerves are the ulnar, common
fibular, tibial, median, radial, and cranial nerves, especially the facial and trigeminal nerves.⁶
The trigeminal (nerve V) and facial (nerve VII) cranial nerves are mixed nerves with motor
and sensory function, with the trigeminal being predominantly sensory and the facial being
mostly motor, both innervating the face.⁷

The trigeminal nerve has a single motor branch which innervates the chewing muscles,
including the masseter.⁸ The facial nerve is a sensory-motor nerve, with its motor portion
responsible for all facial expressions. Lesions in this nerve might cause paresis, in addition to
damaging speech and eating functions.⁹ The frontal branches are responsible for innervating
the frontal muscle and the temporo-facial divides into the temporal and the zygomatic
branches. The zygomatic branch innervates the inferior bundle of the orbicularis oculi and
damage to this nerve causes incomplete eyelid closure, called lagophthalmos.¹⁰ The buccal
nerve innervates the orbicularis oris muscle.¹¹

Different studies reinforce the importance of investigating the zygomatic branch, although
there is little mention of the remaining branches of the facial nerve. Other facial branches may
also be impaired in leprosy, thus indicating the need for attention and a systematic evaluation
by objective means that allow for the quantification of the efficiency concerning facial muscles,
which can be obtained through electrophysiological tests.¹²

Surface electromyography (sEMG) is a noninvasive, pain-free and reproducible procedure
capable of providing objective measurements concerning the investigated muscles. This
may be a relevant resource for facial muscle evaluation in leprosy. It has been used in
neuromuscular evaluation for muscular activity diagnosis by different professionals, such as
The contribution made by the sEMG analysis allows a detailed investigation of the motor integrity to be obtained for the different muscles innervated by the facial nerve. The basic component of the peripheral nervous system evaluated by sEMG is the motor unit action potential (MUAP), that is assessed for duration, amplitude, and number of phases. The classification of a MUAP as normal or neuropathic rests on the Root Mean Square (RMS) and the Mean frequency (Fmean).

In peripheral neuropathies where there is evident axonal involvement, as in leprosy, decreased recruitment of MUAPs occurs in weak muscles immediately with the onset of the lesion. Because some axons and their motor units have been lost, the only way to increase force is to fire the remaining available motor units faster, resulting in a higher Fmean. Furthermore, the process of denervation and reinnervation arising from the maintenance of neural function results in changes in MUAP morphology. MUAPs become longer in duration, higher in amplitude, and polyphasic, reflecting an increased RMS.

Therefore, by evaluating the features of the electromyographic signal from the main facial muscles, the differences between the clinical forms of the disease and the patterns of facial symmetry provide informative data concerning the face of a leprosy patient. In addition, this method can be used to monitor facial motor function during and after the end of treatment, especially in cases of leprosy reaction and in those who have undergone some rehabilitation treatment.

Methods

Subject Selection

We recruited 90 participants, 19 of whom were healthy subjects (control group) and 71 were leprosy patients. From the latter, 13 were from the tuberculoid pole (TT) and 14 from the lepromatous pole (LL), and the remaining individuals were part of the intermediate borderline group, with 22 borderline-tuberculoid (BT), 10 mid-borderline (BB) and 12 borderline-lepromatous (BL) patients. Patients and healthy subjects who showed other possible etiologies of peripheral neuropathy were excluded, namely those with: chronic alcoholism, diabetes mellitus, thyroid disease and/or other hormonal dysfunctions, malnutrition, hereditary neuropathy, hepatitis B or C, HIV, rheumatic and/or autoimmune diseases. Those with facial palsies due to any indeterminate causes including Bell’s palsy in the past were ruled out. We also excluded from the study carriers of other neurodegenerative diseases and those who use botulinum toxin. Patients who had a reaction episode at the time of evaluation were also excluded.

Data Collection

EMG signals were collected with a 16-channel Intan RHD2216 (IntanTechnologies LLC) amplifier with a sampling rate of 5000 Hz. We also used 36 mm disposable passive Ag/Cl (Meditrace 200, Tyco/Kendall, USA) electrodes filled with electrolyte gel SignaGel (Parker Laboratories Inc.). As the area of the electrodes used exceeded the total area of the assessed muscles, the electrodes were adapted in order to avoid crosstalk between the studied and adjacent muscles.
The INTAN amplifier allows for the acquisition of signals from up to eight muscles at the same time, such as the frontalis (right (R) and left (L)), the orbicularis oculi (R and L), the zygomaticus (R and L), and the masseters (R and L). Initially, we simultaneously collected electromyographic signals from the frontalis, zygomaticus, orbicularis oculi and masseter muscles. The signal from the orbicularis oris muscle was collected by removing the electrodes from the left masseter and placing these on the upper lip. Therefore, as our analyses included nine muscles, the data collection was performed in two batches.

Participants were lying on their back and the electrodes were positioned on the face. We asked the participant to perform three isometric contractions with each muscle and to maintain muscular contraction for 20 s, with 5-second breaks between contractions. Firstly, we examined the frontalis muscles. Individuals were told to elevate their eyebrows and keep them raised for 20 s, and two other repetitions were performed after a five-second break. In order to analyze the orbicularis oculi, patients closed their eyes in two different ways, one with maximum strength and then without exerting excessive force. The same five-second break was given between repetitions. For the zygomaticus, we requested the participants to produce an open smile with the zygomaticus major at maximum contraction. For the activation of the masseter muscle, participants were requested to press the upper dental arch strongly against the lower arch. As it is a single muscle with a round shape, orbicularis oris was analyzed with one pair of electrodes only. In order to activate this muscle, we asked individuals to perform a lip protrusion, following the standard procedure applied to the previous muscles.

To avoid bias related to the randomness of the EMG signal, each task was repeated 4 times, with the EMG signal being collected in all repetitions to compose the data set.

DATA ANALYSIS

The facial muscles were analyzed jointly and separately for each leprosy clinical form. For the symmetry analysis, we studied both right (R) and left (L) sides of the face, considering all the muscles together and individually, except for the orbicularis oris muscle as it is a single round-shaped facial muscle.

The EMG signal was filtered by using a 4th order bandpass Butterworth filter with a cut off frequency of 20–500 Hz. EMG features were estimated for the comparison between groups of individuals with each leprosy clinical form and the control group formed of healthy individuals. The facial muscles were analyzed jointly and separately for each leprosy clinical form and healthy individuals.

The peak value of the rectified EMG signal was used for normalization. The investigated features estimated from the electromyographic signal were Root Mean Square (RMS) (Equation (1)) and Mean Frequency (Fmean) (Equation (2)).

$$\text{RMS} = \sqrt{\frac{\sum_{i=1}^{N} (emg(i))^2}{N}}$$  \hspace{1cm} (1)

where:

- $emg$ – emg signal;
- $N$ – number of samples;
- $i$ – $i$th discrete sample of $emg$. 

Evaluating the integrity of facial muscles in leprosy

Figure 1. Electromyographic normalized signal from the orbicularis oculi muscle. Where: (a) EMG signal of a borderline-tuberculoid (BT) leprosy patient and (b) EMG signal of a healthy individual.

\[ F_{\text{mean}} = \frac{\sum_{i=1}^{N} (S_x(i) \cdot f(i))}{\sum_{i=1}^{N} S_x(i)} \]  

(2)

where:
- \( S_x \) – power spectrum of emg;
- \( f \) – frequency of \( S_x \) in Hz.

Figure 1 shows examples of EMG signals collected from the participants. Figure 1a depicts a normalized EMG signal of a participant with BT leprosy, and Figure 1b shows a normalized
Figure 2. Normalized electromyographic signal from zygomaticus muscles of a tuberculoid (TT) leprosy patient. Where: (a) EMG signal from the right side and (b) EMG signal from the left side.

The EMG signal of a healthy individual, the two being male and in the same age range. The normalized signal amplitude is larger for the patient with leprosy.

Figure 2 shows samples of the normalized EMG signal collected from participants, both from the same female participant with the TT form of leprosy. Figures 2a and b show the EMG signal of the right and left zygomaticus muscle, respectively. Here, one notes that the amplitude of the normalized signal is different when comparing both sides of the face, thus characterizing facial asymmetry.
### Table 1. Clinical-epidemiological data of the studied leprosy patients

<table>
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<tr>
<th>Variables</th>
<th>Number of patients</th>
<th>Percentage of patients (%)</th>
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<td><strong>Clinical form</strong></td>
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<td></td>
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<tr>
<td>BT</td>
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<td>30.9</td>
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<tr>
<td>BB</td>
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<td>14.1</td>
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<tr>
<td>BL</td>
<td>12</td>
<td>16.9</td>
</tr>
<tr>
<td>LL</td>
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<td>19.7</td>
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<tr>
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<tr>
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<td>1.4</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1.4</td>
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</tbody>
</table>

### Statistical Analysis

In order to perform the statistical analysis of data, normality of each feature (RMS and Fmean) was verified by the Shapiro–Wilk test, which indicated that the data did not meet the assumption of normality. Accordingly, a non-parametric Kruskal–Wallis test followed by post hoc Dunn–Sidak analysis was performed in order to compare the electromyographic signals of the RMS and Fmean generated in all facial muscles and all muscle groups (frontalis, orbicularis oculi, zygomaticus, masseter and orbicularis oris) referent to the total sampling (healthy and clinical forms).

We performed the non-parametric Wilcoxon signed rank test to compare symmetry between muscles through features estimated from electromyographic signals of both right and left hemiface (all facial muscles and each individual muscle), with each participant being his/her own control (paired). The R Project for Statistical Computing was used across all analyses with a significance level of 5% ($\alpha = 0.05$). The statistical analysis was carried out between December 1, 2020 through February 15, 2021.

A sensitivity analysis was performed per-protocol, but all participants performed the tasks properly, with no exclusion. For example, all male participants that declined to shave would be excluded, as this prevented the attachment of the surface electrodes.

### Results

Seventy-one patients who had been diagnosed with leprosy and nineteen healthy controls were included in this study. The age of the population ranged from 22–70 years, with a mean age of $47.85 \pm 12.15$ for the leprosy group and $44 \pm 14.40$ for the healthy subjects. Table 1 shows the predominance of men in the 40–59 age range. Concerning disease classification, the BT clinical form prevailed.
In relation to the RMS values for the facial muscles analyzed, in conjunction with the healthy subjects, these showed no difference for the LL form, which presented the smallest amplitude among all clinical forms ($p = 0.182$). The remaining forms (TT, BT, BB and BL) presented higher values than those for the healthy subjects, with these differences being statistically significant ($p < 0.001$) (Figure 3). The highest amplitude was for the BB form; BB and LL were different from TT ($p < 0.001$). The tuberculoid pole (TT and BT) was different from BB and LL forms. We found a statistically significant difference between BL and LL in the lepromatous pole, with higher RMS values for BL (Figure 3).

Regarding the Fmean (Figure 5), there was a difference noted between the values of healthy subjects and patients of all clinical forms, except for LL form ($p = 0.986$). The highest frequency values were seen in TT and BL forms, which did not present a significant difference between each other ($p = 0.757$) (Figure 4).

When examining the RMS value of each separate facial muscle, we found impairment in the frontalis muscle in TT, BT and BB forms, where these demonstrated the largest amplitude values (Figure 5). Regarding the orbicularis oculi, a significant difference was found between the RMS values of healthy subjects and all clinical forms. As for the zygomaticus muscles, there was a statistically significant difference for both BB and LL forms, with the first showing higher values and the latter lower values than those for healthy individuals (Figure 5). Leprosy
patients presented significantly higher values for the masseter muscles than healthy individuals for all clinical forms. In contrast, the orbicularis oris muscle was statistically different only in the BT form.

The Fmean value indicated that the frontalis muscle was altered in the TT, BB and BL forms (\( p = 0.003, p = 0.022 \) and \( p < 0.001 \) respectively). The orbicularis oculi presented impairment in the TT, BT and BL forms (\( p < 0.001 \)) (Figure 6). Concerning the zygomaticus muscle, all forms showed abnormalities (\( p < 0.001 \)), although BL stood out with the highest frequencies. We observed alterations in the masseter in the TT, BB and LL forms (\( p < 0.001 \)). In the orbicularis oris in the TT, BB and BL forms, there is a statistical difference with higher values than those for healthy individuals (\( p < 0.001, p = 0.009 \) and \( p = 0.018 \) respectively) (Figure 6).

In order to check for differences between the two sides of the face, we employed the Wilcoxon statistical non-parametric paired test, while comparing the means of the right (R), and left (L) hemiface of the same patient.

In relation to the RMS feature of the electromyographic signal, when considering combined facial muscles, the difference between the left and right sides of the face was significantly different only in the TT clinical form (\( p < 0.001 \)) (Figure 7).

For the Fmean feature, a statistical difference in asymmetry was noted in the TT, BB and LL forms (\( p < 0.001, p = 0.025, p < 0.001 \) respectively) (Figure 8).

Figure 9 shows the separate RMS evaluation of muscles, in which facial asymmetry was noted for the frontalis muscle in all clinical forms, but not in healthy individuals. The
Figure 5. Comparison of the means of the electromyographic signal feature (RMS) from each separate facial muscle of leprosy patients and control group through the Kruskal–Wallis method (multiple comparison, Dunn’s test).

The orbicularis oculi muscle presented asymmetry in BT and LL forms, as well as in healthy individuals. For the zygomaticus, we could find asymmetry in TT ($p < 0.001$), BB ($p = 0.009$) and BL ($p = 0.019$) forms, and in healthy individuals ($p = 0.002$), and for the masseter in healthy individuals, TT ($p < 0.001$) and BB ($p < 0.001$) forms.

Figure 10 shows the asymmetry analyses of the Fmean electromyographic signal feature indicated differences for the frontalis muscle in the healthy group ($p < 0.001$), and in TT, BT, BB and LL forms ($p < 0.001$). For the orbicularis oculi there was asymmetry in BT and BB forms ($p = 0.037$ and $p < 0.001$ respectively). The zygomaticus was asymmetric in all clinical forms and in the healthy group. Asymmetry was also evident in the masseter muscle in the healthy group and in all clinical forms except in BB.

**Discussion**

This study examined facial motor function through surface electromyography in patients with different clinical forms of leprosy, and revealed the impairment of muscles innervated by the facial nerve and its temporal, zygomatic and buccal branches and by the trigeminal nerve and its mandibular branch, indicating neural damage in facial musculature in all forms.
Different approaches to facial muscle assessment have been applied, although they are still not routine for leprosy.\textsuperscript{12,13,16,17} We examined the RMS feature and Fmean feature of the electromyography signal. Both features were complementary to each other in our analysis of facial musculature impairment in leprosy patients, thus presenting more accurate results regarding neural damage.

The results of this analysis, the facial muscular impairment in leprosy were demonstrated in an objective way, notably in TT and in the borderline group forms (BT, BB and BL). The results found in our work can be explained by variations of the intensity of neurological impairment with the spectrum of immune response of the patient. In the TT form, there is an intense granulomatous response with early neural destruction. The same happens in the borderline forms, in which there is great immunologic instability favoring type 1 reactions, causing an aggressive injury to the peripheral nerves in these clinical forms.\textsuperscript{18,19}

With regard to the LL form, the group of facial muscles did not differ from the control group, probably due to the anergy exhibited to \textit{M. leprae}. In this clinical form, the involvement of the peripheral nerve takes place later, and the neural impairment pattern is predominantly sensitive.\textsuperscript{19}
Figure 7. Comparison of the means of the electromyographic signal feature (RMS) from combined facial muscles on the right (R) and left (L) hemiface, through the Wilcoxon method, according to clinical forms of leprosy and control group.

It is important to emphasize the electromyographic evaluation of the orbicularis oculi and zygomatic branches considering the protective function of these muscles against corneal injury. The results indicate a specific impairment of these muscles in the TT, BT and BL forms. Such findings also endorse previous studies that demonstrated that the impairment of the orbicularis oculi does not take place separately, as most of the examined patients had other associated facial muscle damage as well. The impairment occurred mainly in the borderline group forms (BT, BB and BL), reinforcing the association with reactional episodes and immunological instability found in these patients.\textsuperscript{16}

Nonetheless, considering the difficulty in recognizing the neural involvement and even the delay in the diagnosis of leprosy, it is difficult to establish and to specify the number of reactions presented by the patient. This consideration however is extremely relevant and can be used in future works.

In evaluating symmetry, most of the evaluated branches showed an asymmetrical pattern. Therefore, there was asymmetrical motor impairment of the face in most of the cases and also according to the analysis of clinical forms, especially in the borderline group.

In the present study, while in borderline forms there is a predominantly neurogenic impairment (high amplitudes) in most of the muscles, in LL patients there is a more infiltrative/myopathic condition. The higher frequencies and amplitudes observed in borderline forms corroborates with a neurogenic condition (chronic denervation and reinnervation), and in LL patients, the lower frequency and amplitudes, reinforce the hypothesis of a local infiltrative process, especially in the more superficial muscles and close to colder areas.
Figure 8. Comparison of the means of the electromyographic signal feature (Fmean) from combined facial muscles in the R and L hemiface, through the Wilcoxon method, according to clinical forms of leprosy and control group.

Figure 9. Comparison of the means of the electromyographic signal feature (RMS) from each separate muscle (R and L) through the Wilcoxon method, according to clinical forms of leprosy and control group.

The results presented herein point to a generalized impairment of the facial muscles in leprosy, as demonstrated by the RMS and Fmean features of the signal from the surface electromyography applied to the upper, middle and lower facial segments. Our results corroborate
Figure 10. Comparison of the means of the electromyographic signal feature (Fmean) from each separate muscle (R and L) through the Wilcoxon method, according to clinical forms of leprosy and control group.

with previous articles indicating abnormalities in both the upper and lower facial musculature in leprosy.\textsuperscript{12,16}

The present study reinforces the importance of investigating all facial nerve branches, as well as the mandibular branch of the trigeminal nerve in leprosy patients, given that only the ophthalmic branch of the trigeminal is recommended in the routine evaluation of leprosy patients.\textsuperscript{20} The surface electromyography proved to be an auxiliary tool for the diagnosis of motor facial disabilities that are imperceptible to clinical examination, aiding in the prevention of incapacities, which is fundamental for the social inclusion of leprosy patients.

Considering these findings, further longitudinal studies should be carried out, allowing for a more timely analysis of how useful this method can be in preventing disabilities and in rehabilitating leprosy patients.

Ethics statement

This research was carried out according to the recommendations of the Guidelines of the National Board on Research Ethics (CONEP). All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by UFU Research Ethics Committee under the number CAAE: 41933614.3.0000.5152.

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Conflict of interests
Authors report no conflict of interest.

Data sharing
The supporting data for this article can be obtained from the corresponding author on request.

Authors’ contributions
LBP, DEA, DFS, VHGB, AOA and AAP wrote the manuscript and contributed to its analysis and interpretation of data. MFO and IMBG wrote the manuscript, collected and analyzed data, performed the experiment, discussed the results as well as contributed to conception, design, analysis and interpretation of data. All authors read and approved the final manuscript.

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