Epidemiologic Study of Charcot-Marie-Tooth Disease: A Systematic Review

Lidiane Carine Lima Santos Barreto Fernanda Santos Oliveira
Paula Santos Nunes Iandra Maria Pinheiro de França Costa
Catarina Andrade Garcez Gabriel Mattos Goes Eduardo Luis Aquino Neves
Jullyana de Souza Siqueira Quintans Adriano Antunes de Souza Araújo

Núcleo de Pós-Graduação em Medicina da Universidade Federal de Sergipe (UFS), Rua Cláudio Batista S/N Bairro Sanatório, Aracaju, SE, Brazil

Key Words

Charcot-Marie-Tooth disease · Epidemiology · Prevalence · Public health

Abstract

Background: Charcot-Marie-Tooth disease (CMT) is the most common inherited neuropathy. CMT is classified into 2 main subgroups: CMT type 1 (CMT1; demyelinating form) and CMT type 2 (CMT2; axonal form). The objectives of this study were to systematically review and assess the quality of studies reporting the incidence and/or prevalence of CMT worldwide. **Summary:** A total of 802 studies were initially identified, with only 12 meeting the inclusion criteria. CMT prevalence was reported in 10 studies and ranged from 9.7/100,000 in Serbia to 82.3/100,000 in Norway. The frequency of the main subtypes varied from 37.6 to 84% for CMT1 and from 12 to 35.9% for CMT2; the country with the lowest prevalence of CMT1 was Norway, and the country with the highest prevalence of CMT1 was Iceland; on the other hand, CMT2 was least prevalent in the United Kingdom and most prevalent in Norway. **Key Messages:** This review reveals the gaps

that still exist in the epidemiological knowledge of CMT around the world. Published studies are of varying quality and utilise different methodologies, thus precluding a robust conclusion. Additional research focusing on epidemiological features of CMT in different nations and different ethnic groups is needed.

© 2016 S. Karger AG, Basel

Introduction

Charcot-Marie-Tooth disease (CMT) was first described in 1886 by Charcot and Marie in Paris, and Tooth in London, and was referred to as ‘peroneal muscular atrophy’ [1, 2]. It is part of a clinically and genetically heterogeneous group of hereditary motor and sensory neuropathies with a prevalence of 1/2,500 people; it is the most frequently inherited neuropathy and one of the most common neurogenetic disorders [3, 4].

The main clinical features of this disorder are typically childhood onset, familial occurrence, slowly progressive weakness, and muscular atrophy affecting the feet and

legs; later on, the hands may also be affected, and additional clinical features may then include depression of tendon reflexes and slight to moderate distal sensory impairment [1–4].

The classification of CMT type 1 (CMT1), CMT type 2 (CMT2), and intermediate CMT is on the basis of median motor nerve conduction velocity: CMT1, <38 m/s; CMT2, >38 m/s; and intermediate CMT, 25–45 m/s [5–7].

The prevalence of CMT has been studied in western Norway, and 3 hereditary types were distinguished in the area: autosomal dominant CMT with an estimated prevalence of 36/100,000 X-linked recessive CMT with a prevalence of 3.6/100,000; and autosomal recessive CMT with a prevalence of 1.4/100,000 [3]. Furthermore, more than 40 CMT genes have been currently identified [8].

Few epidemiologic studies have reported the prevalence of CMT in the world. The apparent discrepancy in the results of the various prevalence studies may be caused by differences in methodology, including case identification. According to their importance, a systematic review of the literature was performed in order to analyse and synthesize the literature on epidemiologic studies, regarding the distribution of this disease among the worldwide population (countries and regions).

Methods

The current systematic review was performed in accordance with the guidelines for transparent reporting of systematic reviews and meta-analyses (PRISMA statement) [5].

Search Strategy

Four databases (Internet sources) were used to search for appropriate papers that fulfilled the purpose of this study. These included the National Library of Medicine (Medline-PubMed), Web of Science, Scopus, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) using different combinations of the following keywords: CMT disease, epidemiology, prevalence, public health, and cross-sectional studies. The databases were searched for studies conducted in the period from January 1990 to May 2015. The structured search strategy was designed to identify any published document that evaluated epidemiological studies on CMT disease. Additional papers were included in our study after analyses of all references from the selected articles. We did not contact the investigators, nor did we try to identify unpublished data.

Study Selection

All electronic search titles, selected abstracts, and full-text articles were independently reviewed by a minimum of 2 reviewers (L.C.L.S.B., P.S.N., I.M.P.F.C., and C.A.G.). Disagreements over inclusion/exclusion criteria were resolved by reaching a consen-

sus. The following inclusion criteria were applied: epidemiological studies of CMT in different countries or global regions, and reported prevalence and/or frequency data of the disease and its most frequent CMT subtypes in the population. Exclusion criteria were as follows: inappropriate diagnoses, incomprehensive case ascertainment, review articles, meta-analyses, abstracts, conference proceedings, editorials/letters, and case reports. An exception was made for the article by Foley et al. [9], although it was in the form of a letter, due to the lack of epidemiological studies, which were consistent with the inclusion criteria available in the literature.

Quality Assessment

Each of the 2 reviewers independently completed a quality review for each study to assess the study eligibility for inclusion. The quality of the studies was evaluated using an assessment tool designed specifically for this study based on a scoring system suggested by Boyle [10] (table 1). The quality of studies was scored based on a scoring system composed of 8 questions. For studies based solely on registries, the reviewers were asked to mark 'yes' for questions 3, 4, 5, and 6. For studies using multiple sources of ascertainment, the reviewers were asked to mark 'not applicable' for question 4, and quality was thus scored out of 7. A score of 8/8 or 7/7 was considered high quality, while a score of 1/8 or 1/7 was considered low quality. A third reviewer was consulted in cases for which there was a lack of consensus between the primary reviewers.

Data Extraction

Data were extracted by one reviewer using standardised forms and were checked by a second reviewer. Extracted information included data regarding setting, source (authors, year), objective and study design, country, population denominator, affected individuals/families, timescale (prevalence date), case ascertainment method, diagnostic method, outcome (prevalence per 100,000 population), prevalence of CMT1 and CMT2 subtypes, and potential bias/methodological limitations.

Results

In the literature search, we found 1,158 titles. After excluding 301 duplicate articles and 57 review articles, we proceeded with the reading of 802 titles and abstracts; these included 567 articles on PubMed; 117 on Scopus; 86 on Web of Science and 32 on CINAHL. Thirty articles were selected for full reading. After the assessment of articles not shown in full; duplicates; case studies; articles not in English, Spanish, or Portuguese; and articles with objectives that were not relevant to this study, 12 remaining articles were finally selected (fig. 1).

The most common types of studies were epidemiological and they reported the prevalence and frequency of the genetic subtypes; 4 were retrospective, 3 were prospective, 3 were transversal, 1 was a cohort study, and 1 was a cross-sectional community-based study (table 2). The

Table 1. Quality assessment scores of CMT disease incidence and prevalence studies

Study	Q1 target population described?	Q2 cases from entire population/ probability sampling?	Q3 response rate >70%?	Q4 nonresponders clearly described?	Q5 sample representative of population?	Q6 data collection methods standardized?	Q7 validated criteria to assess disease?	Q8 were estimates given with CI?	Total score
Braathen et al. [23]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8/8
Holmberg et al. [14]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	7/8
MacMillan and Harper [25]	Yes	Yes	No	No	Yes	Yes	Yes	Yes	6/8
Morocutti et al. [26]	Yes	Yes	Yes	No	No	Yes	Yes	No	5/8
Nicolaou et al. [27]	Yes	Yes	Yes	No	Yes	Yes	Yes	No	6/8
Kandil et al. [12]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	7/8
Gudmundsson et al. [21]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	7/8
Foley et al. [9]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	7/8
Kurihara et al. [13]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	7/8
Mladenovic et al. [15]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8/8
Gess et al. [22]	Yes	Yes	No	Yes	Yes	Yes	Yes	No	6/8
Mostacciolo et al. [11]	Yes	Yes	No	No	No	Yes	Yes	Yes	5/8

Fig. 1. Flow diagram of selection of CMT disease incidence and prevalence studies during the period January 1, 1990–May 31, 2015.

Table 2. Details of included studies

Author/years/ country	Objective/design of the study	Population/ geographical area	Study period/ prevalence estimated on	Case ascertainment method	Diagnostic method	Outcome	Potential bias/ methodological limitations
Braathen et al. [23], 2011, Norway	Population-based study of prevalence and gene frequencies of different CMT genotypes. Retrospective study	297,539/eastern Akershus county, Norway	1990–2005/–	Institute of Medical Genetics, University of Oslo Akershus University Hospital. Geneticist/neurologist records classified clinically, neurophysiologically and genetically	Clinical information, median motor conduction velocity and DNA confirmed diagnoses	Prevalence of CMT 82.3/100,000 Women: 1/1,130 Men: 1/1,313 CMT1: 37.6% CMT2: 35.9%	None identified
Holmberg et al. [14], 1994, Sweden	Population-based epidemiological and clinical study. Transversal study	518,742/ Norrbotten and Vasterbotten, northern Sweden	1988–1991/ December 31, 1991	Departments of Internal Medicine, Geriatrics, Pediatrics and Orthopedics in the hospitals of the region and to the Health Care Stations	Family history and pedigree analysis and DNA analysis. CMT type 1 or 2 on the basis of median motor nerve conduction velocity, electromyography	Prevalence of CMT: 20.1/100,000 CMT1: 16.2/100,000	None identified
MacMillan and Harper [25], 1994, UK	Population-based study of the clinical and genetic characteristics of HMSN I adult population. Prospective study	939,3 (adult: 742.1)/ Glamorgan, South Wales	May 1989–June 1991/ June 1, 1988	Department of Neurology, University Hospital of Wales, Cardiff. Department of Neurophysiology, University Hospital of Wales	Standard clinical, electrophysiological and, wherever available, histological criteria	Prevalence of CMT: 18.1/100,000 CMT1: 10.9/100,000 CMT2: 2.7/100,000	Not available on the penetrance in childhood
Morocutti et al. [26], 2002, Italy	Population-based study of prevalence of CMT and to determine the relative percentage of subtypes. Prospective study	332,155/Molise, a central- southern region of Italy	March 1998– June 2000/ December 31, 1999	All the practicing neurologists and neurophysiologists of the county and obtained their collaboration	Neurological and electroneurographic evaluation and bio-molecular analysis	Prevalence of CMT 17.5/100,000	None identified
Nicolaou et al. [27], 2010, Turkey	Population-based study of epidemiological, clinical and genetic characteristics of CMT. Transversal study	794,000/Cyprus	January 15, 2009	The clinical and neurogenetic data bases of the Cyprus Institute of Neurology and Genetics	Based on standard motor and sensory nerve conduction studies performed on all family members available	Prevalence of CMT: 16/100,000 CMT1: 52% CMT2: 33% CMT intermediate: 15%	None identified
Kandil et al. [12], 2012, Egypt	Population-based study of prevalence, patterns, and predictors of peripheral neuropathies. Cross-sectional community-based study	42,223 Urban: 13,288 Rural: 28,935/ council, Assiut	January 1, 1997– December 31, 1997/ December 31, 1997	Four rural study sites: northeast, northwest, southeast and southwest of the governorate. Four urban areas were selected within assut itself	Neurological examination, routine laboratory tests, neurophysiology, and neuroimaging (magnetic resonance)	Prevalence peripheral neuropathy of 3181/100,000 HMSN: 12/100,000	Alcoholic neuropathy was not recorded. Nutritional causes of neuropathy may have been underestimated

Table 2. (continued)

Author/years/ country	Objective/design of the study	Population/ geographical area	Study period/ prevalence estimated on	Case ascertainment method	Diagnostic method	Outcome	Potential bias/ methodological limitations
Gudmundsson et al. [21], 2010, Iceland	Population-based study of prevalence and clinical spectrum of CMT. Retrospective study	307,672/ Iceland	1983–2006/ January 1, 2007	Based on information from all practicing neurologists, both neurophysiology laboratories and the only neurology department in the country	Clinical features and neurophysiological testing. DNA testing was regarded as confirmatory	Prevalence of CMT: 12/100,000 CMT1: 10/100,000 CMT2: 2/100,000	None identified
Foley et al. [9], 2012, England	Population-based study of prevalence all types of CMT. Prospective study	2.99 million people with 259,500 in Newcastle upon Tyne Northern England	1995–2010/ September 1, 2010	The neurogenetic clinical service, the molecular diagnostic service and the clinical neurophysiology service	Clinical presentation, positive family history, electrophysiological studies and molecular genetic testing	Prevalence CMT of 11.8/100,000 196 men/ 156 women	Underestimate due to the insidious nature and variable penetrance of the disease
Kurihara et al. [13], 2002, Japan	Population-based study of prevalence and genetic features of CMT. Transversal study	176,086/ Yonago and Sakaiminato, in the Tottori in western Japan	–/April 2000	Departments of Neurology, Child Neurology and Orthopedics of Tottori University. Questionnaires were sent to other hospitals, clinics and health facilities. Non-responders were interviewed directly over the phone	Electrophysiological and pathological studies were performed using a standard protocol. Genomic DNA	Prevalence of CMT 10.8/100,000	Wide clinical variation and several mildly affected phenotypes. Underestimated in Japan
Mladenovic et al. [15], 2011, Serbia	Population-based study of prevalence and 15-year survival in CMT disease. Retrospective study	1,576,124/ Belgrade, Serbia	January 1, 1988– December 31, 2007/–	Belgrade neurological institutions. Two neurologists	Clinical and CMT diagnosis established according to European CMT Consortium criteria	Prevalence of CMT: 9.7/100,000 CMT1: 7.1/100,000 CMT2: 2.3/100,000 15-year survival: 85.6±7.8%	Underestimation for lack of a protocol official
Gess et al. [22], 2013, Germany	Population-based study of frequencies of mutations in CMT genes from large patient cohorts	Cohort of 776 patients/ Germany	2004–2012/–	Germany neuromuscular center	Analyzed patient histories, electrophysiological and genetic testing	Frequency of CMT subtypes CMT1: 60% CMT2: 26% HNPP: 14%	Germany it is not known whether CMT genes were tested in all patients
Mostacciolo et al. [11], 1991, Italy	Population-based study for the realistic estimate of the prevalence of HMSN I. Retrospective study	1,067,130/ Padua and Rovigo of Veneto Northeastern Italy	1960– 1987/1987	Neurology departments of all the general hospitals of 2 contiguous provinces and Regional Center for Neuromuscular Disorders of Padua University	Nerve biopsies and EMGs	Prevalence of HMSN I 9.37/100,000	Underestimated

HMSN = Hereditary motor and sensory neuropathy; HNPP = hereditary neuropathy with liability to pressure palsies; HMSN I = type I hereditary motor and sensory neuropathy.

Table 3. Genetic epidemiology of CMT in the general population

Country	Affected individuals, n	Families, n	CMT prevalence/100,000 population	CMT1, % (prevalence/100,000) (n)	CMT2, % (prevalence/100,000) (n)	Others, % (n)
Norway	245	116	82.3	37.6 (–) (92)	35.9 (–) (88)	2.9 (intermediate CMT: 7) 23.6 (unknown neurophysiological phenotype: 58)
Sweden	104	52	20.1	81 (16.2) (84)	15 (–) (16)	4 (4)
UK	133	49	18.1	56 (10.9) (69)	12 (2.7) (15)	31 (CMT3: 1; CMT5: 7; spinal CMT: 9; not classified: 22)
Italy	58	13	17.5	64 (–) (37)	25 (–) (15)	1 (6)
Turkey		33	16	52 (–) (18 families)	33 (–) (11 families)	15 (intermediate CMT: 4 families)
Egypt	5	–	12	–	–	–
Iceland	37	18	12	84 (10) (31)	16 (2) (6)	–
England	352	275	11.8	56.7 (–) (126)	17.6 (–) (39)	25.8 (57)
Japan	19	11	10.8	–	–	–
Serbia	161	–	9.7	73 (7.1) (119)	23 (2.3) (37)	4 (5)
Germany	776 (589*)	–	–	60 (–) (355)	26 (–) (151)	14 (HNPP: 83)
Italy	100	30	–	– (9.37) (100)	–	–
Total	1,990	597				

* Five hundred eighty nine patients with nerve conduction studies.

longest time interval investigated was 27 years (1960–1987), in the retrospective study of Mostacciuolo et al. [11]. A high level of heterogeneity among studies precluded a firm conclusion.

The selected studies were performed in different countries, including Egypt, England, Germany, Iceland, Italy (2), Japan, Norway, Serbia, Sweden, Turkey, and the United Kingdom. The studies were conducted between 1991 and 2013. The number of participants per study varied widely, ranging from 5 to 776 individuals with CMT and from 1 to 275 families (table 3).

The most commonly used diagnostic tools were family history, neurological and neurophysiological investigations, and molecular genetic investigations. Ten studies assessed the prevalence of CMT, with reported rates ranging from 9.7/100,000 in Serbia to 82.3/100,000 in Norway (table 3).

The frequency of the main CMT subtypes in countries varied from 37.6 to 84% for CMT1 and from 12 to 35.9% for CMT2; CMT1 was least prevalent in Norway and

most prevalent in Iceland; on the other hand, CMT2 had the lowest prevalence in the United Kingdom and the highest prevalence in Norway. A disproportion in the CMT1/CMT2 relationship was observed in different countries; for example, Iceland, which had the greatest difference, had a CMT1 to CMT2 ratio of 5:1, while Norway had the most homogenous sample with a 1:1 ratio. Among the included studies, only 3 did not report information on CMT1 and CMT2 subtypes; Kandil et al. [12] performed a study on various peripheral neuropathies in Egypt, Kurihara et al. [13] reported data on CMT prevalence in the general population, and Mostacciuolo et al. [11] presented only CMT1 data.

Regarding the different strategies for collecting epidemiological data, the studies used self-administered questionnaires, and clinical and electrophysiological data analysis in retrospective, prospective, and databases studies. Note that self-administered questionnaires and interviews are common ways to obtain morbidity information, frequency of symptoms, and prevalence of variables.

Discussion

Although there is a growing interest in CMT research, epidemiological studies of this disease are still scarce, and knowledge of CMT epidemiology in different parts of the world remains extremely limited.

It is difficult to assess the prevalence of CMT due to a wide variation of clinical symptoms and the different forms of the disease [14]. These difficulties account for the high variability in the prevalence rates reported in epidemiological studies. The problem with estimating minimal prevalence in chronic disorders is to identify all the patients in the general population/geographical region. According to Mladenovic et al. [15], CMT prevalence varies in different populations and different regions within countries.

In our review, we found articles from several countries, but most studies were performed in European countries. This is probably due to the fact that there are major centres for CMT diagnostics in Europe.

Regarding the types of studies included in this review, it seems that the retrospective study was the most predominant, which is due to the fact that the review of medical records is a widely used method of data collection, despite certain limitations [16]. Prior knowledge about certain characteristics of what is being observed introduces distortions in the record of an event, and years later, for the conduction of a historical cohort study, verification may aggravate these distortions for the same reasons [17].

Regarding epidemiological studies, most have investigated the prevalence of general CMT; most of the remaining studies have investigated the prevalence of CMT1, the most common subtype of the disease [18]. Prevalence studies evaluating only CMT2 are rare. Patients and families affected by CMT2 may be more difficult to identify than those affected by CMT1. The age of onset for CMT1 is often during the younger years, while that for CMT2 is often during the older years. The presence of other hereditary neuropathies is more frequent with advancing age, and CMT may thus be more difficult to discern from other neuropathies.

The clinical diagnosis of peripheral neuropathies can be difficult [19]. However, in relation to diagnostic methods used in studies, neurophysiological findings and family history with multiple affected individuals can further support the diagnosis of CMT, which is the most common inherited neuropathy [20]. The systematic screening of multiple close relatives is important [21, 22].

According to Gudmundsson et al. [21], there have recently been major advances in understanding the genetics

of CMT. Genetic testing is helpful in subdividing CMT, but this is not a prerequisite for the diagnosis of CMT. DNA abnormalities are not known to exist for some forms of CMT, or corresponding tests are not commercially available. Gess et al. [22] reported that the genetic heterogeneity of CMT is enormous, and over 40 genes have been shown to cause CMT. Thus, it is important to design rational diagnostic procedures, including the evaluation of the most common causative genes. In particular, the most common genes and their cumulative rates in CMT are of interest.

When analysing the prevalence of CMT (9.37–20.1/100,000), it can be inferred that the lower prevalence rate (9.37/100,000) was reported in an older study [11], in which the only diagnostic methods were nerve biopsies and electromyography; this was also a retrospective study. The second study with the lowest prevalence was also a retrospective study [15], and diagnosis was confirmed only by clinical and CMT diagnosis established according to European CMT Consortium criteria.

In addition to this difference in the diagnostic method used in each study, another factor that may have changed the prevalence reported in each study is that some affected individuals may have mild or no symptoms. This presents a problem in identifying cases of CMT, and most prevalence studies have included a number of individuals with few or no symptoms that were only discovered when seemingly unaffected family members were studied. This may explain the somewhat higher prevalence found in some studies [21].

In the study by Braathen et al. [23], a meticulous effort was made to include all people with CMT in eastern Akershus County, Norway; perhaps that is the reason why their study reported the highest prevalence of CMT (82.3/100,000).

Gudmundsson et al. [21] also reported a high prevalence of CMT in Iceland (12/100,000 population), and improved methods were discussed when comparing another Icelandic study performed in the 1960s, with a reported CMT prevalence of 1.6/100,000.

Regarding the prevalence of CMT subtypes (CMT1 and CMT2), a majority of studies found through genetic testing that CMT1 was more prevalent than CMT2; in most studies, the duplication of chromosome 17p11.2 occurred more frequently, indicating a diagnosis of CMT1 [14, 15, 22].

The only study that found that CMT2 was more prevalent than CMT1 was from Braathen et al. [23], but there was a relatively small difference (CMT2, 49.4% and CMT1, 48.2%). The authors found an equal distribution

of CMT1 and CMT2 in the general Norwegian population, and this was in contrast to previous studies based on clinical populations, which found that CMT1 was significantly more frequent than CMT2.

According to Sackett [24], the different neurophysiological distribution in the general and clinical populations are probably caused by ascertainment differences, as selection bias is more pronounced in clinical populations than in the general population. Thus, Braathen et al. [23] reported that it is likely that their results are more representative than the results from clinical populations, reinforcing this statement by the fact that the ratio between the total number of affected people and the total number of families was similar for both CMT1 and CMT2 (2.3:1 and 2.1:1, respectively).

Conclusion

In conclusion, most studies were performed in European countries, and this is probably due to the fact that there are major centres for CMT diagnostics in Europe. Also, the most widely used diagnostic method was surveying family history with multiple affected individuals, and the survey was further associated with other methods, since the systematic screening of multiple close

relatives is important. The prevalence of CMT varied in different populations and different regions within countries, as did the relative frequency of subtypes CMT1 and CMT2. However, most studies found that CMT1 is the most prevalent subtype of CMT. However, the retrospective nature of these studies might contribute to biases in data collection. Future studies using uniform diagnostic criteria and longitudinal follow-up can help identify temporal trends and geographic variations of the epidemiologic features of CMT in different regions of the world.

This review reveals the gaps that still exist in the epidemiological knowledge of CMT in the world. Published studies are of varying quality and utilize different methodologies, thus precluding a robust conclusion. Future research focusing on epidemiological features of CMT in different nations and different ethnic groups is therefore needed.

Acknowledgments and Funding

We would like to thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico/CNPq/Brazil and Fundação de Amparo à Pesquisa do Estado de Sergipe/FAPITEC-SE for the financial support. We would like to thank Editage (www.editage.com.br) for their English language editing services.

References

- 1 Charcot JM, Marie P: Sur une forme particulière d'atrophie musculaire progressive, souvent familiale, débutant par les pieds et les jambes, et atteignant plus tard les mains. *Rev Med (Paris)* 1886;6:97–138.
- 2 Tooth HH: The Peroneal Type of Progressive Muscular Atrophy. London, H.K. Lewis, 1886.
- 3 Skre H: Genetic and clinical aspects of Charcot-Marie-Tooth's disease. *Clin Genet* 1974; 6:98–118.
- 4 Martyn CN, Hughes RA: Epidemiology of peripheral neuropathy. *J Neurol Neurosurg Psychiatry* 1997;62:310–318.
- 5 Dyck PJ, Lambert EH: Lower motor and primary sensory neuron diseases with peroneal muscular atrophy. I. Neurologic, genetic, and electrophysiologic findings in hereditary polyneuropathies. *Arch Neurol* 1968;18:603–618.
- 6 Davis CJ, Bradley WG, Madrid R: The peroneal muscular atrophy syndrome: clinical, genetic, electrophysiological and nerve biopsy studies. *J Genet Hum* 1978;274:775–780.
- 7 Harding AE, Thomas PK: The clinical features of hereditary motor and sensory neuropathy types I and II. *Brain* 1980;103:259–280.
- 8 Høyer H, Braathen GJ, Busk ØL, et al: Genetic diagnosis of Charcot-Marie-Tooth disease in a population by next-generation sequencing. *Biomed Res Int* 2014;2014: 210401.
- 9 Foley C, Schofield I, Egton G, et al: Charcot-Marie-Tooth disease in Northern England. *J Neurol Neurosurg Psychiatry* 2012;83:572–573.
- 10 Boyle MH: Guidelines for evaluating prevalence studies. *Evid Based Mental Health* 1998; 1:37–39.
- 11 Mostacciolo ML, Micaglio G, Fardin P, et al: Genetic epidemiology of hereditary motor sensory neuropathies (type I). *Am J Med Genet* 1991;39:479–481.
- 12 Kandil MR, Darwish ES, Khedr EM, et al: A community-based epidemiological study of peripheral neuropathies in Assiut, Egypt. *Neurol Res* 2012;34:960–966.
- 13 Kurihara S, Adachi Y, Wada K, et al: An epidemiological genetic study of Charcot-Marie-Tooth disease in western Japan. *Neuroepidemiology* 2002;21:246–250.
- 14 Holmberg BH, Holmgren G, Nelis E, et al: Charcot-Marie-Tooth disease in northern Sweden: pedigree analysis and the presence of the duplication in chromosome 17p11.2. *J Med Genet* 1994;31:435–441.
- 15 Mladenovic J, Milic Rasic V, Keckarevic Markovic M, et al: Epidemiology of Charcot-Marie-Tooth disease in the population of Belgrade, Serbia. *Neuroepidemiology* 2011;36:177–182.
- 16 Mendes W, Travassos C, Martins M, et al: Review of studies on the assessment of adverse events in hospitals. *Rev Bras Epidemiol* 2005; 8:393–406.
- 17 Reichenheim ME, Moraes CL: Pillars for assessing validity in epidemiological studies. *Rev Bras Epidemiol* 1998;1:131–148.
- 18 Mostacciolo ML, Schiavon F, Angelini C, et al: Frequency of duplication at 17p11.2 in families of northeast Italy with Charcot-Marie-Tooth disease type I. *Neuroepidemiology* 1995;14:49–53.
- 19 Boerkoel CF, Takashima H, Garcia CA, et al: Charcot-Marie-Tooth disease and related neuropathies: mutation distribution and genotype-phenotype correlation. *Ann Neurol* 2002;51:190–201.

- 20 Dyck PJ, Karnes JL, Windebank AJ, et al: Minimal pathologic expression of a mutant gene for hereditary motor and sensory neuropathy. *Mayo Clin Proc* 1983;58:419–425.
- 21 Gudmundsson B, Olafsson E, Jakobsson F, et al: Prevalence of symptomatic Charcot-Marie-Tooth disease in Iceland: a study of a well-defined population. *Neuroepidemiology* 2010;34:13–17.
- 22 Gess B, Schirmacher A, Boentert M, et al: Charcot-Marie-Tooth disease: frequency of genetic subtypes in a German neuromuscular center population. *Neuromuscul Disord* 2013;23:647–651.
- 23 Braathen GJ, Sand JC, Lobato A, et al: Genetic epidemiology of Charcot-Marie-Tooth in the general population. *Eur J Neurol* 2011;18:39–48.
- 24 Sackett DL: Bias in analytic research. *J Chronic Dis* 1979;32:51–63.
- 25 MacMillan JC, Harper PS: The Charcot-Marie-Tooth syndrome: clinical aspects from a population study in South Wales, UK. *Clin Genet* 1994;45:128–134.
- 26 Morocutti C, Colazza GB, Soldati G, et al: Charcot-Marie-Tooth disease in Molise, a central-southern region of Italy: an epidemiological study. *Neuroepidemiology* 2002;21:241–245.
- 27 Nicolaou P, Zamba-Papanicolaou E, Koutsou P, et al: Charcot-Marie-Tooth disease in Cyprus: epidemiological, clinical and genetic characteristics. *Neuroepidemiology* 2010;35:171–177.

Erratum

The article by Barreto et al., entitled ‘Epidemiologic study of Charcot-Marie-Tooth disease: a systematic review’ [Neuroepidemiology 2016;46:157–165, DOI: 10.1159/000443706] includes false statements when it refers to the study by Nicolaou P, Zamba-Papanicolaou E, Koutsou P, et al., entitled ‘Charcot-Marie-Tooth disease in Cyprus: epidemiological, clinical and genetic characteristics’ [Neuroepidemiology 2010;35:171–177, DOI: 10.1159/000314351]. The term *Turkey* needs to be replaced by *Cyprus* in the text and the tables.

In addition, the list of authors shall read: Lidiane Carine Lima Santos Barreto, Eduardo Luis de Aquino Neves, Jullyana de Souza Siqueira Quintans, Paula Santos Nunes, Iandra Maria Pinheiro de França Costa, Catarina Andrade Garcez, Fernanda Santos Oliveira, Cynthia Coelho Souza, Gabriel Mattos Goes, and Adriano Antunes de Souza Araújo.