

Assessment of Mizaj in Patients with Carpal Tunnel Syndrome: an Observational and Analytical Study

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ABSTRACT

Background: Carpal Tunnel Syndrome (CTS) is the most prevalent peripheral mononeuropathy. *Khadar* is the word used for CTS in Iranian Traditional Medicine (ITM), and the effect of cold Temperament (*Mizaj*) as one of its causing factors is emphasized.

Objectives: The purpose of this study was to determine the *Mizaj* of patients suffering from CTS.

Methods: This study was conducted at Imam Khomeini hospital, Tehran, Iran. General *Mizaj* of 170 patients with CTS was assessed using the Salmannejad questionnaire. Electrophysiological testing and clinical examination were done and patients were categorized into mild, moderate and severe CTS. Findings were analysed with SPSS software.

Results: Regardless of CTS severity, total preponderance of cold-wet *Mizaj* was observed (n=49, 28.8%). Considering CTS severity, cold *Mizaj* and wet *Mizaj* were the highest prevalent singular *Mizaj* in all groups of CTS severity. Cases with cold-wet *Mizaj* made up the highest compound *Mizaj* percentage in all categories of CTS severity (mild=32.35%, moderate=27.3%, severe=29.2%). However, according to statistics, the difference of warmth-coldness, and wetness-dryness scores among different groups of CTS severity was not significant (P=0.05).

Conclusion: Cold-wet *Mizaj* was most prevalent in our study. *Mizaj* identification may help individuals at high risk for CTS to prevent the disease by *Mizaj* correction. Especial recommendations according to *Mizaj* may help patients, too.

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INTRODUCTION

Carpal Tunnel Syndrome (CTS) is the commonest peripheral nerve entrapment mononeuropathy.⁽¹⁻⁵⁾ This compression neuropathy of median nerve, which makes up around 90% of all entrapment neuropathies.^(6, 7) causes sensory dysfunction described by patient as hand pain, numbness, and tingling. Motor deficit symptoms also occur including lack of strength in index and middle finger and weakness in thumb abduction and opposition.^(2, 7) The most important symptom is pain or paraesthesia in the route of median nerve at night.⁽⁸⁾ CTS is seen in women almost twice than men.⁽³⁾

Different studies have reported different rates of incidence and prevalence in general population worldwide. Each year, about one million American adults happen to suffer from CTS which needs medical treatment (6). In 2000, in UK the number of new CTS patients in primary care were 1952 women and 877 men (3). In 2001, in the Netherlands, the overall incidence rate of CTS was 1.8 per 1000 without gender consideration.⁽⁹⁾ All these huge numbers will eventually impose high cost to the health care systems. In addition, work-related carpal tunnel syndrome is a major cause of long-lasting disability.⁽¹⁰⁾

CTS pathophysiology is multifactorial. The key element is increased pressure of intracarpal tunnel.⁽¹¹⁾ This pressure can cause direct nerve injury, ischemia of median nerve due to compression of vessels in the perineurium and impairment of axonal transport.⁽¹²⁾ In idiopathic CTS, the underlying pathology is noninflammatory fibrosis that happens in connective tissue around flexor tendons. It is suggested

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that this fibrous and vascular proliferation may happen due to mechanical stresses (11). Obesity or increased body mass index,⁽¹³⁻¹⁵⁾ diabetes,^(16, 17) rheumatoid arthritis,⁽¹⁷⁾ hypothyroidism,⁽¹⁷⁾ and pregnancy⁽¹⁸⁾ are some conditions associated with CTS. Others are connective tissue diseases, hand osteoarthritis⁽¹⁹⁾ and occupational factors.⁽²⁰⁾

The most precise way of CTS diagnosis is combining results of clinic and electrodiagnostic study.⁽²¹⁾ Mild CTS is considered as: Distal Sensory Latency >3.6 ms. The moderate form has Distal Sensory Latency >3.6 ms and Distal Motor Latency >4.2 ms. If in addition to these two parameters, motor amplitude is less than 5.5 mv, CTS is considered to be severe.⁽²²⁾

In managing symptoms of CTS, these strategies may be addressed: conservative treatment and surgical treatment.^(6, 23) The commonest non-surgical ones include: oral intake (24) or injection of glucocorticoids,⁽²⁵⁾ wrist splinting,^(24, 26) and occupational and physical therapies such as nerve-gliding exercises.⁽²⁷⁾ Myofascial massage and use of complementary and alternative medicine are other ways of possible therapy. The World Health Organization (WHO) suggests using capacities of traditional medicine because it is available, affordable, and culturally acceptable.⁽²⁸⁾

Reports show that most supportive therapies have short-term efficacy.^(29, 30) Surgical decompression is an effective treatment for CTS⁽³¹⁾ in suitable cases; but also exposes patients to the risk of surgical complications. Overall, evidence supports initial non-surgical treatment.⁽³²⁾ Regarding challenges in management options of CTS, emphasis on prevention of the disease is necessary.

From Iranain Traditional Medicine (ITM) viewpoint, patients with CTS share some common features, especially Temperament (*Mizaj*). ITM emphasizes on lifestyle changes and disease prevention by six essential principles known as *Setteh-e-zarurieh* including: foods and drinks, climate and weather, sleep and wakefulness, movement and rest, mental movement and repose, evacuation and retention.⁽³³⁾

Mizaj is the result of contact of the four classical elements (fire, water, earth and air with four natures of warmness, coldness, dryness and wetness) with each other, and interactions between their antagonistic qualities. The conclusion is a new homogenous quality called *Mizaj*. In general, *Mizaj* can be divided in two categories, moderate and non-moderate. If a *Mizaj* is displaced from its moderate center toward the edges of the quality spectrum, the person is susceptible to *su-e-mizaj* (dys temperament). Non-moderate *Mizaj* is composed of eight types, four singular (warm, cold, wet, and dry) and four combined (warm-wet, warm-dry, cold-wet, cold-dry) types.⁽³⁴⁾ Determining the type of a person's *Mizaj* is done using the *Mizaj* questionnaire.

It seems that medieval physicians had recognised CTS by other terminologies and names. "*vaja al-asab*", which refers to the pain originated from nerve, was used as an expression in medieval medical manuscripts for describing pain conditions.⁽³⁵⁾ Famous Iranian physicians such as Avicenna (980-1037 CE) have defined 15 types of pain precisely; one of them is the term "*Khadar*". *khadar* describes sensory neuropathy and it may

happen in one organ as a result of peripheral neuropathy, similar to what is seen in CTS.⁽³⁶⁾ Other Iranian scholars like Aghili Alavi Shirazi (12th century) in *Khulasah al-Hikmah*,⁽³⁷⁾ Rhazes (865-925 CE) in *Al-havi fi al-tibb*⁽³⁸⁾ and Haly Abbas (949-982 CE) in *Kamel al-Sana'a al-Tebbiya*⁽³⁹⁾ have described this sensory impairment with the symptoms (like numbness, paraesthesia, tingling and hypoesthesia), causes and treatments.

MATERIAL AND METHODS

The present study was an observational, qualitative cross-sectional study conducted in the Physical Medicine and Rehabilitation Clinic of Imam Khomeini Hospital of Tehran University of Medical Sciences, Tehran, Iran. 184 patients with CTS, of any age group and either sex, irrespective of the grade of CTS, who attended the above out-patient clinic were included based on the following inclusion criteria: Being at least 20 years old; willingness of the individual to participate in the research project; the presence of clinical signs and symptoms of CTS (tingling, numbness, paraesthesia, pain at night, positive Phalen test, positive Tinnel test, and positive compression test) as well as confirmatory electrophysiological testing; confirmation of CTS and clinical examination by a specialist to rule out any pathology; ability to read and write Persian. Cases with these exclusion criteria were excluded: medical history of any type of acute trauma; addiction to drugs, alcohol, and sedatives; and psychological problems.

Statistical Analysis

The sample size was calculated using the following formula; $N=200$, $p=0.24$ and $d=0.02$. The estimated sample size was 177, and 184 cases were included. Finally, and after eliminating missing data, 170 valid data were analysed.

All included cases were examined, and CTS was diagnosed by a specialist. Sample size was calculated statistically taking the previously available prevalence as reference. The duration of the study was from May to June 2020. The patients fulfilling the inclusion criteria were informed about the study and were included after obtaining their written informed consents. In all cases, demographic information such as age, weight, BMI, height, education, occupation, city of birth, as well as city of residence were obtained and recorded in each patient's personal profile. The Salmanezhad's twenty-questionnaire for determining *Mizaj* was given to all patients for completion.

Finally, all the information obtained were analysed using SPSS 26 statistical software (IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA). The type of *Mizaj* was determined depending on the severity of the CTS. In this study, average descriptive statistics, and appropriate statistical tests including Kolmogorov-Smirnov test, nonparametric tests such as Kruskal Wallis and Spearman tests were used to analyse the data. The significance level in this study is less than 0.05.

Mizaj Identification Questionnaire

Salmanezhad's twenty-questionnaire has 15 questions regarding identification of coldness and warmness of *Mizaj*; and 5 questions about wetness and dryness of *Mizaj*. Each question has five scores ranging from one to five. If sum of

scores related to the first 15 questions is less than or equal to 46, *Mizaj* of the patient is cold; if this number is 47-49, the case has moderate *Mizaj*; and if this number is 50 or more, warm *Mizaj* is recorded for the patient. In case the total sum of numbers in the last five questions is 14 or less, *Mizaj* of the case is wet, if this number is 15 or 16, the person is moderate in dryness and wetness; and 17 or more is regarded to be dry. The questionnaire has shown reliability and validity.⁽⁴⁰⁾

Ethical considerations

This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Ethical approval was received from Tehran University of Medical Sciences (ID: IR.TUMS.IKHC.REC.1399.070). The goal of the study was explained to the participants and patients were assured that their information was kept confidential and there will be a general final report. Then the patients signed informed written consent. In the case that any of the participants wanted to know their *Mizaj*, their test result was explained to them.

RESULTS

Study was done on 184 CTS patients. Total study participants with valid data were 170. Most of the participants were female (n= 153, 90.0%). Median age of the patients was 48.91(±10.92). According to the definition mentioned previously, 20.00% of patients had mild CTS, 55.88 % had moderate and 24.12% had severe form of CTS.

A large percent of participants were housewives (77.6%). 10.0% worked on their own and 5.3% were employees. Slightly more than this number (5.9%) did not work at all and 1.2 % were workers. Approximately half of the respondents were under diploma (53.5%). with diploma made up 34.7. % of respondents,

Table 1: Demographic profile of the study subjects (N = 170)

Variables	Number of patients (N)	Percentage (%)
Age (years)	Median(±IQR): 48.91 (±10.92)	Range: 25- 83
BMI	Median(±IQR): 29.88 (±4.71)	Range: 20.78- 50.60
gender		
Male	17	10.0
Female	153	90.0
Education level		
Under diploma	91	53.5
Diploma	59	34.7
Some university courses	3	1.8
Bachelor	9	5.3
Master	6	3.5
PhD	2	1.2
Occupation		
Housewife	132	77.6
Employee	9	5.3
Working on their own	17	10.0
Worker	2	1.2
Jobless	10	5.9

while 5.3% of them had bachelor’s degree and only 3.5% belonged to the group with master’s degree. Next were participants who had taken Some university courses (1.8) and then PhD (1.2). Table 1 shows demographic characteristics of patients.

Results of Mizaj regardless of CTS severity

Considering singular *Mizajs* and as seen in Table 2, total preponderance of the cold *Mizaj* was observed (n=75, 44.1%). Then were warm patients (N=64, 37.6%). Less than one fifth of the respondents had moderate *Mizaj* from warmness-coldness view (N=31, 18.2%). More than half of the patients (N=100, 58.8%) had wet *Mizaj*. Next were the patients with moderate *Mizaj* from wetness and dryness point of view (N=42, 24.7%), and patients with dry *Mizaj* made up 16.5% of cases (N=28).

About combined *Mizaj* s and as is illustrated in figure 1, overall, the most patients (28.8%) had cold-wet *Mizaj*, while the least (4.1%) were moderate in warmness-coldness and dry. Warm-wet (22.9%) and warm-moderate (10.0%) participants stood at the second and third position in this list while cold-moderate *Mizaj* with its 9.4% cases was in fourth position. As the data suggests, warm-dry cases consisted of 6.5% patients which was less than moderate-wet (7.6%) and more than cold-dry cases (5.9%) respectively. Moderate-moderate cases included 4.7% of total study participants.

Results of Mizaj regarding CTS severity

As shown in Table 3, in all groups of CTS severity, cold *Mizaj* was the highest singular prevalent *Mizaj*. This *Mizaj* was observed in half of cases with mild CTS (n=17), 43.1% of moderate CTS group (n=41), and 41.4% of patients suffering from severe CTS (n=17). The most number of patients with cold *Mizaj* belonged to moderate CTS severity group (n=41, 54.6%). The second highest prevalent *Mizaj* was warm, seen in 11, 38 and 15 patients of mild CTS (32.3%), Moderate CTS (40.0%), and severe CTS (36.5%). Patients with moderate *Mizaj*

Table 2: *Mizajs* of studied CTS patients

		Wetness- dryness			Total
		Dry	Moderate	Wet	
Warmness-coldness	Warm	11	18	35	64
	Moderate	7	8	16	31
	Cold	10	16	49	75
Total		28	42	100	170

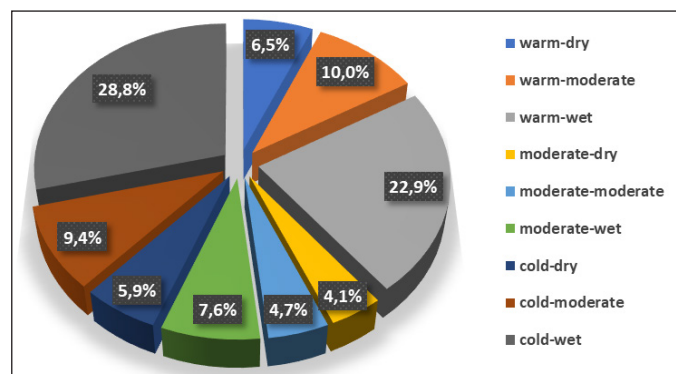


Fig. 1: *Mizaj* distribution of total study participants

Table 3: Number of cases regarding warmness- coldness and wetness-dryness according to CTS severity

		Warmness- coldness			Total
		Warm	Moderate	Cold	
CTS severity	mild	11	6	17	34
	moderate	38	16	41	95
	severe	15	9	17	41
Total		64	31	75	170

		Wetness- dryness			Total
		dry	moderate	wet	
CTS severity	mild	4	12	18	34
	moderate	17	24	54	95
	severe	7	6	28	41
Total		28	42	100	170

from warmness-coldness view, accounted for 17.6% (n=8) of mild CTS cases, 16.8% (n=16) of moderate CTS patients, and 21.9% of severe CTS cases (n=9).

Wet Mizaj was also the most prevalent in all three groups of CTS severity (mild=18 individuals, equal to 52.9%; moderate=56.8% and 54 cases; severe=68.2% and 28 patients), and the highest number of individuals with wet Mizaj was seen among patients with moderate CTS (54%). Details are given in Table 3.

As figure 2 illustrates, about combined Mizajs, cases with cold-wet Mizaj made up the highest amount in all three categories of CTS severity. In severe CTS group, this number was equal to that of warm-dry (29.27%). The other types of Mizaj had a smaller percentage in this group. Order of highest to lowest included: moderate-wet Mizaj (9.76%); cold-dry and moderate-moderate both 7.32%; cold-moderate, moderate-dry and warm-dry equally 4.88%; and warm-moderate 2.44%.

Following cold-wet Mizaj in moderate CTS group (27.37%), warm-wet patients made the next prevalent Mizaj (25.26%). Individuals with warm-moderate Mizaj comprised 11.58% of cases who suffered from moderate CTS. 9.47% of cases in this group had cold-moderate Mizaj and the next percentage (6.32%) was equal between cold-dry and warm-dry Mizaj. 5.26% of cases in this group had moderate-moderate Mizaj and the same number had moderate-dry Mizaj. The least frequent Mizaj belonged to subjects with moderate-moderate Mizaj (3.16%).

Among patients who had mild CTS, after cold-wet Mizaj (32.35%), the next percentage belonged to warm-moderate and cold-moderate Mizaj (both 14.71%). While warm-moderate participants made up 14.71% of total mild cases, warm-wet and warm-dry had the same number and percentage (8.82%). individuals with moderate-moderate Mizaj composed 5.88% of mild CTS group. None of the patients categorized in this group had moderate-dry Mizaj.

Normality of warmness-coldness, and wetness-dryness scores of Mizaj was evaluated using Kolmogorov-Smirnov test. Since these scores did not have normal distribution (p=0.030, and p=0.001, respectively), non-parametric tests were used. Kruskal-Wallis and Spearman tests were used to analyse the relationship between scores of warmness-coldness and wetness-dryness of Mizaj, and CTS severity.

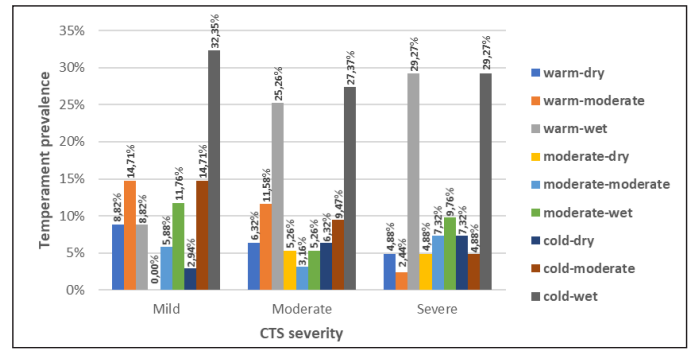


Fig. 2: Mizaj prevalence according to CTS severity

Kruskal-Wallis non-parametric test showed that the difference of warmness-coldness score among different groups of CTS severity is not significant (p=0.856). Wetness-dryness score was not significantly different among the three groups of CTS severity, either (p=0.272).

The Median of warmness-coldness score was the highest in moderate CTS severity group (53). Patients with severe CTS had a lower Median (49) and the lowest warmness-coldness score pertained to severe CTS group (46.5). The highest Median of wetness-dryness score (15) was also related to the group of moderate CTS severity. Mild and severe CTS group had the next Median of this score (14 and 13 respectively).

DISCUSSION

Mizaj, which is produced from action and reaction among elements, is mentioned as singular or combined depending on whether only one quality of classical elements is dominant, or two qualities reveal their features simultaneously. Mizaj has a leading role in health maintenance, diagnosis and treatment of diseases. In Persian medicine, some criteria are used to determine Mizaj of an individual which are almost qualitative features. Using a standard questionnaire makes it possible to change qualitative data into quantitative ones. Thus, data may be used in studies in order to compare different factors and study their relationship.⁽⁴¹⁾

This study is one of the very first times that Mizaj of patients with CTS is studied. There are some factors affecting Mizaj such as climate in place of living, and season of the year.

In 2013, Siciliani Scalco et al. have studied effect of seasons of the year on frequency of neuropathies, including 4260 cases with CTS. The results revealed that the highest frequency of CTS diagnosis was in winter (50.8%) and the lowest frequency in summer (38.9%).⁽⁴²⁾ This is a noticeable variation which complies with Persian medicine principles.

Most of patients lived in nearly the same climate. Since study was done in two months with almost the same weather conditions, the effect of season and climate on Mizaj may be ignored.

Although there is hardly another study found on subject of Mizaj identification and CTS or neuropathies, Ansari et al. have done a wider study.⁽⁴³⁾ The authors evaluated the concordance of Mizaj of individuals and Mizaj of their diseases in 400 cases. Their study was done in National Institute of Unani Medicine

of Bangalore in India, in which they assessed *Mizaj* of each patient. Then, the disease of every individual was evaluated and by considering the related objective and subjective signs and symptoms, a *Mizaj* was attributed to the disease. The concordance of these two *Mizaj* was analysed. They found a significant concordance between cold *su-e-mizaj* and diseases of the cases. The same was seen about cold-wet *Mizaj* and patients' diseases.⁽⁴³⁾

In our study, regardless of CTS severity, total preponderance of the cold *Mizaj* was observed (n=75, 44.1%) and more than half of the patients (N=100, 58.8%) had wet *Mizaj*. Overall, slightly less than one third of total study participants (n=49, 28.8%) had cold-wet *Mizaj*.

Considering CTS severity, cold *Mizaj* was the highest prevalent singular *Mizaj* in all groups of CTS severity (mild=50.0%, moderate=43.1%, severe=41.4%). Wet *Mizaj* was also the most prevalent singular *Mizaj* from wetness-dryness viewpoint (mild=50.0%, moderate=43.1%, severe=41.4%). Cases with cold-wet *Mizaj* made up the highest compound *Mizaj* percentage in all three categories of CTS severity (mild=32.35%, moderate=27.3%, severe=29.2%). In our study the same *Mizajs* are found to be most prevalent, and the results comply with Ansari's study. However, according to statistical tests, the difference of warmness-coldness, and wetness-dryness scores among different groups of CTS severity was not significant.

The relationship of cold *Mizaj* and neuropathies has been mentioned by ITM scholars many times. In addition to Avicenna, Rhazes and Haly Abbas have emphasized on cold and cold *su-e-mizaj* as an important cause of *khadar*. Aghili Alavi Shirazi mentions that the patient who has *Khadar* in his hand, can not grip and keep things in hand.⁽³⁷⁾ Esmail Jorjani, another Iranian scholar (1042-1137) writes in his book, *Zakhireh Kharazmshahi*, that one of the causes of *khadar* is cold *Mizaj* of the organ.⁽⁴⁴⁾ His other book *alaghraz ol tebbiyeh* counts cold *Mizaj* as the reason of weakness in nature of organ.⁽⁴⁵⁾ Arzani, who is another famous scholar of Iranian Traditional Medicine in 11th and 12th century, gives a complete explanation in his book *Tebb-e-akbari*.⁽⁴⁶⁾ He mentions degrees of sensation problem in *Khadar* which depend on the strength of cause. The cause of tingling sensation is either cold *Mizaj* or overwhelm of nerve by blood (warm-wet *Mizaj*). He continues with nerve compression, cold thick humour or wetness of nerve, and external coldness of the environment as three of eight detailed causes of *Khadar* (46). In his *Mizan-ol-tebb*, Arzani notes ways of treatment in warm-wet, cold-wet and dryness dominancy.⁽⁴⁷⁾ Nazem Jahan in his book, *Exir-e-azam*, writes about phlegmatic and wet *Khadar*, as well as sanguinic, and dry *Khadar*.⁽⁴⁸⁾

In Canon of medicine, Avicenna has mentioned a main rule for treatment of nerve diseases which is *Mizaj* improvement and modification. Thus, removal of materials with cold nature (*mavad-al-barede*) is essential in CTS as a mononeuropathy.⁽³⁶⁾

According to the *Mizaj* of each individual, it is possible to propose a healthy lifestyle and correction of *setteh-e-zaruriyeh* to prevent CTS. In this regard, a suitable diet can be recommended to the individual. For example, the appropriate

regimen for wet and cold *Mizaj* has been studied and proposed considering both modern nutrition science and traditional resources.⁽⁴⁹⁾

One of the restrictions of this study was the preponderance of female sex. Although according to previous studies, CTS is more prevalent among women, since gender affects *Mizaj* of patients generally, it is suggested to do further studies with more study population of both genders.

CONCLUSION

Regarding the high prevalence of CTS, its effect on quality of life, its financial burden, and challenges in management options of CTS, prevention of the disease may be one of the best possible ways for both individuals and health systems. *Mizaj* identification may help individuals at high risk for CTS prevent the disease by *Mizaj* correction. ITM uses *setteh-e-zaruriyeh* for *Mizaj* correction, which include: foods and drinks, climate and weather, sleep and wakefulness, movement and rest, mental movement and repose, evacuation and retention. Also, if each patient is given appropriate recommendations and education in each of these fields based on his/ her *Mizaj*, the treatment will have a better result.

The results of this study showed that cold and cold-wet *Mizaj* was most prevalent in CTS. This may be used to warn the patients at risk and teach them to change their lifestyle in order to live a healthier life with less complications including CTS.

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AUTHOR CONTRIBUTIONS

All authors did the literature search and drafted sections of the manuscript. PN combined and edited the drafts. MK did conceptualization, methodology and statistical analysis. ShK prepared the figures and helped in resources. MH, SZEM and MA helped in physical examination and electrodiagnostic study. SZEM and MA supervised the manuscript and did the project administration. All authors subsequently revised the manuscript.

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