Original Article

Prevalence and Severity of Central Sensitization in Post-Polio Syndrome: Associations with Clinical Measures and Quality of Life

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Abstract

Objectives: To investigate the presence and severity of central sensitization (CS) and its associations with clinical measures and quality of life (QoL) in individuals with a history of paralytic poliomyelitis with and without post-polio syndrome (PPS). **Methods:** In this cross-sectional study, we included 98 individuals with a history of poliomyelitis, in whom 82 (83.6%) met the criteria of PPS. We used CS Inventory (CSI) to evaluate the presence and severity of CS. We evaluated the severity of fatigue, pain, polio-related impairments, and QoL using a Numerical Rating Scale in addition to Fatigue Severity Scale, Self-reported Impairments in Persons with late effects of Polio rating scale (SIPP), and Nottingham Health Profile (NHP). **Results:** CS was present in 52.4% of patients with PPS, of which 63% are classified as severe to extreme. Those with CS reported more severe symptoms, more polio-related impairments, and worse QoL than those without CS. Severity of CS showed significant positive correlations with severity of fatigue, pain, SIPP, and NHP scales in those with PPS. CSI did not indicate CS in any of those without PPS. **Conclusion:** CS was present in more than half of the individuals with PPS and correlated with more severe pain, fatigue, and more polio-related impairments, in addition to poorer QoL. These findings suggest that CS may contribute to the clinical picture in a subgroup of individuals with PPS. Thus, identification and appropriate management of CS patients may potentially help alleviate their symptoms and improve their QoL.

Keywords: Central sensitization, pain, poliomyelitis, post-polio syndrome, quality of life

Introduction

Poliomyelitis is an infectious disease caused by an enterovirus, and it mainly involves the anterior horn cells of the spinal cord and/or brain stem. It can cause varying degrees of paralysis, permanent disability, and even death. After long-term stability following recovery, some patients with or without remaining disability may develop new neuromuscular symptoms, defined as "post-polio syndrome" (PPS).[1] Although the pathophysiological mechanisms underlying PPS have not been clearly understood, different theories have been proposed, including noncompensated denervation of the enlarged motor units, overuse and degeneration of those motor units, genetic factors, persistent viral infection, and immunopathological factors.[1]

Classic symptomatology of PPS includes new or increasing fatigue, muscle weakness, and pain, which can be quite debilitating and can decrease life satisfaction.[1-3] Among these symptoms, early studies have primarily focused on muscle weakness and fatigue. PPS has been believed to be a "painless" disease, stemming from a lack of sensory involvement. However, in recent years, several studies have been conducted assessing pain in PPS. These studies have indicated that pain is a persistent problem in PPS, with up to 91% of people with PPS reporting pain and discomfort.[4]

PPS pain has been shown to be chronic in nature and localized in both muscles and joints; it has been graded from moderate to severe intensity, and it significantly affects daily life.[3,4] It was initially believed to be mainly nociceptive in character, possibly due to disuse or overuse of weakened muscles, postural changes or abnormal biomechanics, joint instability or deterioration, and secondary conditions such as arthritis or tendinitis.[5] However, other types of pain, particularly neuropathic pain, have also been reported.[6] A recent study investigated the characteristics of PPS pain.[7] The pain was mostly found to be of a deep aching character and was combined with muscle cramps, which are not the usual features of a nociceptive pain. It has been stated that neuropathic pain is unexpected in the course of polio since no sensory nerve fiber is affected. The authors noted that the pain appeared to

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be specific to PPS and might have resulted from a combination and/or an impaired modulation of pain, and suggested the term "post-polio muscular pain."[7]

However, we have recently demonstrated that fibromyalgia syndrome (FMS), which is a widespread chronic pain syndrome with somatic symptoms, is common in people with PPS.[8] Depending on the diagnostic criteria used, we found the prevalence of FMS to range from 15% to 35% in 60 people with PPS, which is higher than the prevalence in people with polio without PPS and in the general population. Moreover, coexisting FMS was found to correlate with more severe PPS symptoms, decreased quality of life (QoL), and more severe polio-related impairments. These findings raised the question of whether central sensitization (CS) could contribute to clinical presentation of PPS, which warrants further investigation.

CS is defined as a neurophysiological entity in which dysregulation in the central nervous system leads to an increased responsiveness to various sensory inputs, resulting in enhancement of pain and/or hypersensitivity to external stimuli such as sound, light, or chemical substances.[9] Emerging evidence suggests that it is the key mechanism of FMS and it contributes to the proposed pathophysiology of overlapping chronic painful conditions with unclear etiology, including but not limited to temporomandibular joint dysfunction, irritable bowel syndrome, chronic back pain, headache, and chronic pelvic pain. These "unexplained" disorders are referred to as "central sensitivity syndromes," all of which share overlapping symptoms, such as pain, sleep disturbances, fatigue, anxiety, and depression, of which CS is a common etiology.[10]

The observation that many symptoms of PPS also overlap with CS syndrome suggests that there may be a central contribution to the clinical presentation of PPS. The high prevalence of FMS that we reported recently also supports this assumption.[8] Therefore, our objectives were to investigate the presence and severity of CS in individuals with a history of poliomyelitis with and without PPS using the Central Sensitization Inventory (CSI), a valid and reliable scale to determine CS.[11-13] In addition, we evaluated whether CS was associated with the presence and severity of fatigue and pain, polio-related impairment, and QoL in people with PPS. We hypothesized that CS is common and may contribute to the clinical characteristics and QoL in a group of individuals with PPS.

Methods

This study was designed in a cross-sectional fashion. Participants were enrolled from the patients who applied to the post-polio outpatient clinic of Ege University Medical Faculty, Department of Physical and Rehabilitation. One-hundred and forty patients with a history of paralytic poliomyelitis were screened for the eligibility criteria. After detailed neuromuscular examination was conducted, nerve conduction studies and needle electromyography (EMG) investigations were performed on those who did not have a previous satisfactory EMG report, to confirm the presence of poliomyelitis, determine which limb was affected by polio, and evaluate the presence of other pathologies such as neuropathies and radiculopathies. Patients with a confirmed diagnosis of paralytic poliomyelitis who were willing to participate in the study were included. Exclusion criteria were those with comorbidities that can induce pain, fatigue, and muscle weakness, such as hypertension, diabetes, hepatic, cardiac, renal, rheumatologic, metabolic/endocrine diseases, vitamin D or B12 deficiencies, and other neurologic disorders including discogenic or neuropathic pain; those taking any medication that could relieve pain and depression or induce fatigue; those over 60 years of age; and wheelchair users. Blood tests, radiographic examinations, and consultations were performed in some participants to exclude these comorbidities. Preexisting FMS was not excluded. The ethics committee of Ege University Hospital approved the study protocol before the commencement of trial. Participants were asked to sign a printed version of the consent form after an investigator informed them about the study.

After the assessment of subjects for the inclusion and exclusion criteria, a total of 98 participants were enrolled in the study. Demographic and clinical characteristics of all the participants were recorded. PPS was determined according to the criteria of March of Dimes.[14]

PPS symptoms, polio-related impairments, QoL, presence of FMS, and CS features were assessed in all participants using the following scales and inventories:

***Numerical Rating Scale (NRS) for pain*:** Participants' average pain level during the previous week was questioned by an 11-item NRS, where zero indicated "no pain" and 10 indicated the "worst imaginable pain."

***Fatigue Severity Scale (FSS)*:** Fatigue severity was assessed using the Turkish version of FSS.[15] Validity and reliability of the scale have been previously established in PPS.[16] The scale consists of nine questions, and each item is rated on a seven-item Likert scale (1 meaning complete disagreement to 7 meaning complete agreement). A maximum score of 7 indicates more severe fatigue.

***Self-reported Impairments in Persons with late effects of Polio rating scale (SIPP)*:** Polio-related functional loss was assessed by SIPP.[17] The scale consists of 13 questions that assess symptoms over the previous 2 weeks: fatigue, weakness, joint or muscle pain during physical activity or at rest, sensory disturbance, respiratory problems at rest or during physical activity, intolerance to cold, sleep problems, concentration problems, memory complaints, and mood swings. Each item is rated from 1 to 4, with higher scores indicating higher symptom severity.

***Nottingham Health Profile (NHP)*:** The first section of NHP was used to assess QoL. Its validity for Turkish patients was studied by Kücükdeveci *et al*.[18] It consists of 38 items and six subdivisions: energy, sleep, emotional reactions, physical

mobility, pain, and social isolation. The scores of each item are added to obtain a score of 0–100 for each subdimension, and a total score of 0–600 is obtained by summing the scores of the six subdimensions. Higher scores denote a greater level of distress.

American College of Rheumatology (ACR) 2016 criteria for FMS: Diagnosis of FMS was made according to the ACR 2016 criteria,[19] which requires all the following criteria to be met: 1) generalized pain, defined as pain in at least four of five regions; 2) presence of symptoms at a similar level for at least 3 months; 3) widespread pain index (WPI) ≥7 and symptom severity scale (SSS) score ≥5 or WPI 4–6 and SSS score ≥9; and 4) a diagnosis of FMS is valid irrespective of other diagnoses. In these criteria, WPI refers to the number of painful areas (0–19) and SSS is the sum of the severity scores of the three symptoms (fatigue, waking unrefreshed, and cognitive symptoms) (0–9) plus the presence of three somatic symptoms (headaches, pain or cramps in lower abdomen, and depression) (0–3), giving the final score of 0–12.

***CSI*:** CSI is a self-reported screening questionnaire used to assess the presence of symptoms related to CS. It was developed in 2012 by Mayer *et al*.[12] to identify patients with symptoms that may be related to CS syndrome, with a proposed common etiology of CS. Validity and reliability of the scale have been demonstrated in various painful conditions.[13] The Turkish version of CSI was used for this study.[11] CSI consists of 25 questions related to common CS symptoms (i.e. sleep problems, unrefreshing sleep, concentration difficulties, sensitivity to light, spreading of pain, stress as an aggravating factor, sensitivity to odors, restless leg syndrome). Each answer is scored from 0 (never) to 4 (always). A score of more than 40 out of 100 points has been reported to be the clinically relevant cutoff value to distinguish the presence of CS.[20] CSI severity levels have also been proposed for clinical interpretation: scores of 0–29 indicate subclinical, 30–39 indicate mild, 40–49 indicate moderate, 50–59 indicate severe, and 60–100 indicate extreme CS.[20]

Statistical analysis

Statistical analysis was conducted using Statistical Package for the Social Sciences version 23.0 (IBM Corporation, Armonk, NY, USA). For the nominal variables, frequency analyses were performed. The assessment for normal distribution of the continuous data was done by Shapiro–Wilk test. Most variables did not show a normal distribution; for this reason, comparison and correlation analyses were performed using nonparametric statistical methods. Variance of categorical variables was evaluated using the Chi-square test. Subjects with a CSI score of 40 or above were defined as CS (+) and those below 40 were defined as CS (−).[20] Variables were compared between those subjects with and without PPS and between those who were classified as CS (+) and CS (−) using the Mann–Whitney U test and the Welch's unequal variances *t*-test. Correlation with the CSI total scores of SIPP and NHP were assessed using the nonparametric Spearman correlation analysis. *P* values of 0.05 or less were accepted as statistically significant.

Results

Table 1 shows the demographic and clinical characteristics of the study subjects grouped by the presence of PPS. Of the total 98 participants, 82 (83.6%) met the criteria of PPS. We did not detect a statistically significant difference between those subjects with and without PPS in terms of age and the number of polio-affected limbs $P \leq 0.05$). Females predominated in those with PPS, and males in those without PPS ($P \leq 0.05$). The predominant symptoms reported by those with PPS were fatigue (90%) and pain (85%), with moderate to severe intensity. Fatigue and sleep problems were more frequently reported by those with PPS compared to those without ($P \leq 0.05$). NHP showed the highest levels of distress in the energy, physical mobility, and pain subdimensions in those with PPS. Subjects with PPS had significantly higher severity of pain and fatigue, more polio-related impairments, and worse QoL than those without PPS ($P \leq 0.05$).

Table 1: Demographic and clinical characteristics of subjects and comparison between groups according to the presence of PPS

	PPS (+) (*n*=82)	PPS (−) (*n*=16)	*P*
Age	50.8 (8.2)	49.4 (6.9)	0.887
Sex (F/M)	58/24	4/12	0.001
Assistive device use (+)	48 (58%)	9 (56%)	0.86
Duration of PPS (months)	49±24	42±28	0.30
Polio-affected limbs			
One limb	12 (14.6%)	4 (25%)	
Two limbs	58 (70.7%)	12 (75%)	0.012
Three limbs	4 (4.9%)	0	
Four limbs	8 (9.8%)	0	
Symptoms reported			
Fatigue	74 (90.2%)	2 (16.6%)	0.000
Pain	70 (85.4%)	7 (43.7%)	0.102
Sleep problems	52 (63.4%)	2 (16.6%)	0.000
Cold intolerance	42 (51.2%)	8 (50.0%)	0.572
Clinical scales			
SIPP scale (13–52)	32.3±7.2	17.7±2.3	0.000
NRS pain (0–10)	6.3±2.7	3.7±3.1	0.012
FSS (0–7)	4.9±2.1	1.7±0.3	0.000
NHP			
Physical mobility (0–100)	49.4±22.9	32.6±17.1	0.007
Pain (0–100)	47.3±36.3	9.1±16.5	0.000
Sleep (0–100)	39.5±28.2	13.2±9.8	0.012
Energy (0–100)	63.4±46.7	11.2±12.9	0.001
Emotional reaction (0–100)	36.2±15.3	14.7±7.1	0.000
Social isolation (0–100)	23.6±29.4	10.6±23.5	0.001
Total (0–600)	259.4±132	76.7±38.3	0.000

Categorical data are presented as numbers (percentages) and continuous variables as mean±standard deviation. F=female, FSS=Fatigue Severity Scale, M=male, NHP=Nottingham Health Profile, NRS=Numerical Rating Scale, PPS=post-polio syndrome, SIPP=Self-reported Impairments in Persons with late effects of Polio rating scale

Table 2 presents the CSI scores for the whole sample, grouped by sex and presence of PPS. Overall, mean CSI scores were significantly higher in females compared to males ($P \leq 0.05$). The average CSI score of those with PPS was 39.3 (between 5 and 77), of which 43 (52.4%) scored 40 or above, indicating the presence of CS. Of these 43 subjects with CS, 16 (19.5%) were classified as having a moderate level, 15 (18.3%) as having a severe level, and 12 (14.8%) as having an extreme level of CS-related symptom severity. However, all subjects without PPS had a CSI score below 40, with a mean value of 13 (between 4 and 31). Of these, 12 (75%) were classified as having a mild level of CS-related symptom severity.

Comparisons of demographic and clinical features between CS (+) and CS (−) subjects among those with PPS are presented in Table 3. There were no statistically significant differences regarding age and number of polio-affected limbs between them ($P > 0.05$). Females were predominant in CS (+) and males in CS (−) subjects ($P \leq 0.05$). CS (+) subjects reported more severe pain and fatigue and had more polio-related impairments and worse QoL ($P \leq 0.05$). The number of limbs with newly reported weakness was significantly higher in CS (+) subjects compared to CS (−) subjects ($P \leq 0.05$).

Total CSI scores showed significant positive correlations with NRS, FSS, SIPP, and NHP scales in those with PPS [Table 4].

Among 82 patients with PPS, 30 (36.5%) met the ACR 2016 criteria for FMS, while none of those without PPS met these criteria [Table 5]. The average CSI scores and the severity levels of CSI were higher in those with FMS compared to those without FMS ($P \leq 0.05$). Among 30 patients with FMS, 24 (80%) had a CSI score of 40 or above [Table 5]. Total CSI scores showed significant positive correlations with the WPI, SSS, and FS scores (not shown in the table; $P \leq 0.05$).

Table 2: Comparison of the CSI scale scores according to the presence of PPS

	PPS (+) (*n*=82)	PPS (−) (*n*=16)	*P*
Total CSI score (0–100)	39.3±16.2	17.0±8.2	0.000
Females (58/4)	41.1±19.1	24.1±11.1	0.000*
Males (24/12)	29.8±14.6	10.1±2.3	
CSI severity levels			
Subclinical (0–29)	28 (34.1%)	12 (25%)	
Mild (30–39)	11 (13.4%)	4 (75%)	0.001
Moderate (40–49)	16 (19.5%)	-	
Severe (50–59)	15 (18.3%)	-	
Extreme (60–100)	12 (14.8%)	-	

Nominal variables are presented as numbers (percentages), and continuous data variables as mean±standard deviation. *Comparison between females and males within the group. CSI=Central Sensitization Inventory, PPS=post-polio syndrome

Table 3: Comparison of demographic and clinical features between subjects with and without CS

	CS (+) (*n*=42)	CS (−) (*n*=40)	*P*
Age	51.1 (6.2)	49.5 (8.4)	0.527
Sex (F/M)	34/8	16/24	0.032
Polio affected limbs			
One limb (*n*=12)	5 (11.9%)	7 (17.5%)	0.247
Two limbs (*n*=58)	34 (80.9%)	24 (60%)	
Three limbs (*n*=4)	3 (7.1%)	1 (2.5%)	
Four limbs (*n*=8)	6 (14.2%)	2 (5%)	
Number of limbs with reported new weakness			
One limb	20 (47.6%)	24 (60%)	0.004
Two limbs	12 (28.5%)	16 (40%)	
Three limbs	10 (23.8%)	0	
Clinical scales			
SIPP scale (13–52)	34.2±6.7	22.5±3.3	0.000
NRS pain (0–10)	7.1±3.4	4.4±2.4	0.005
FSS (0–7)	5.9±2.1	3.1±2.3	0.000
NHP			
Physical mobility (0–100)	53.4±22.9	39.1±18.2	0.024
Pain (0–100)	58.3±29.3	23.6±21.5	0.000
Sleep (0–100)	61.3±30.6	17.7±23.9	0.000
Energy (0–100)	84.5±30.6	24.1±33.1	0.000
Emotional reaction (0–100)	33.7±30.5	14.1±34.1	0.000
Social isolation (0–100)	27.8±33.1	17.6±22.7	0.024
Total (0–600)	317.3±110	136.1±99.1	0.000

Categorical variables are presented as numbers (percentages) and continuous variables as mean±standard deviation. CS=central sensitization, F=female, FSS=Fatigue Severity Scale, M=male, NHP=Nottingham Health Profile, NRS=Numerical Rating Scale, SIPP=Self-Reported Impairments in Persons with late effects of Polio rating scale

Discussion

This is the first study to investigate the presence of CS in individuals with a history of poliomyelitis with or without PPS. Presence of CS was assessed by CSI, which is a valid and reliable scale to identify CS in various conditions. We found that more than half (51.2%) of those with PPS had a CSI score of 40 points or above, indicating the presence of CS. Among those with CS, 63% were classified as having a severe to an extreme level of CS-related symptom severity. Mean total score of CSI was found to be 39.3 in this population, which appears to be higher than the values reported in healthy persons (mean value of 21.5) and close to those reported in chronic pain patients (mean value of 41.6).[12,20] We found higher rate of CS in females than males, which is in line with the previous studies reporting higher prevalence of chronic widespread pain in females.[21] Moreover, CS (+) subjects reported more severe pain and fatigue and had more polio-related impairments and worse QoL compared to CS (−) subjects. In addition, statistically significant correlations were found among the CSI score, severity of pain and fatigue, polio-related impairments, and the NHP scale, indicating that the higher the CSI score, the more severe are the pain and fatigue and the worse is the functional status and QoL. However, none of those without PPS showed the presence of CS. In agreement with our previous study, we found coexisting FMS in 36% of patients with PPS.[8] We also found that, 80% of FMS patients were classified as

Table 4: Correlations of CSI and other study scores in participants with PPS

Clinical scales	CSI score	
	R	*P*
SIPP scale	0.827	0.000
NRS pain	0.455	0.003
FSS	0.755	0.000
NHP		
Physical mobility (0–100)	0.328	0.037
Pain (0–100)	0.567	0.000
Sleep (0–100)	0.719	0.000
Energy (0–100)	0.774	0.000
Emotional reaction (0–100)	0.476	0.031
Social isolation (0–100)	0.573	0.000
Total (0–600)	0.818	0.000

Spearman correlation analysis. FSS=Fatigue Severity Scale, CSI=Central Sensitization Inventory, NHP=Nottingham Health Profile, NRS=Numerical Rating Scale, PPS=post-polio syndrome, SIPP=Self-Reported Impairments in Persons with late effects of Polio rating scale

Table 5: CSI scores according to the presence of FMS in patients with PPS

	FMS (+) (*n*=30)	FMS (−) (*n*=52)	*P*
Total CSI score (0–100)	54.3±12.1 32–77	30.65±11.0 5–48	0.000
CSI severity levels			
Subclinical (0–29)	-	29 (56%)	
Mild (30–39)	4 (13.3%)	5 (9.6%)	0.001
Moderate (40–49)	7 (23.3%)	18 (34.6)	
Severe (50–59)	11 (36.7%)	-	
Extreme (60–100)	8 (26.7%)	-	
CSI ≥40	24 (80%)	19 (36.5%)	0.000

Nominal variables are presented as numbers (percentages) and continuous data variables as mean±standard deviation and min–max. CSI=Central Sensitization Inventory, FMS=fibromyalgia syndrome, PPS=post-polio syndrome

having CS syndrome, and that the severity of FMS increases as the severity of CS increases. Considering the major role of CS in the pathogenesis of FMS, this is an expected finding which supports previous studies.[22,23] However, we also found CS in 36.5% of PPS patients without FMS, although the severity level was lower compared to those with FMS. These findings may support our hypothesis that CS mechanisms may contribute to the clinical picture in a subgroup of individuals with PPS, and that those with most severe CS present with FMS.

The findings of our study may provide insights into the pathogenesis of PPS. The presence of CS in PPS can be explained in the context of neuroinflammation, one of the proposed mechanisms in the pathogenesis of both PPS and CS. While abundant evidence indicates that CS becomes apparent following peripheral noxious stimuli, nerve damage, or tissue injury, recent studies also suggest that CS may also be driven by neuroinflammation in the peripheral and central nervous system.[24] Neuroinflammation results from neuroglial and neuroimmune interactions in the peripheral or central nervous system, leading to increased release of inflammatory mediators including cytokines and chemokines. Previous studies have shown that sustained increases in cytokines, chemokines, and other glia-produced mediators circulating in CSF can lead to the induction and maintenance of CS.[25] It is now recognized that neuroinflammation leads to chronic widespread pain via CS and contributes to the pathophysiology of chronic overlapping pain conditions.[20]

Although PPS has been mostly considered a condition resulting from uncompensated denervation of enlarged reinnervated motor units, there is now increasing evidence that there may be an ongoing inflammatory process in PPS. Several studies presented evidence of inflammation in various locations, including cerebrospinal fluid, central nervous system, muscles, blood, and peripheral nerves in people with previous polio with or without PPS. Muscle biopsies showed inflammatory changes in addition to increased expression of prostaglandin E2 synthetic pathway enzymes.[26] The inflammatory process theory was further supported by increased levels of proinflammatory cytokines and peptides such as tumor necrosis factor-α, interferon-γ, and leptin in the serum and cerebrospinal fluid of individuals with PPS.[27] Identification of a proposed inflammatory process in PPS has led to studies of immune-modulatory treatment of PPS via intravenous immunoglobulin (IvIG) therapy. These studies have shown that IvIG therapy significantly reduces cytokine levels in PPS patients.[28] Therefore, our findings suggest that neuroinflammation-induced CS may be the underlying etiology of the new neuromuscular symptoms in a subset of individuals with PPS. However, further studies investigating the relationship of CS with evidence of neuroinflammation in the central nervous system are needed to prove this hypothesis.

The results of the present study raise the question of whether those with CS symptoms such as widespread pain and extreme fatigue may be considered as a specific subgroup of PPS. It was speculated that a progressive form of PPS, with more rapid deterioration of function, that is to a greater extent accompanied by other symptoms such as fatigue and pain, is driven by immunological and inflammatory processes and responds well to IvIG treatment.[29,30] Based on the present study, we can also speculate that a subgroup of individuals with PPS may have an inflammatory background if they have the symptoms related to CS. It is not possible to conclude whether this subgroup was a more progressive form of PPS, but our finding that the number of limbs with newly reported weakness is higher in those with CS than in those without CS may indirectly support this assumption.

Our findings may also suggest that pain is nociplastic in character in a group of individuals with PPS. Nociplastic pain is defined as pain that occurs due to actual or potential tissue damage that causes activation of peripheral nociceptors

or a change in nociception, although there is no evidence of disease or lesion in the somatosensory cortex.[31] Nociplastic pain encapsulates many mechanisms such as peripheral, spinal, and supraspinal mechanisms, typically seen in the process of peripheral sensitization and CS.[32] Since the presence of PPS brings the individuals with polio further disability through altered movement mechanics, the pain associated with musculoskeletal problems can lead to chronic nociceptive pain, which almost universally evolves into nociplastic pain, mediated through peripheral sensitization first and eventually CS. These proposals do not seem to contradict with the possible involvement of neuroinflammation in patients with PPS; instead, many of the mechanisms in the process of nociplastic pain involve inflammatory changes such as altered chemokines and cytokines peripherally or evidence of findings compatible with inflammation in the central nervous system. Thus, both the presence of PPS and the process of the nociplastic pain might be contributing to ignition of this fire.

The findings obtained in our study may also provide insights into the management of PPS. Detailed examination and diagnosis of PPS and making a distinction between those with and without CS may be important in the selection of treatment options. Targeting neuroinflammation via immunomodulatory treatment to inhibit cytokines and chemokines and use of alternative neuromodulatory approaches such as electrical and magnetic stimulation, transcranial magnetic stimulation, and acupuncture may result in symptom relief and improvement of QoL in those with CS. Targeting CS by centrally acting medications such as tricyclic antidepressants, serotonin–norepinephrine reuptake inhibitors, and α2δ ligands and by nonpharmacologic approaches such as cognitive behavioral therapies may also be effective in these people.[9] Indeed, a few studies have shown that centrally acting medications can be beneficial in individuals with PPS. In a study conducted in 1995, it was reported that approximately half of the patients with PPS responded well to amitriptyline treatment.[33] In another study, we reported that lamotrigine treatment led to improvement in symptoms and QoL of individuals with PPS.[34] However, randomized and controlled, double-blind studies are needed to demonstrate the efficacy of these agents, as well as newer centrally acting drugs and nonpharmacologic and neuromodulatory approaches in the subgroup of PPS patients who have features of CS.

The present study has several limitations. First, the number of subjects without PPS was exceedingly low. This was probably because those with existing symptoms were more likely to seek tertiary care. Therefore, further studies with a larger number of patients both with and without PPS would be needed to support our findings. Second, although CSI is a valid and reliable scale to identify CS, future studies should apply more sophisticated methods such as laboratory neurotransmitters, imaging, and quantitative sensory testing for quantifying clinical findings of CS in PPS. Third, although NHP includes items assessing psychological status, we did not measure patients' levels of depression and anxiety, which are known to be closely related to pain. Lastly, due to the cross-sectional design of the study, it could not be determined whether CS-positive individuals had a more progressive form of PPS, which warranted the use of longitudinal designs to find an answer to that question.

In summary, this study demonstrated the presence of CS in more than half of individuals with PPS. The severity of CS was found to be associated with the severity of pain and fatigue, polio-related impairments, and worse QoL. These findings could hypothetically be explained by the concept of neuroinflammation and may indicate the nociplastic nature of pain in a subgroup of individuals with PPS. Therefore, identification and appropriate management of CS can potentially help alleviate PPS symptoms, particularly pain and fatigue, and improve QoL of these patients. However, further studies with a longitudinal design and with larger sample sizes are needed to properly address these issues.

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Conflicts of interest

There are no conflicts of interest.

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