

# Quality of life in patients with Charcot-Marie-Tooth disease type 1A

Análise da qualidade de vida de pacientes com a doença de Charcot-Marie-Tooth tipo 1A

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## ABSTRACT

We assessed the functional impairment in Charcot-Marie-Tooth resulting from 17p11.2-p12 duplication (CMT1A) patients using the Short-Form Health Survey (SF-36), which is a quality of life questionnaire. Twenty-five patients of both genders aged  $\geq 10$  years with a positive molecular diagnosis of CMT1A were selected. Age- and gender-matched Control Group (without family history of neuropathy), and the sociodemographic and professional conditions similar to the patients' group were selected to compare the SF-36 results between them. The results showed that the majority quality of life impairments in CMT1A patients occurred in the social and emotional domains. Functional capacity also tended to be significantly affected; other indicators of physical impairment were preserved. In conclusion, social and emotional aspects are mostly neglected in the assistance provided to CMT1A Brazilian patients, and they should be better understood in order to offer global health assistance with adequate quality of life as a result.

**Key words:** quality of life, questionnaires, Charcot-Marie-Tooth Disease.

## RESUMO

Avaliou-se o comprometimento funcional de pacientes com Charcot-Marie-Tooth provenientes da duplicação 17p11.2-p12 (CMT1A), utilizando o SF-36, que é um questionário para medir a qualidade de vida. Vinte e cinco pacientes de ambos os sexos com idades  $\geq 10$  anos e diagnóstico molecular de CMT1A foram selecionados. Idade, sexo, condições sociodemográficas e profissionais foram pareados com o Grupo Controle (sem histórico familiar de neuropatia). Os resultados mostraram que o maior impacto da CMT1A na qualidade de vida ocorreu nos domínios social e emocional dos pacientes avaliados. A capacidade funcional também tende a ser significativamente afetada, enquanto outros indicadores de deficiência física foram preservados. Por fim, os aspectos sociais e emocionais dos pacientes acometidos por CMT1A costumam ser negligenciados na assistência médica prestada aos pacientes brasileiros, e devem ser melhor compreendidos a fim de oferecer uma assistência global à saúde, resultando em adequada qualidade de vida.

**Palavras-Chave:** qualidade de vida, questionários, Doença de Charcot-Marie-Tooth.

Charcot-Marie-Tooth disease (CMT) or hereditary motor and sensory neuropathy (HMSN) is the most common inherited neuropathy with an estimated prevalence of 40 in 100,000 people<sup>1</sup>. It belongs to a large, heterogeneous, and complex group of genetically determined neuropathies with autosomal dominant, autosomal recessive, or X-linked inheritance. At least 51 genes have already been associated with the condition; however, the actual number is expected to range between 50 and 100 genes.

CMT affects mainly muscle strength distally in the lower limbs. The impact on sensory function is variable, although loss of balance and pain occurs. *Pes cavus*, hammertoes, and kyphoscoliosis

are common features. The disease phenotype is quite variable, but most CMT patients are situated in the benign side within the spectrum of the peripheral neuropathies. Although onset usually happens in the two first decades of life, most patients have a slowly progressing disease<sup>2-4</sup>. However, there are patients with a more severe disease phenotype carrying genetic mutations that seems to be prone for such clinical presentation<sup>5</sup>.

Even patients with benign manifestations of CMT have functional impairment that may be accompanied by physical limitations, disability, and negative impact on quality of life as a whole<sup>4,6</sup>.

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According to the definition of the World Health Organization (WHO), quality of life refers to one's perception of his/her position in life in the context of culture and values of the place where one lives and sets his/her goals, expectations, standards, and concerns<sup>7</sup>. Therefore, a patient's perception of his/her disease will affect his/her quality of life, interfering with his/her health status and other aspects of life in general<sup>8</sup>.

A number of scales are currently used to assess quality of life, especially the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36), whose usefulness and adequacy are recognized worldwide<sup>9</sup>. In Brazil, the scale was culturally adapted and validated by Ciconelli et al.<sup>9</sup> and has been used in different disciplines of health sciences, both in research settings for the assessment of quality of life and in clinical practice, with the purpose of helping patients to take decisions concerning their treatment<sup>8</sup>.

About the quality of life assessment in CMT patients, other studies conducted in the United States, Australia and Italy have shown that the disease has a negative impact on quality of life<sup>10-12</sup>. There are several psychosocial issues faced by CMT patients<sup>10</sup>, which include quality of life domains, obstacles to perform daily-life activities such as working, feelings of anger, guilt, and fear, and aspects related to self-esteem. Some studies suggested that CMT-related weakness may be mentally disabling and cause significant physical effects. As a whole, inherited neuropathies result in deterioration in quality of life, and the physical aspects of quality of life seems to be most commonly associated with disability<sup>11,12</sup>. Also, according to these studies, the mental domain of quality of life is affected by depression, and women tend to have more severe symptoms, although the reason for this is not understood. Those authors suggest that analyzing quality of life is crucial for the development of future therapies<sup>11,12</sup>.

The recognition of functional and quality of life impairments might favor more adequate interventions and adaptation of CMT patients.

To our knowledge, the quality of life of CMT patients was never investigated in Brazil, and considering that it is subject to social and cultural influences, a study in this specific context is important. Therefore, the aim of this study was to assess self-reported quality of life of CMT resulting from 17p11.2-p12 duplication (CMT1A) Brazilian patients, regarding sociodemographic variables in comparison to a Control Group.

## METHODS

The present study was conducted at the Division of Neurogenetics of the Ribeirão Preto Medical School University Hospital, being approved by the local Ethics Committee for Medical Research (Process HCRP 12219/2004). Twenty-five

patients of both genders aged  $\geq 10$  years with a positive molecular test for duplication in region 17p11.2-p12 were selected. The patients' medical records were reviewed and those with concomitant diseases were excluded.

An age- and gender-matched Control Group was chosen and underwent the same assessments under the same conditions. Participants of the Control Group presented similar characteristics to the patients' group, but no family history of neuropathy. Sociodemographic and professional conditions were also used as selection criteria to form the Control Group; therefore, we opted to include control participants whose profiles were more similar to those of the patients.

The quality of life of patient and control groups was assessed by utilizing the instrument SF-36, which consists of 36 items divided into eight domains. These comprise functional capacity, physical aspects, pain, general health status, vitality, social aspects, emotional aspects, and mental health.

The SF-36 was completed at the patient's follow-up appointment. First, participants were given an explanation of the study and, when consent for participation in this study was provided, the questionnaire was completed through an interview. For the Control Group, the study was explained and, according to the volunteer's availability and interest to participate, an interview was scheduled for the completion of the questionnaire. All of them were conducted by the same researcher who had received a training for this purpose.

The presence or absence of occupation was extracted from the patients' medical records, and confirmed during the interview.

Data concerning results were assessed using descriptive statistics, and they were submitted to the normality test (Shapiro-Wilk). The groups were compared using chi-square tests, and for the data that did not adjust to the normal curve, nonparametric ones, like Mann-Whitney's, was carried out. The influence of sociodemographic characteristics was analyzed using Mann-Whitney and Spearman's correlation tests. The level of statistical significance adopted in this study was  $p < 0.05$ .

## RESULTS

Among the 25 CMT1A Brazilian patients enrolled, most were female (60%) and their ages ranged from 10 to 68 years-old, with a mean of 34.16 (standard deviation –  $SD \pm 15.24$  years).

None of the participants presented relevant physical restrictions and use of canes, crutches, or wheelchairs was not observed. From the patients interviewed, 32% had an occupation, 20% were students; while 48% had no occupation or were housewives, retired, pensioned or inactive. The mean duration of disease was 14.8 years, ranging from 4 to 59.

Among the 25 participants in the Control Group, most of them were female (64%) and their ages ranged from 10 to

68 years, with a mean of 33.92 years (SD±14.84 years). Thirty-two percent of healthy participants had an occupation, 28% were students; while 40% had no occupation or were housewives, retired, pensioned, or inactive.

The comparison analysis regarding the presence (workers and students) or absence (retired, inactive, pensioned) of occupation between patients and control groups was analyzed by Mann-Whitney's test that yielded  $p=1.00$ . This result indicated that the occupational status did not differ between the Groups, which reflects that the disease does not affect the professional skills.

Table 1 presents the comparison between patients and controls for the domains assessed with the SF-36. Significant differences were found between CMT1A patients and controls in social ( $p=0.02$ ) and emotional aspects ( $p=0.04$ ). The groups did not differ in any other remaining domains assessed. Table 2 shows the statistical correlation analysis of the quality of life assessed by the SF-36 with age, gender, and occupation variables in CMT1A patient group. No significant correlations were found between any of the domains of the SF-36 and the sociodemographic variables in CMT1A patients (Table 2), nor in the Control Group (data not shown). "No occupation" refers to housewives, retired people, or inactive participants. "With occupation" is the performance of work or study activities of the participants. Finally, duration of the disease was weakly correlated with age (Pearson=0.31) and with depression (Pearson=-0.30) in CMT1A patients.

## DISCUSSION

The mensuration of quality of life using the SF-36, a self-rated instrument, is important not only because of the information concerning the patient's quality of life, but also for directly involving the patient in the process of perceiving and assessing such information. This may increase patient's awareness about the disease and its complications, resulting in enhanced interest and participation in future therapies, and in the design of treatments encompassing the physical and emotional status simultaneously.

The data obtained showed that, in comparison with the control subjects, the quality of life in CMT1A Brazilian patients affected mostly the social and emotional aspects. Although functional capacity tends to be more impaired in this clinical group, other indicators for the assessment of physical impairment were preserved, in contrast with Padua et al.<sup>12</sup>, who found that physical aspects significantly affected quality of life. The authors justify this influence of physical aspects at quality of life with an adaptation process from expectation to reality. In the study carried out by Padua et al.<sup>12</sup>, the social and emotional domains presented no significant differences across the enrolled groups, and the authors explained that this could be due to the adaptation previously mentioned or to the slow progression of the disease. The pain domain was the most significant in the Italian patients studied by Padua et al.<sup>12</sup>, suggesting that pain is the most relevant symptom in the patients assessed.

**Table 1.** Mean scores of patients with Charcot-Marie-Tooth 1A and healthy controls in the domains of the Short-Form Health Survey.

Domain	Means		Standard deviation		p-value
	Patients	Controls	Patients	Controls	
Functional capacity	61.20	76.00	30.76	22.41	0.08
Physical aspects	72.00	78.00	39.74	36.31	0.56
Pain	64.36	69.92	26.37	25.11	0.37
Global health status	61.92	64.04	22.15	13.23	0.87
Vitality	61.40	64.60	20.74	19.73	0.63
Social aspects	86.50	74.00	25.75	23.64	0.02*
Emotional aspects	88.00	70.66	27.02	37.67	0.04*
Mental health	75.52	70.40	22.70	19.80	0.18

\*statistically significant difference.

**Table 2.** Correlation significance of the Short-Form Health Survey domains with age, gender, and occupational status in the Charcot-Marie-Tooth 1A patient group.

Domain	Age <sup>a</sup>		Gender <sup>b</sup>		Occupation <sup>b</sup>		Mean
	r-value	p-value	Z-value	p-value	Z-value	p-value	
Functional capacity	-0.116	0.579	0.53	0.61	0.08	0.94	61.20
Physical aspects	-0.239	0.250	0.97	0.40	1.26	0.27	72.00
Pain	0.331	0.106	0.28	0.81	1.51	0.14	64.36
Global health status	-0.143	0.495	0.61	0.57	0.49	0.62	61.92
Vitality	0.182	0.383	1.41	0.18	0.33	0.65	61.40
Social aspects	-0.302	0.142	1.72	0.18	2.23	0.07	86.50
Emotional aspects	0.062	0.768	1.07	0.46	1.21	0.41	88.00
Mental health	0.296	0.150	0.84	0.43	0.74	0.47	75.52

<sup>a</sup>Spearman's correlation coefficient and analysis of correlations between age and perceived quality of life; <sup>b</sup>Mann-Whitney's test.

Although CMT1A tends to deteriorate the physical ability over the years, aging was not related to worse perception of quality of life in this group of patients presently studied, as also reported by Pfeiffer et al.<sup>6</sup>. However, this finding must be relativized since, according to another research, the instrument used here may not be able to detect minor changes occurring over short periods in a slowly progressing disease<sup>13-16</sup>. Evidence highlighting the need for further investigation on this aspect is provided by Vinci et al.<sup>17,18</sup>, who observed that age and duration of symptoms are strongly associated with deterioration of quality of life, which did not occur with the subjects investigated in the present study. Cultural and social characteristics of a population are likely to be accountable for these discrepancies<sup>11</sup>, although the small number of patients studied may also have influenced the final results.

No relationship between quality of life and age or duration of symptoms in CMT patients was found by Shy and Rose<sup>4</sup>. They reported, however, differences in perceived quality of life between men and women, and its association with pain, depression, and occupational status. They also noted that quality of life is dynamic and may therefore vary in the course of the disease. We found no interactions between gender and domains of quality of life assessed, as well as no significant correlations between occupational status and perceived quality of life. Pain and other physical aspects were not significant when the investigated groups were compared. However, the domains related to social and emotional aspects such as feelings, friendship, group, and family relationships, exhibited a considerable difference between patient and control groups. Our results contrast with findings obtained in other countries, for example Italy and Australia, where other domains had greater relevance. In the Italian study, Padua et al.<sup>12</sup> found significant results for the pain domain, while no significant differences were seen between patients and healthy controls for the remaining domains. Regarding to Australians, Redmond et al.<sup>11</sup> encountered differences in functional capacity seen between patients and controls. This fact strengthens Redmond's view that cultural and social characteristics of a population might determine which domains of quality of life are most affected<sup>11</sup>.

The majority of indicators of physical health were preserved in the CMT1A patients, probably as a result of the slow progression of the disease, with impairment of upper limbs occurring later in relation to the lower limbs<sup>3</sup>. The initial physical condition of the patients corresponded to the typical presentation of CMT1A. Some of them had difficulties to perform daily life activities such as changing clothes; others were unable to work because of their physical limitations,

which is an example of the functional impairment caused by the disease. We had hypothesized significant variations in the domains related to physical health between patients and controls. However, the results obtained in the present study showed that social and emotional domains were the only ones significantly different between CMT1A patient and Control Groups. Such fact indicates that the consequences of the physical disease were more important than the physical disability itself. These findings have important clinical consequences and deserve to be studied in greater depth. Besides, CMT1A patients should receive adequate attention not only regarding their physical problems, but also emotional and social aspects of their condition.

Differently from what was expected, the psychosocial issues faced by CMT1A patients proved to be highly relevant in daily life, including aspects of quality of life, changes in daily life activities, feelings of anger, guilt, and fear, self-esteem issues, and safety concerns. The disease may be invisible to some patients, but the disability and emotional impacts cause significant results to others. In the psychological aspect, we assessed the patient's satisfaction with his/her health status, with life in general, and we intended to investigate symptoms of depression and anxiety through another methodologies of evaluations. In the social sphere, family, occupational, and social aspects were assessed. We found out that patients' dissatisfaction regarding their health and the loss of independence to work or even to perform daily activities (such as washing, cooking, or shopping) had a direct impact on social functioning, which may result in symptoms of depression and anxiety. In this study, the impact and relevance of psychosocial issues on the patients' perception was observed as an important factor to consider during the disease development.

According to Arnold et al.<sup>10</sup>, the individual perception of disability and of the diagnosis depends on one's personal experiences with the disease, personality, family, and social support network, and also on the experience of previous generations affected<sup>10</sup>.

It is imperative to understand what really affects the quality of life of CMT1A patients in order to make proper interpretations of the disease's natural history and to investigate alternatives to improve these patients' quality of life. In conclusion, social and emotional aspects are mostly neglected in the assistance provided to CMT1A Brazilian patients and should be better understood in order to offer global health assistance, with adequate quality of life as a result. Therefore, social and emotional aspects should be taken into account in future treatments and therapeutic trials for CMT1A.

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