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Association of central sensitization with pain and quality of life among patients with chronic musculoskeletal pain disorders– A cross sectional study

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Abstract
Background: Chronic musculoskeletal pain disorders (CMPDs) are among the leading causes of disabilities across populations, resulting in high social and financial burden. This persistent pain condition may include the central sensitization (CS) phenomenon, which may be associated with severity of pain and quality of life that may be taken into account in CMPD treatment.
Objective: The aim of the study was to explore association of CS with pain intensity and quality of life.
Methods: In present cross-sectional study total of 185 gujarati participants aged 18-75, suffering from several CMPDs were included. CS symptoms were measured with the Gujarati Version of the CSI, pain intensity was measured by VAS and quality of life was measured by WHOQOL BREF Gujarati version. Statistical analysis was done by using SPSS 15 version. Spearman's rank correlation coefficient test, Mann Whitney U test and Kruskal wallis test were applied for co-relation and between group comparisons respectively. Significance level was set at $p<0.05$.
Results: There were statistically significant moderate positive correlation exists between CSI score and VAS score (Rho = 0.46, P = <0.001) and also there was statistically significant moderate negative correlation exist between CSI score and WHOQOL score (Rho = -0.60, P = <0.001).
Conclusion: There is moderate association exist between CSI score with pain intensity and quality of life. In light of these results, it is recommended that clinicians supplement their assessment with the CSI in CMPDs for improved decision-making during treatment.

Keywords: central sensitization, CMPDs, association, pain, quality of life

Introduction

Musculoskeletal disorders (MSDs) are a diverse group of complex regional syndromes leading to acute or chronic pain, impaired physical function, and disability. The prevalence of musculoskeletal disorders increases with age, obesity, and physical inactivity [1]. Musculoskeletal disorders are a major cause of morbidity, influence health and quality of life and impose an enormous burden on our healthcare system. The burden of musculoskeletal disorders is global, and looking at the gravity of the situation the World Health Organization (WHO) had declared 2000-2010 as the Bone and Joint decade. India is no exception to this situation [1]. WHO estimates that approximately 40% of people over 70 years suffer from osteoarthritis (OA) knee and 80% of individuals experience low back pain (LBP) pain during their lives [2]. A prevalence study conducted by the Indian Council of Medical Research reported an overall prevalence of musculoskeletal disorders to be 7.08%–11.5%. [1]. High prevalence of OA and spinal pain is associated with lifestyle factors, level of physical activity, occupation, and psychosocial factors [3].

Twenty per cent of the general population experiences prolonged or recurrent pain for at least 3 months, such pain is then considered to be chronic [4,5]. Musculoskeletal disorders commonly known as chronic musculoskeletal pain disorders (CMPDs), these conditions lead to increased risk of developing other chronic health conditions, as well as decline in mental health. [6]. CMPDs account for the greatest proportion of persistent pain across geographies and ages, and prevalence increases with aging and obesity [6-8]. The economic consequences of chronic pain include direct costs of medical care and pain management treatments, as well as indirect costs of decreased work productivity and sick leave, and of disability and sickness retirement. [5,9].

The Global Burden of Disease study shows that CMPDs such as low back pain (LBP), headache disorders, neck pain, and others are within the top leading causes of years lived with disability and disability- adjusted life-years (DALY) worldwide [10]. Specifically, in the European Union, musculoskeletal disorders account for 10.3% of the total DALY [11]. CMPDs are therefore responsible for disability and high social and financial burden [12].

Chronic pain is a multi-factorial condition which has an impact on physical or body structures and functions, on psychological processes and on daily activities and quality of life of individuals [5, 13, 14]. Limited functioning or capacity to perform everyday tasks (essential for an independent living) affects individuals with chronic pain in their mobility and self-care, social relationships, work and leisure [15]. Individuals' functioning is composed of

body functions (body level)—described by impairments they experience, and of activities and participation (personal and social levels, respectively) described by capacity and performance tests [14, 16].

Under musculoskeletal conditions, some symptoms such as pain cannot be explained by a specific organic cause. [17]. This has led to a growing interest in central sensitization (CS) to explain some cases of "nonorganic" symptoms. This neuro-physiological phenomenon is defined as an amplification of neural signaling within the central nervous system, which provokes an abnormal increase in pain [18]. In the past decennia, a relevant subsample of patients with chronic pain, including individuals with chronic low back pain (CLBP), have shown an increased responsiveness to noxious and non-noxious stimuli, described as CS [19]. CS is a result of an imbalance in the nociceptive pathways ('pain pathways') and supraspinal structures due to an amplified facilitation and/or reduced inhibition [18, 20, 21]. The phenomenon, CS, is manifested by an amplified pain perception regarding its intensity (hyperalgesia and allodynia), duration (aftersensations and temporal summation) and distribution (expansion of the receptive field), as well as a reduced conditioned pain modulation (CPM) [21]. CS can explain why patients with musculoskeletal disorders suffer from pain, disability, and other symptoms in the absence of a clear nociceptive input or tissue damage [22].

Because patients with CS are more reactive to stimuli and their pain experience is enhanced, the presence of CS and/or higher levels of CS could plausibly be associated with lower physical functioning and participation in patients with CMPD, and vice versa. More severe symptomatology of CS, decreased parasympathetic/vagal activity or altered somatosensory responses have been associated with greater self-reported pain-related disability [23-29].

Given the need to transfer the CS concept to clinical management of persistent pain [18, 30], the Central Sensitization Inventory (CSI) was designed as a screening instrument to help identify if a patient's symptoms may be related to CS [31]. This tool has shown strong psychometric properties and that it is a clinically useful outcome measure [32, 33] Scored from 0 to 100 [34], a cutoff score of 40 is considered to identify >82% of central sensitization pain patients [35]. This cutoff score was integrated as part of an algorithm to classify patient pain as neuropathic pain, nociceptive pain, or CS pain [36]. Moreover, five severity levels have been proposed to help in the clinical interpretation of CSI score [37]. Since the CSI was developed, there has been growing evidence of the presence of CS phenomena under CMPD, such as LBP [38], shoulder pain [39, 40], chronic whiplash [41], knee pain [42], and tendinopathies [43]. Indeed, there is evidence that suggests that treatment for patients with predominant CS symptoms should be different from that of patients suffering from persistent painful conditions without CS. [44].

Although the increase in the frequency of CS in patients with chronic pain is known, data on the association of CS with pain and quality of life is not fully understood by previous literature. Hence there was a need to study the relationship of CS with pain and quality of life among the patients with CMPDs. Thus the aim of the present study was to determine whether there was any association of CS with severity of pain and quality of life (QOL) among patients with CMPDs.

Aims and Objectives of the Study

The aims and objectives of the present study covered by this research proposal were

1. To determine whether there is any association between CS and severity of pain among patients with CMPDs.
2. To determine whether there is any association between CS and quality of life (QOL) among patients with CMPDs.

Hypotheses

1. **Null Hypothesis (Ha0):** There is no significant association between CS-related symptoms and severity of pain among patients with CMPDs.
   Alternatiev Hypothesis (Ha1): There is significant association between CS- related symptoms and severity of pain among patients with CMPDs.
2. **Null Hypothesis (Hb0):** There is no significant association between CS-related symptoms and quality of life among patients with CMPDs.
   Alternative Hypothesis (Hb1): There is significant association between CS-related symptoms and quality of life among patients with CMPDs.

Methodology

Study Design: Cross sectional study.

Study Population: Patients with any of chronic musculoskeletal pain disorder.

Sampling Technique: Convenient sampling

Study Duration: 8 months

Sample Size: Sample size for present study was calculated by considering the proportion of chronic musculoskeletal pain disorder patients among OPD of S.S. Agrawal institute of Physiotherapy and Medical Care Education, Navsari (i.e. 14% of total OPD) i.e. $N = Z^2\ pq/d^2 = (1.96)^2\ (0.14)\ (1\text{-}0.14) / (0.05)^2 = 184.93 = 185$ with different CMPDs was included in this study. Where, Z = Level of significance i.e. 95% = 1.96, p = Proportion of CMPDs by one month pilot survey i.e. 14%, q = 1-p, d = allowable error = 5%

Study Setting: S.S. Agrawal institute of Physiotherapy and Medical Care Education, Navsari.

Inclusion Criteria [45]:
- Subjects with any chronic musculoskeletal pain disorder.
- Subjects suffering from MPD for at least 3 months duration.
- Both male and female with age group 18 to 75 years.
- Subjects who can read and write Gujarati language.
- Subjects willing to participate.

Exclusion Criteria [45]:
- Subjects consuming analgesics or non-steroidal anti-inflammatory drugs (NSAIDs).
- Subjects underwent any surgical intervention in the last three months.
- Subjects diagnosed of specific medical conditions that can negatively affect the central nervous system, including cancer, brain or spinal cord injury, neurological disease or injury,
- Subjects with rheumatoid arthritis, fibromyalgia, polyarthralgia or any other systemic wide spread pain disease.
- Subjects with primary diagnosis of neuropathic pain and
- Subjects experiencing pain as a result of infection.
- Subjects with known psychiatric disorders.

Material and Tools:
- Consent Form
- Chair
- Pen
- Screening Form
- All the outcome measures scales sheets.
- Data recording Sheet

Outcome Measures

1. The Central Sensitization Inventory Gujarati (CSI-G) version to identify symptoms of CS [46].

The CSI is a measure that is used to identify symptoms related to CS and to ascertain the degree of symptoms represented in a 100-point scale. The CSI is the first instrument developed to identify key symptom manifestations of CS, rather than focus on those found in each separate disorder [31]. There are 25 questions that ask about variables related to CS, each a Likert scale of 0–4, where 0 corresponds to the respondent experiencing the event "never" and 4 to "always." A score ≥40/100 is consistent with a larger degree of CS symptomatology. Recently, five severity levels (subclinical = 0–29; mild = 30–39; moderate = 40–49; severe = 50–59; and extreme = 60–100) have been developed to help in the clinical interpretation of the CSI. [37] The CSI has very acceptable internal consistency with Cronbach's alpha at 0.88 and stability with test-retest reliability of r = 0.82. [35] The study by D. Bid *et al* provided us with the evidence that the CSI-G is a reliable and valid measure to assess CS in Gujarati-speaking patients [46].

2. Visual analogue Scale (VAS) to measure Pain Severity [47].

The patients pain severity will be evaluated with a 10-cm horizontal visual analogue scale (VAS) ranging from "0 cm" (no discomfort) to "10 cm" (worst imaginable).

3. WHO Quality of Life instrument (WHOQOL-BREF) Scale Gujarati Version to assess quality of life in all patients with CMPDs [48].

The WHOQOL-BREF produces scores for four domains related to quality of life: physical health, psychological, social relationships and environment. The WHOQOL-BREF contains a total of 26 questions. To provide a broad and comprehensive assessment, one item from each of the 24 facets contained in the WHOQOL-100 has been included. In addition, two items from the overall quality of Life and General Health facet have been added.

Procedure

He study was approved by Institutional ethics committee of Sarvajanik College of Physiotherapy, Surat. The subjects were screened on the basis of inclusion and exclusion criteria and their demographic data were taken by an assessment Performa. Prior to the commencement of the study, detailed procedure of the study was explained to the participants and a signed written informed consent form was taken from them. All the participants then assessed for all the outcome measures described in outcome measures section.

After the collection of data the severity of CS symptoms was correlated with the pain and quality of life for whole sample. Then participants were divided into two groups on the basis of significant (≥40) and non-significant (<40) symptoms of CS on CSI score. Patients with CMPD whose CSI Score <40 and patients with CMPD whose CSI Score ≥40 to compare for any differences in terms of demographics and outcome measures. Mean of age, BMI, duration of symptoms, VAS (Pain intensity) score and WHOQOL BREF (Quality of life) score were compared between groups.

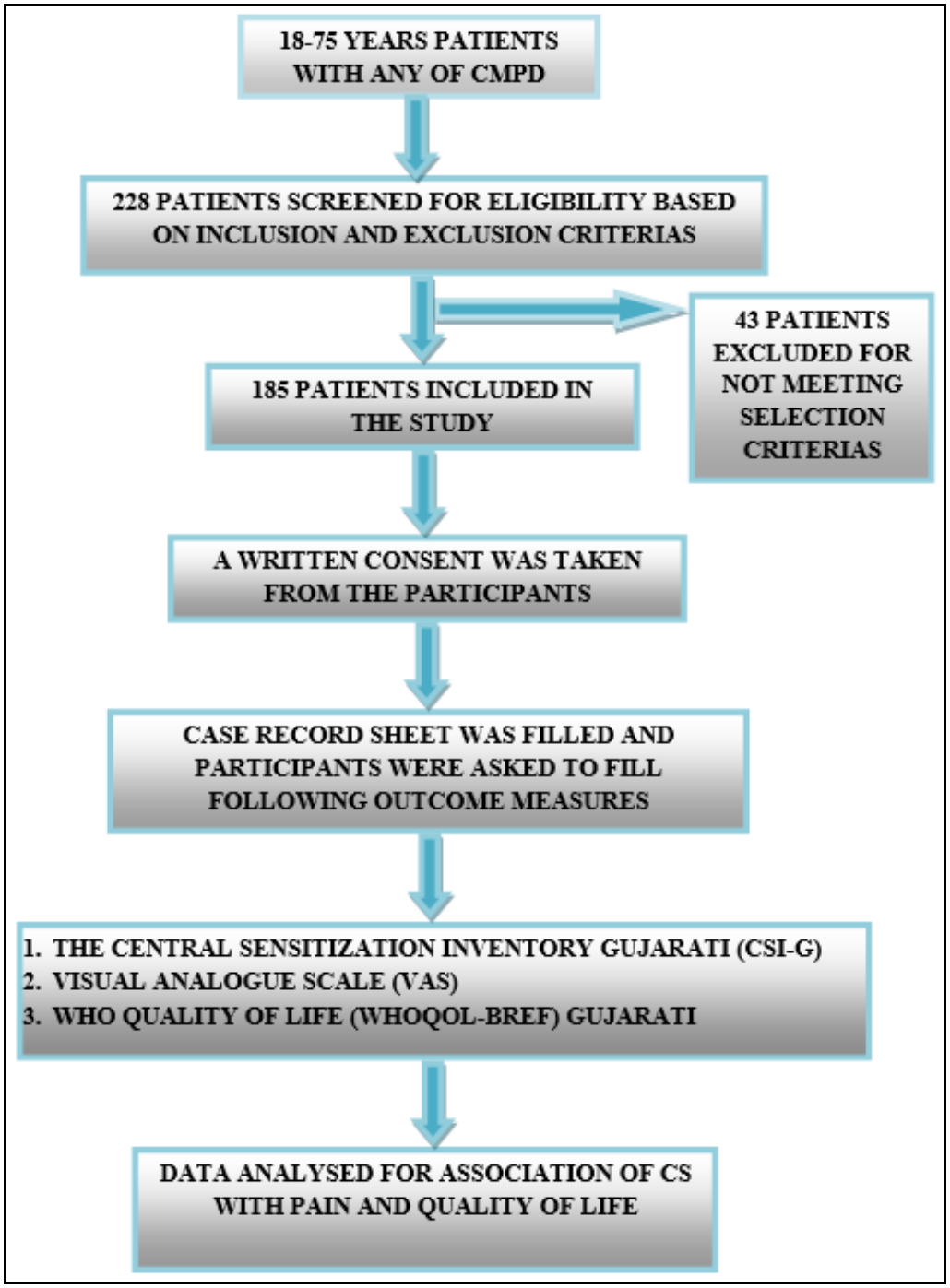


Fig 1: Study Layout

Statistical Analysis

The data was entered using Microsoft Excel 2017 and it was analyzed using SPSS 15 version. Demographic Data were analyzed by mean, median and standard deviation. Normality of data was analyzed by Kolmogorov Smirnov test. All the parameters of this study were not normally distributed. Based on that, data were analyzed by non-parametric tests i.e. spearman's rank correlation coefficient test, Mann Whitney U test and Kruskal wallis test for co-relation and between group comparisons respectively. Absolute significant correlation coefficients were considered clinically relevant only if >.30, according to the suggestion of Cohen (1992) [67]. The level of significance was set at $\alpha = 0.05$.

Results

A total of 228 patients with different CMPDs were screened for this study out of that 185 participants were included in the study and 43 patients were excluded for not meeting selection criteria. The mean age was 50.66 (SD=14.96) years, mean BMI was 26.18 (SD=4.81) kg/m^2 and Mean duration of symptoms was 21.54 (SD=27.30) months of all participants. The mean total CSI score was 24.73 (SD=15.28) points. Mean pain intensity measured by VAS was 4.90 (SD=2.02) cm and mean quality of life measured by WHOQOL score was

94.51(SD=16.36) points. More details of demographics and outcome measures data of sample are given in Table 1.

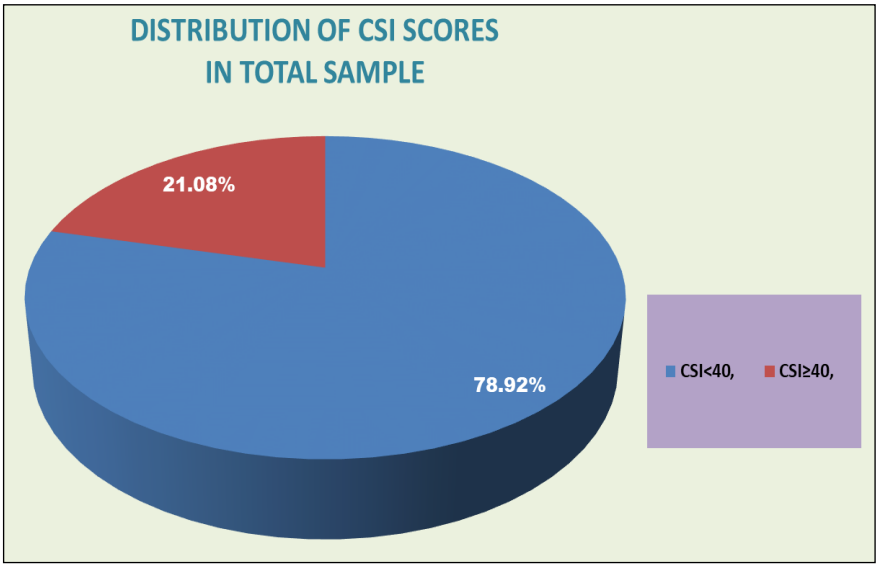
Table 1: Patient's Demographic Variables

(N=185)

VARIABLES	MEAN ± SD	MEDIAN	MIN	MAX
Age (years)	50.66 ± 14.96	52	18	76
BMI (kg/m^2)	26.18 ± 4.81	25.83	16	41.54
Duration (months)	21.54 ± 27.30	12	3	120
Total CSI Score	24.73±15.28	22	0	66
VAS Score (Cm)	4.90±2.02	5	0.3	10
Total WHOQOL Score	94.51±16.36	94	56	130

Among total 185 participants 76 (41.1%) were males and 109 (58.92%) were females. The frequency of CS was higher for females 28.44% (N=31) than males 10.53% (N=8). The most frequent diagnoses were LBP 26.49% (N=49) and Shoulder pain 26.49% (N=49), followed by knee pain 24.86% (N=46) and Neck pain 22.16% (N=41). From the total sample, 146 (78.92%) subjects had a CSI score <40 points (cutoff score), whereas the remaining 39 (21.08%) subjects had CSI score ≥40.

As shown in Table 2 the results of the spearman's rank correlation coefficient test showed statistically significant moderate positive correlation between CSI score and VAS score (Rho=0.46, P=<0.001) and also there was statistically significant moderate negative correlation exist between CSI score and WHOQOL score (Rho= -0.60, P=<0.001). While there were no statistically significant correlations found between CSI Score and age, BMI and duration of symptoms.



Graph 1: Pie-chart representing the distribution of CSI scores in total sample

Comparison of various variables and outcome measures between two groups divided by CSI score <40 or ≥40 points, calculated by mann whitney U test are shown in Table 3. There were statistically significant differences of Duration of symptoms, VAS score and WHOQOL score were found between the CSI <40 and CSI ≥40 groups (P = 0.00064, <0.00001 and <0.00001, respectively).

Table 2: Correlations of the CS (SCI Score) Scores with pain (VAS) and quality of life (WHOQOL Score) calculated by spearman's rank correlation coefficient.

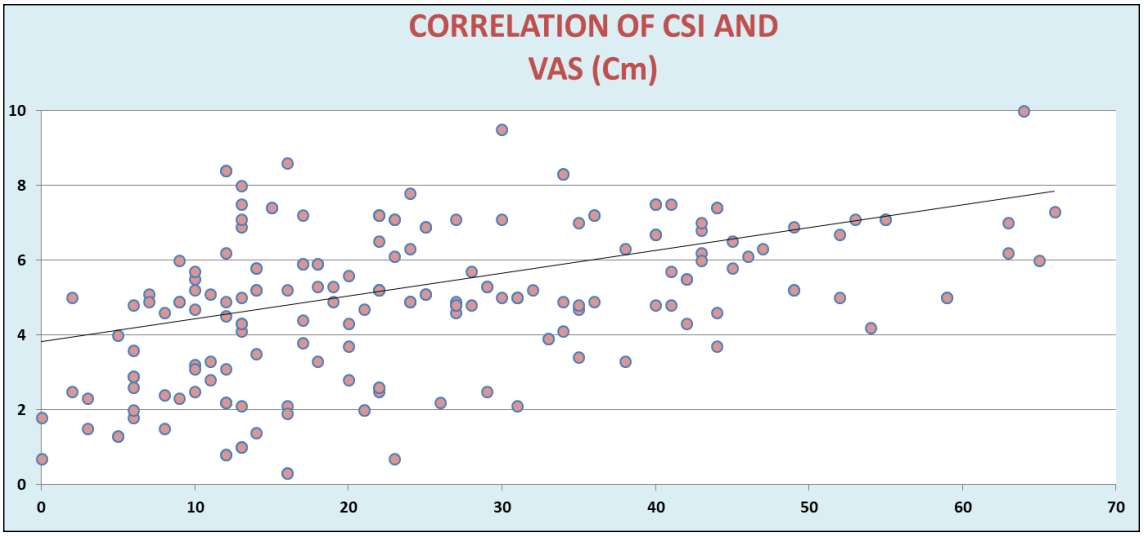
Variables	Correlation coefficient (Rho)	P Value
CSI Score –VAS (cm)	0.46	<0.001
CSI Score – WHOQOL Score	-0.60	<0.001

Bold denotes statistical significance

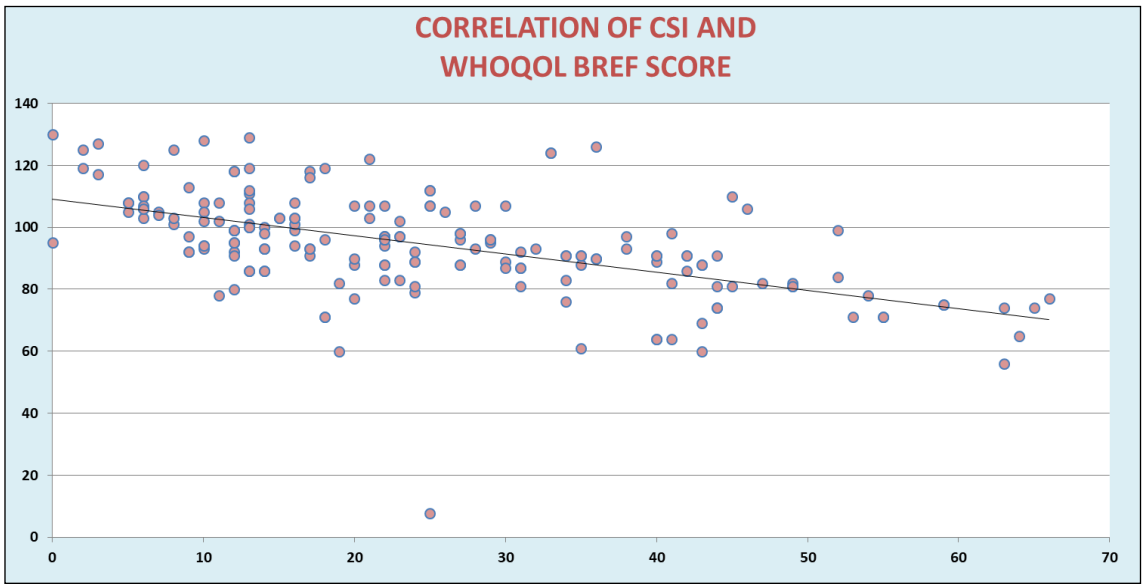
Table 3: Comparison of outcome measures between two groups divided by CSI score <40 or ≥40 points, calculated by mann whitney U test.

Variables	CSI <40 (N=146)	CSI ≥40 (N=39)	P Value
VAS (cm)	4.9	6.2	<0.00001
WHOQOL Score	97	81	<0.00001

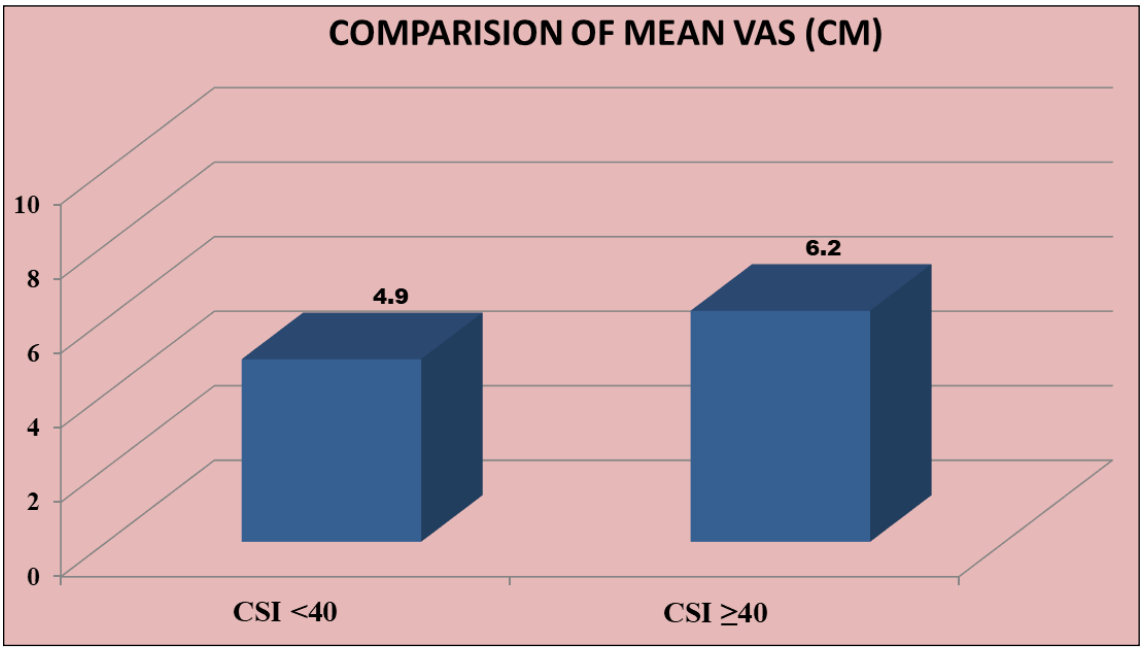
Bold denotes statistical significance



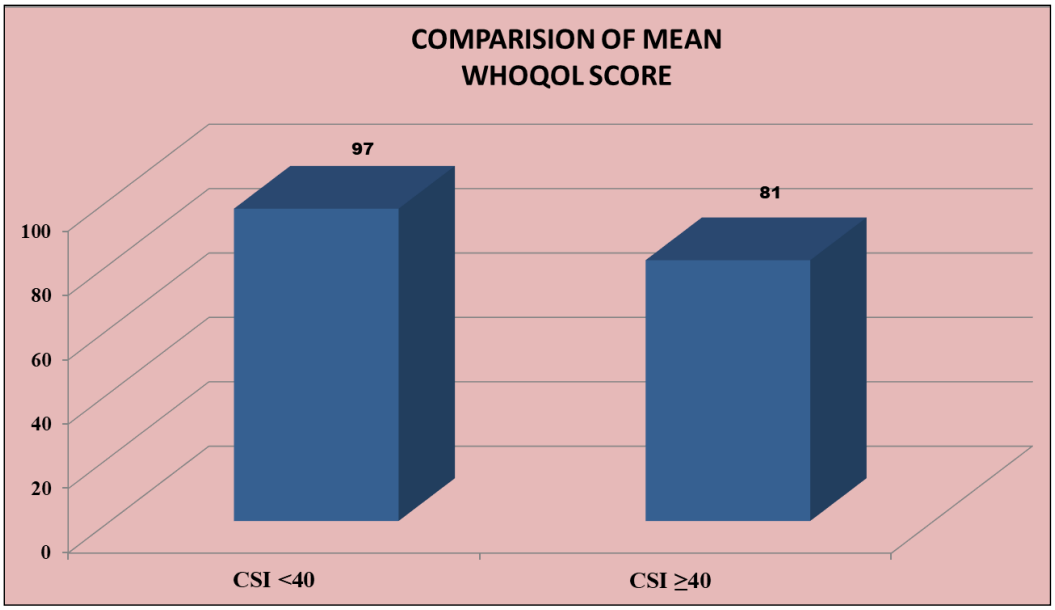
Graph 2: Scatter diagram representing the correlation between CSI total score and VAS Score.



Graph 3: Scatter diagram representing the correlation between CSI total score and WHOQOL BREF score.



Graph 4: Bar diagram representing the difference of mean VAS between CSI<40 and CSI≥40 groups



Graph 5: Bar diagram representing the difference of mean WHOQOL Score between CSI<40 and CSI≥40 groups

Discussion

When considering the hypothesis of the present study it was expected to test whether CS would be associated with measures of pain intensity and quality of life or not. The results of the study confirmed the moderate relationship between CSI score levels with pain intensity (Measured by VAS score) and quality of life (measured by WHOQOL BREF -G) in patients with chronic musculoskeletal pain disorders, which confirm the alternative hypothesis. Hence the null hypothesis is rejected and alternative hypothesis is accepted.

The results of present study suggest that as the CSI score levels increased, the pain intensity and quality of life tended to get worse. The comparison of various variables and outcome measures between two groups divided by CSI score <40 or ≥40 points showed statistically significant differences of Duration of symptoms, VAS score and WHOQOL score were found between the CSI <40 and CSI ≥40 groups. These findings further strengthen the correlation or association of CS with pain intensity and quality of life. These results also support previous studies which reported that the CSI score/severity levels correlate with disability, QOL and pain intensity [23]. Many authors have described similar results of comparisons.

Kregel *et al*. reported that higher CSI total scores showed a moderate correlation with current higher pain intensity and strong correlations with lower physical and emotional quality of life. Higher CSI total scores showed moderate correlations with higher pain disability and higher pain catastrophizing in a nonspecific chronic spinal pain population [23], Gervais *et al*. reported positive correlations between the CSI and PPT/TS in people with knee osteoarthritis [49], and Coronado *et al*. found significant correlations between the CSI and PPT in a shoulder pain cohort. [50]. Neblett *et al*. found the associations among the CSI severity-level groups and patient-reported depressive symptoms, perceived disability, sleep disturbance, and pain intensity [37]. Previous studies also reported that features of CS include lowered pain thresholds and elevated pain ratings to standardized stimuli local to the primary area of pain and at remote regions (e.g., widespread pain sensitivity) [18] which supports the association of CSI with pain intensity and quality of life.

Limitations and Suggestions

- In this study only four, more prevalent non-traumatic and non-operative musculoskeletal disorders were included because of the conveniences and availability of the patients. Future study can be carried out including other MSDs i.e. traumatic, operative, arthropathies etc.
- CSI is a patient-reported outcome, as used to assess a patient's symptoms or functional status at a specific time. However, this information is subjective. Future research should supplement CSI data with objective measures.
- In this study total score of CSI was correlated with total score of WHOQOL for finding out association, further correlation of CSI total score can be carried out with four domains of WHOQOL BREF i.e. physical health, psychological, social relationship and environment separately, so that further information regarding which component of quality of life is more associated with CS related symptoms could be known.

Conclusion

Present study conclude that there is moderate association exist between CSI score with pain intensity and quality of life. In light of these results, it is recommended that clinicians supplement their assessment with the CSI in CMPDs for improved decision making during treatment.

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