

Original Research

Hand Numbness among Patients with Musculoskeletal Pain: A link to Neck Pain and Vitamin D deficiency—A Case-control study

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Abstract

Objective: Peripheral neuropathy is common in the general population. A pinched nerve in the neck typically causes neck pain, a widespread musculoskeletal complaint worldwide. Preliminary observations revealed a high prevalence of neck pain and arm numbness in patients with musculoskeletal pain (MSP) and vitamin D deficiency. This study aimed to determine the prevalence of self-reported peripheral neuropathy in relation to neck pain among patients with MSP. **Study Design:** Case-control study. **Methods:** A total of 232 patients with MSP and age- and sex-matched controls participated in this study. Serum plasma vitamin D (VitD), plasma parathyroid hormone (PTH), and serum calcium (S. Ca) levels were measured. **Results:** A significantly higher prevalence of vitamin D deficiency was observed in MSP patients (91.3%) compared to controls (51.7%) ($p < 0.001$). Elevated PTH levels were found in 50% of the cases, while most had normal S. Ca levels. Females comprised 85.3% ($n = 198$) of the participants. Weakness was reported by 74.1% of patients with MSP, compared to 0.0% in controls. Neck pain was present in 72.8% of the cases, while numbness in the hand, fingers, or palm was reported in 55.2%. Binary logistic regression identified neck pain as the only predictor of hand numbness (OR = 2.108, 95% CI: 1.130–3.93, $p = 0.019$). Several published studies strongly support the benefits of vitamin D and calcium supplementation in patients with MSP. **Conclusion:** Vitamin D deficiency, neck pain and arm numbness are prevalent among patients with MSP. Arm numbness was associated with neck pain. These findings underscore the importance of assessing patients with neck pain and hand numbness for vitamin D deficiency and related symptoms. Additionally, the evidence highlights the potential benefits of vitamin D and calcium supplementation for patients with multi-site MSP including those with neck pain.

Keywords: vitamin D, neck pain, arm numbness, musculoskeletal pain.

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INTRODUCTION

Peripheral neuropathy is a common condition in the general population, with prevalence rates ranging from 1% to 7%, increasing to 8% in older adults¹. Idiopathic cases account for 25% to 46% of all peripheral neuropathy cases¹. Common causes include diabetes mellitus, nerve compression or injury, alcohol use, toxin exposure, hereditary disorders, and nutritional deficiencies. The most common identifiable causes of hand peripheral neuropathy are nerve compression or injury, such as carpal tunnel syndrome (CTS) and cervical radiculopathy (pinched nerve in the neck).

A pinched nerve in the neck is a condition caused by compression or impairment of any of the spinal nerve roots, resulting in neurological dysfunction that may extend beyond

the neck to the arms, chest, upper back, and shoulders¹⁻⁴. This condition typically causes neck pain and radiating arm pain or numbness, tingling, weakness in the hand and fingers, as well as sensory deficits or motor dysfunction in the neck and upper extremities^{2,3}.

Neck pain is one of the most common musculoskeletal complaints worldwide, with a prevalence of 30%–50% in the general population. Its prevalence has been reported to increase with age and is higher in women than in men⁵. Neck pain can cause significant discomfort and disability across various age groups, imposing a substantial personal and socioeconomic burden^{6,7}. It is commonly attributed to muscle spasm or hyperactivity^{2,6-10}. Although most of symptoms typically resolve over time or with minimal intervention, the recurrence rate of neck pain remains high. Several conventional therapies are available for chronic neck pain, including exercise, stretching, physical therapy, massage, cervical collars, anti-inflammatory medications, and muscle relaxants^{5,8}. While these conventional therapies may provide temporary relief, their long-term use remains debatable⁵.

Vitamin D is the most commonly deficient vitamin worldwide, and MSP and weakness are frequently associated with vitamin D deficiency¹¹. The classical functions of vitamin D include maintaining calcium and phosphate homeostasis, promoting bone mineralization and preventing hypocalcemic tetany¹². Over the past two decades, following the discovery of nuclear



and membrane vitamin D receptors in skeletal muscle¹³⁻¹⁵, the role of vitamin D has been found to extend beyond calcium and phosphate homeostasis; it also appears to play a significant role in skeletal muscle health¹⁶. Current evidence suggests that vitamin D insufficiency may contribute to MSP, sarcopenia, myopathy, and an increased risk of falls. Vitamin D is essential for the normal development and growth of muscle fibers. It stimulates de novo muscle fiber synthesis and enhances muscle function¹⁷. Vitamin D deficiency may lead to symptoms of rickets in children and osteomalacia in adults, while also contributing to or exacerbating osteopenia, osteoporosis, and fractures in adults^{18,19}. The classical symptoms of osteomalacia include skeletal pain in the lower spine, pelvis, hips, legs, feet, and ribs, which may worsen with physical activity. In addition, it can result in decreased muscle tone, muscle weakness, or stiffness in the arms and legs¹⁷⁻¹⁹. However, such symptoms are often subtle and can remain undetected in the initial stages^{18,20,21}. Besides, vitamin D deficiency is often missed in medical diagnosis as it can manifest with widely varying types of pain in different individuals²².

Based on our preliminary data^{23,24}, we observed a high prevalence of neck pain (58.1% -72.8 %) and arm numbness in patients with vitamin D deficiency and MSP. To the best of our knowledge, no published studies have examined the relationship between vitamin D status and the occurrence of neck pain and arm numbness.

This research was conducted with the aim of finding the prevalence of self-reported peripheral neuropathy in relation to neck pain among patients with MSP.

METHODS

Participants and Setting

This case-control study involved 232 patients who experience musculoskeletal pain and 232 gender- and age-matched healthy controls. Participants were recruited from physical therapy clinics, neurology clinics, and the radiology department at King Abdullah University Hospital (KAUH), the main tertiary teaching hospital in northern Jordan. The control group subjects were apparently healthy volunteers with no history of MSP, general weakness or fatigue, or peripheral neuropathy, and their ages were within the same five-year age of the case group. Controls were recruited from both sexes, including individuals visiting various clinics for checkups, patients' family members, and university campus attendees²⁴⁻²⁸. Recruitment period started on May 1st 2021, and ended on Oct 1st 2021.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board Committee of Jordan University of Science and Technology. Written informed consent was obtained from all participants. To minimize confounding factors, exclusion criteria included subjects with chronic diseases such as chronic renal failure, chronic liver disease, neurodegenerative conditions, or diseases

affecting the nerves (e.g., diabetes mellitus, thyroid disease, rheumatoid arthritis, lupus, multiple sclerosis), as well as those taking vitamin D supplements within the past two months.

Participants completed guided self-assessment questionnaires that gathered information on their demographics, health status and disease conditions. For patients with MSP, the questionnaire also addressed MSP duration (<3 months, 3 months-12 months, >1 year), frequency (daily, weekly, monthly), location of MSP sites of usual pain by marking the specified pain sites that were included in the questionnaire. Those pain sites were neck, shoulder, lower back, arms, hand, fingers, wrist, palm, forearm, upper leg, lower leg, knee, and foot. The number of painful sites was calculated as a continuous variable for pain assessment as evaluate MSP severity over the last month. Pain severity was measured using the 0-10 Numerical Rating Scale (NRS), (0, no pain; 10, maximum pain)²⁴⁻²⁸, as well as mild, moderate and severe.

Assessment of peripheral neuropathy

Questions about the symptoms of peripheral neuropathy were also included in the questionnaire. Patients were asked whether they experienced peripheral numbness, tingling, weakness, and pain in the hand, fingers, or palm. Also, participants were asked if they experience neck stiffness and/or stiffness between shoulders usually or during sleep or as awake in the morning and tingling or numbness in shoulder or arm or hand during sleep or after waking up in the morning. Other data collected from participants will be published elsewhere.

Laboratory analysis

Non-fasting blood samples were obtained by venipuncture into a vacutainer with or without anticoagulant. Serum plasma levels of 25-hydroxyvitamin D (25(OH)D) and plasma parathyroid hormone (PTH) were measured using a chemiluminescent assay (Modular E Analyzer, Roche). Serum calcium (Ca) levels were measured using a Modular P Analyzer (Roche). All assays were performed at KAUH laboratory. Serum 25(OH)D, levels were assessed in 211 out of 232 patients and all 232 controls, whereas PTH and calcium levels were evaluated in 200 out of 232 patients due to logistic difficulty.

Statistical Analysis

Data were analyzed using the Statistical Package for Social Science (SPSS, version 21.0). Data were presented as frequencies and means with standard deviations, as appropriate. An independent sample t-test was used for comparisons between two groups. Spearman's correlation was performed to assess the correlation between MSP severity and selected parameters. The chi-square (X^2) test was used to compare categorical variables. Binary logistic regression analysis was conducted to identify predictors of hand numbness among patients with MSP. A P-value of <0.05 was considered statistically significant for all analyses.



RESULTS

Characteristics of the study population

Data were collected from 232 participants with MSP and sex- and age-matched controls, aged between 18 and 65 years (mean \pm SD: 32.23 \pm 11.23 for patients and 32.35 \pm 11.58 for controls, $p = 0.913$). Females represented 85.3% ($n = 198$) of the participants.

General weakness/fatigue was reported by 74.1%, $n = 172$ of patients with MSP compared to 0.0% ($n = 0$) the controls. Statistical analysis further revealed that most participants had normal BMI with mean \pm SD of 25.73 \pm 5.56 for cases and 24.51 \pm 4.19 for controls ($p = 0.007$).

Patients with MSP reported pain in the following areas: neck (169, 72.8%), shoulder (156, 67.2%); forearm (72, 31%), arm (96, 41.4%), wrist (81, 34.9%), hand and fingers (111, 47.8%), palm (33, 14.2%), lower back (166, 71.6%), hip (14, 6.03%), upper leg (82, 35.3 %); lower leg (96, 41.4%), knee (71, 30.6%), and foot (88, 37.9%). In the MSP group, 60.8% (141/232) of participants reported a pain duration of ≥ 1 year, and 59.9% ($n=139$) experienced daily pain. The average pain score on NRS was 6.19 \pm 2.03.

Biochemical parameters among study population

The patient group had significantly lower vitamin D levels compared to the controls (mean \pm SD: 10.12 \pm 7.18 vs. 22.19 \pm 12.58, $p < 0.001$). A significantly higher incidence of vitamin D deficiency was observed among patient cases as compared to controls ($p < 0.001$). Vitamin D deficiency (<19.9 ng/ml) was reported in 90.9% ($n = 192$) of patients, compared to 48.7% ($n = 113$) of controls. Vitamin D sufficiency was observed in only 1.4% ($n = 3$) of patients compared to 26.7% ($n = 62$) of controls. Hyperparathyroidism was identified in 50% ($n = 100$) of patients. Serum calcium levels were normal in most participants (Table 1).

Patient characteristics with and without neck pain

Baseline characteristics were compared between patients with neck pain ($n = 169$) and those without neck pain ($n = 63$). Statistical analysis showed significant differences in the following variables: average MSP severity ($p = 0.012$), MSP severity (NRS 0-10) ($p=0.013$), number of MSP sites ($p <0.001$), MSP duration ($p <0.001$) and MSP frequency ($p = 0.016$). However, no significant differences were observed between the two groups in terms of age, sex, general weakness/fatigue, BMI, serum vitamin D levels, PTH levels, or serum calcium levels, (Table 2).

Self-reported hand numbness in relation to neck pain

Baseline statistical analysis revealed that the prevalence of numbness or tingling in the hand, fingers, or palm among patients with MSP was 55.2% ($n = 128$), and 22.4% ($n = 52$)

Table 1. Participants characteristics by case-control ($n = 464$).

Variable †	Cases ($n = 232$)	Healthy controls	P-value*
		($n = 232$)	
Age (Years) mean \pm SD	32.23 \pm 11.23	32.35 \pm 11.58	0.913
Age Categories (Years)			0.819
<30	119 (51.3)	124 (53.4)	
30-39	47 (20.3)	48 (20.7)	
40-65	66 (28.4)	60 (18.6)	
Sex			1
Male	34 (14.7)	34 (14.7)	
Female	198 (85.3)	198 (85.3)	
Marital status			0.853
Single	118 (50.9)	116 (50)	
Married	114 (49.1)	116 (50)	
General weakness/ Fatigue			<0.001
Yes	172 (74.1)	0 (0)	
No	60 (25.9)	232 (100)	
BMI (Kg/m ²) mean \pm SD	25.73 \pm 5.56	24.51 \pm 4.19	0.007
BMI Categories (Kg/ m ²)			0.042
Underweight (<18.5)	13 (5.6)	14 (6.0)	
Normal weight (18.5–24.9)	106 (45.7)	121 (52.2)	
Overweight (25–29.9)	71 (30.6)	76 (32.8)	
Obese (≥ 30)	42 (18.1)	21 (9.0)	
Serum Vitamin D level (ng/mL) mean \pm SD	10.12 \pm 7.19	22.19 \pm 12.58	<0.001
Serum Vitamin D level (ng/mL) Categories			<0.001
Normal (≥ 30)	3(1.4)	62(26.7)	
Insufficiency (20-29.9)	16(7.6)	57(24.6)	
Deficiency (10-19.9)	71(33.6)	62(26.7)	
Severe deficiency (<10)	121(57.3)	51(22)	

† Data expressed as numbers and percentage within parenthesis, *P value <0.05 was considered statistically significant.

respectively (Table 3). Additionally, numbness or tingling in the shoulder, arm, or hand during sleep or upon waking was reported by 53.4% ($n = 124$) of patients. Neck stiffness and/or shoulder pain, commonly experienced during sleep or upon waking, were reported by 75% ($n = 174$) of patients (Table 3). Interestingly, as shown in Table 3, our results revealed that significantly higher percentages of patients with neck pain experienced numbness in their hands, fingers, or palms (60.4%, $n = 102$; $P = 0.009$);



Table 2. Patient characteristics with neck pain.

Descriptive Variables †	Total (232)	Neck Pain		*P value
		Yes (n=169)	No (n=63)	
Age Categories (Year)				0.13
<30	119 (51.3)	80 (47.3)	39 (61.9)	
30 - 39	47 (20.3)	38 (22.5)	9 (14.3)	
40 - 65	66 (28.4)	51 (30.2)	15 (23.8)	
Age (mean ± SD)	32.35 ± 11.57	33.73 ± 11.90	30.06 ± 10.38	0.05
Sex				0.749
Male	34 (14.7)	24 (14.2)	10 (15.9)	
Female	198 (85.3)	145 (85.8)	53 (84.1)	
Marital status				0.04
Single	118 (50.9)	79 (46.7)	39 (61.9)	
Married	114 (49.1)	90 (53.3)	24 (38.1)	
General weakness/Fatigue				0.211
Yes	172 (74.1)	129 (76.3)	43 (68.3)	
No	60 (25.9)	40 (23.7)	20 (31.7)	
BMI Categories				0.289
Underweight (<18.5)	13 (5.6)	11 (6.5)	2 (3.2)	
Normal weight (18.5–24.99)	106 (45.6)	71 (42)	35 (55.5)	
Overweight (25–29.99)	71 (30.9)	55 (32.6)	16 (25.4)	
Obese (≥30)	42 (18.1)	32 (18.9)	10 (15.9)	
BMI (Kg/m2) mean ± SD	25.74 ± 5.53	25.68 ± 6.19	25.86 ± 5.29	0.841
Serum Vitamin D Level Categories (ng/ml)				0.518
Normal (≥30)	3 (1.4)	3 (2)	0 (0)	
Insufficient (20-29.9)	16 (7.6)	10 (6.6)	6 (10)	
Deficient (10-19.9)	71 (33.6)	53 (35.1)	18 (30)	
Severe deficiency (<10)	121 (57.4)	85 (56.3)	36 (60)	
Serum Vitamin D level (ng/ml) ± SD	10.12 ± 7.19	10.56 ± 7.60	8.99 ± 5.93	0.115
Parathyroid hormone level (PTH) (pg/ml) categories				1
Hyper (>54)	100 (50)	73 (50)	27 (50)	
Normal (10-54)	100 (50)	73 (50)	27 (50)	
Hypo (<10)	0 (0.0)	0 (0.0)	0(0.0)	
Parathyroid hormone level (PTH) (pg/ml) mean ± SD	59.99 ± 28.95	58.95 ± 95	62.80 ± 30.33	0.41
Serum calcium (mmol/l) categories				0.547
Hyper (>2.6)	4 (2)	2 (1.4)	2 (3.7)	
Normal (2.1-2.6)	191 (95.5)	140 (95.9)	51 (94.4)	
Hypo (<2.1)	5 (2.2)	4 (2.7)	1 (1.9)	
Serum calcium (mmol/l) mean ± SD	2.36 ± 0.51	2.37 ± 0.586	2.38 ± 1.94	0.623
Average MSP severity				0.012
Mild	56 (24.1)	33 (19.5)	23 (36.5)	
Moderate	121 (52.2)	90 (53.3)	31 (49.2)	
Severe	55 (23.7)	46 (27.2)	9 (14.3)	



Pain severity (0-10 Numerical Rating Scale (NRS) (mean ± SD)	6.19 ± 2.03	6.38 ± 2.02	5.67 ± 1.94	0.013
Number of MSP sites MSP duration	5.55 ± 3.10	8.30 ± 2.79	4.06±2.09	<0.001
≤3 months	31 (13.4)	15 (8.9)	16 (25.4)	<0.001
>3 months-<1 year	60 (25.9)	41 (24.2)	19 (30.2)	
≥1year	141 (60.7)	113 (66.9)	28 (44.4)	
MSP frequency				0.016
daily	139 (59.9)	110 (65.1)	29 (46)	
weekly	77 (33.2)	47 (27.8)	30 (47.6)	
monthly	16 (6.9)	12 (7.1)	4 (6.4)	

† Data expressed as numbers and percentage within parenthesis, *p-value <0.05 was considered statistically significant.

Table 3. Self-reported peripheral numbness in relation to neck pain.

Variables †	Total (232)	Neck pain		P value*
		Yes (n=169)	No (n=63)	
Tingling in hand, fingers, or palm				
Yes	52 (22.4)	40 (23.7)	12 (19)	0.453
No	180 (77.6)	129 (76.3)	51 (81)	
Numbness in hand, fingers or palm				
Yes	128 (55.2)	102 (60.4)	26 (41.3)	0.009
No	104 (44.8)	67 (39.6)	37 (58.7)	
Tingling and/or numbness in hand, fingers or palm				
Yes	136 (58.6)	107 (63.3)	29 (46)	0.017
No	96 (41.4)	62 (36.7)	34 (54)	
Weakness in hand, fingers or palm				
Yes	79 (34.1)	63 (37.3)	16 (25.4)	0.089
No	153 (65.9)	106 (62.7)	47 (74.6)	
Pain in the hand fingers or palm				
Yes	108 (46.6)	84 (49.7)	24 (38.1)	0.116
No	124 (53.4)	85 (50.3)	39 (61.9)	
Neck stiffness and/or stiffness between shoulder usually or during sleep or as you awake in the morning				
Yes	174 (75)	149 (88.2)	25 (39.7)	<0.001
No	58 (25)	20 (11.8)	38 (60.3)	
Tingling or Numbness in shoulder or arm or hand during sleep or after waking up in the morning				
Yes	124 (53.4)	97 (82.9)	27 (42.9)	0.048
No	108 (46.6)	20 (17.1)	36 (57.1)	

† Data expressed as numbers and percentage within parenthesis, *P value <0.05 was considered statistically significant

tingling or numbness in the shoulder, arm, or hand during sleep or upon waking (53.4%, n = 124; P = 0.048); and neck stiffness and/or stiffness between shoulders, typically occurring during sleep or upon waking (88.2%, n = 149, p <0.001), compared

to patients without neck pain. Other variables such as tingling, weakness, and pain in the hands, fingers or palms, were not significantly associated with neck pain (Table 3). It is worth mentioning that none of the controls experienced MSP, tingling



or hand numbness in addition to weakness.

Spearman correlation between MSP severity and selected variables (n=232)

Correlation analysis was conducted to evaluate the relationships between MSP severity, number of MSP sites, age, BMI, vitamin D levels, serum calcium, and PTH, among patients with MSP (n = 232). Spearman correlation revealed that MSP severity was significantly and positively correlated with age ($r^2 = 0.284$, $P < 0.001$), BMI ($r^2 = 0.224$, $P = 0.001$), and the number of MSP sites ($r^2 = 0.275$, $P < 0.001$).

It is worth mentioning that age was positively correlated with BMI ($r^2 = 0.485$, $P < 0.001$), while vitamin D levels were negatively correlated with PTH ($r^2 = -0.306$, $P < 0.001$).

Factors associated with hand numbness

Chi-square (χ^2) correlation analysis was conducted to evaluate the relationships between hand numbness and various factors, including age, sex, marital status, general weakness, BMI, vitamin D levels, serum calcium, PTH, and neck pain among patients with MSP (Table 4). The results revealed significant correlations of hand numbness with age ($p < 0.001$), marital status ($p = 0.001$), BMI ($p = 0.013$), and neck pain ($p = 0.007$).

Independent predictors of numbness

The results of the binary logistic regression analysis showed that patients with neck pain were 2.1 times more likely to experience hand numbness (OR = 2.108, 95% CI: 1.130-3.930, $p = 0.019$). In contrast, age, marital status, and BMI were not significant predictors of hand numbness (Table 5).

Table 4. Patient characteristics with hand numbness.

Descriptive Variables	Total (232)	Hand Numbness		*P value
		Yes (n=128)	No (n=104)	
Age Categories (Year)				
<30	119 (51.3)	56 (43.8)	63 (60.6)	<0.001
30 - 39	47 (20.3)	22 (17.2)	25 (24)	
40 - 65	66 (28.4)	50 (39)	16 (15.4)	
Age (mean \pm SD) †	32.35 \pm 11.57	34.38 \pm 11.78	29.86 \pm 10.89	0.003
Gender				
Male	34 (14.7)	20 (15.6)	14 (13.5)	0.643
Female	198 (85.3)	108 (84.4)	90 (86.5)	
Marital status				
Single	118 (50.9)	53 (41.4)	65 (62.5)	0.001
Married	114 (49.1)	75 (58.6)	39 (37.5)	
General weakness/Fatigue ‡				
Yes	172 (74.1)	99 (77.3)	73 (70.2)	0.139
No	60 (25.9)	29 (22.7)	31 (29.8)	
BMI Categories				
Underweight (<18.5)	13 (5.6)	4 (3.1)	9 (8.7)	0.013
Normal weight (18.5–24.99)	106 (45.7)	52 (40.6)	54 (51.9)	
Overweight (25–29.99)	71 (30.6)	41 (32)	30 (28.8)	
Obese (≥ 30)	42 (18.1)	31 (24.2)	11 (10.6)	
BMI mean \pm SD	25.74 \pm 5.53	26.77 \pm 5.72	24.45 \pm 5.02	0.001
Serum Vitamin D Level Categories (ng/ml)				
Normal (≥ 30)	3 (1.4)	3 (2.7)	0 (0)	0.396
Insufficient (20-29.9)	16 (7.6)	8 (7.1)	8 (8.1)	
Deficient (10-19.9)	71 (33.7)	39 (34.8)	32 (32.3)	
Severe deficiency (<10)	121 (57.3)	62 (55.4)	59 (59.6)	



Plasma Vitamin D level (ng/ml) mean ± SD	10.12 ± 7.19	9.85 ± 7.72	9.85 ± 6.56	0.615
Parathyroid level (PTH) Categories (pg/ml)				
Hyper (>54)	100 (50)	51 (48.1)	49 (52.1)	0.335
Normal (10-54)	100 (50)	55 (51.9)	45 (47.9)	
Hypo (<10)	0 (0)	0 (0)	0 (0)	
Parathyroid level (PTH) (pg/ml) mean ± SD	59.99 ± 28.95	60.78 ± 27.60	59.11 ± 26.35	0.662
Serum calcium Categories (mmol/l)				
Hyper (>2.6)	4 (2)	3 (4.2)	1 (0.9)	0.165
Normal (2.1-2.6)	191 (95.5)	87 (91.6)	104 (98.1)	
Hypo (<2.1)	5 (2.5)	4 (4.2)	1 (0.9)	
Serum calcium (mmol/l) mean ± SD	2.36 ± 0.51	2.41 ± 0.67	2.31 ± 0.16	0.172
Neck Pain	169 (72.8)	67 (64.4)	102 (79.7)	0.007
	63 (27.2)	37 (35.6)	26 (20.3)	
Average MSP severity ‡				
Mild	56 (24.1)	25 (19.6)	31 (29.8)	0.088
Moderate	121 (52.2)	67 (52.3)	54 (51.9)	
Severe	55 (23.7)	36 (28.1)	19 (18.3)	
MSP duration				
≤3 months	31 (13.3)	15 (11.7)	16 (15.4)	0.699
>3 months-<1 year	60 (25.9)	33 (25.8)	27 (26)	
≥1year	141 (60.8)	80 (62.5)	6 (58.6)	
MSP frequency				
daily	139 (59.9)	84 (65.6)	55 (52.9)	0.173
weekly	77 (33.2)	37 (28.9)	40 (38.4)	
monthly	16 (6.9)	7 (5.5)	9 (8.7)	
† Data expressed as Mean± Standard Deviation, ‡ Data expressed as numbers and percentage within parenthesis, *P value <0.05 was considered statistically significant.				

DISCUSSION

The most notable finding of the current of the current study is the presence of a significantly higher prevalence of vitamin D deficiency (<20 ng/mL), neck pain, and hand numbness among patients with MSP compared to healthy controls. Specifically, 90.9% of patients with MSP had vitamin D deficiency, compared to 48.7% of the control group (P < 0.001). Additionally, neck pain was present in 72.8% of MSP cases, and hand numbness was reported by 55.2% of patients. Notably, logistic regression analysis demonstrated that neck pain was the sole significant predictor of hand numbness, with an odds ratio of 2.108 (P = 0.019). As a case-control study, these findings indicate an association rather than causality, as several potential confounders, such as lifestyle factors, may influence these relationships.

Vitamin D is a fat-soluble vitamin that influences pain manifestation through its anatomic, hormonal, neurological, and immunological effects. Vitamin D deficiency has been

reported in individuals with musculoskeletal pain and is associated with defective mineralization, myopathy, and symptoms such as joint pain, joint stiffness, bone pain, muscle pain, and muscle weakness^{29-32,33}. In our study, we observed a significantly higher prevalence of vitamin D deficiency (<20 ng/mL) among patients with MSP (91.3%) compared to the control group (51.8%) (P < 0.001). This finding is consistent with our previously published articles^{24,27} and the work of Plotnikoff and Quigley²⁹ who reported that 93% of participants with persistent nonspecific MSP had vitamin D levels <20 ng/mL. On the other hand, the control group which reported no pain at the time of enrollment, showed 51.7% of participants with vitamin D deficiency. These results are consistent with our previously published findings^{23,24,32,34} and the work of Shiekh et al.²¹ and Nadeen et al.³⁵. It has been estimated that 15 – 89.14% of individuals with vitamin D deficiency are asymptomatic, making the condition a challenging clinical entity to detect^{35,36}.

In the current study, patients with MSP and symptoms of vitamin D deficiency reported experiencing pain in multiple



Table 5. Predictors of hand numbness

Variable	Value	B (SE)	OR	Confidence interval	P-value†
Age (Years)	<30 (reference)				
	30 - 39	0.753(.494)	2.12	0.806-5.598	0.127
	40 - 65	0.410(0.580)	0.663	0.249-1.768	0.412
BMI (Kg/m ²)	<25 (reference)				
	25–29.99	-0.172(0.336)	0.842	0.436-1.628	0.609
	≥30	0.736(0.446)	0.479	0.200-1.148	0.099
Marital status	Single (reference)	-0.723(0.432)			
	Married		0.485	0.208-1.132	0.094
Neck pain	No (reference)				
	Yes	0.746(0.446)	2.108	1.13-3.935	0.019

†Binary logistic regression (dependent variable: Hand Numbness), $p < 0.05$ was considered statistically significant. B, coefficient (intercept); SE, standard error; OR, odds ratio; BMI, Body Mass Index.

locations, mostly commonly in the neck (72.8%), lower back (71.6%) and shoulders (67.2%). These multiple locations were significantly and positively associated with pain severity ($r^2 = 0.275$, $P < 0.001$). This suggests that individuals with MSP and multi-site pain are more likely to experience neck pain, which may contribute to hand numbness. Specifically, patients with neck pain were found to be 2.1 times more likely to report hand numbness (OR = 2.108; 95% CI: 1.130–3.930, $P = 0.019$). Additionally, neck pain was significantly correlated with the severity, duration, and frequency of MSP.

Interestingly, in the current study, 88.2% (149 out of 169) of patients with neck pain reported experiencing neck stiffness and/or stiffness between the shoulders particularly upon waking in the morning.

Neck strain typically develops due to muscle spasms, particularly in the levator scapulae muscle, a skeletal muscle which located at the back and side of the neck that connects the cervical spine to the shoulders³⁷.

Strong evidence supports the benefits of vitamin D and calcium supplementation in patients with MSP. This is demonstrated in our previously published articles²⁴⁻²⁶, as well as in prospective case series involving patients with multiple sites of chronic pain and low serum vitamin D levels³ and other published studies³⁹.

In our previous studies that involving patients with MSP^{24,25}, two months of vitamin D supplementation combined with increased dairy-product intake resulted in a significant reduction in MSP severity and the number of pain sites. Neck pain decreased from 69.4% to 30% in one study²⁴ and from 62.5% to 10% in

another²⁵. Similar findings were reported by Le Goaziou et al.³⁹.

Together, these observations highlight the importance of screening patients with neck pain for hypovitaminosis D. Vitamin D supplementation is a cost-effective treatment option for MSP, offering the potential for symptom resolution. This is particularly significant given that neck pain is one of the most common musculoskeletal disorders, with a high economic burden due to treatment costs, reduced productivity and job-related problems⁷.

Calcium is the most abundant mineral in the body, mostly found in milk and milk products⁴⁰. Approximately, 99% of the body's calcium resides in the bones and teeth, while the remaining calcium is involved in various physiological functions including vascular contraction and vasodilation, muscle function, nerve transmission, intracellular signaling, and hormonal secretion⁴⁰. The clinical features of hypocalcemia include muscle cramps, numbness and tingling of the extremities and other symptoms⁴¹. In the current study, 63.3% of the patients had hand numbness and tingling with normal serum calcium levels. This is because blood calcium levels are tightly regulated by the action of PTH, 1,25-dihydroxyvitamin D (the active form of vitamin D) and calcitonin. When vitamin D levels decrease, intestinal calcium absorption is significantly reduced, prompting the release of PTH to restore extracellular fluid calcium levels to normal^{42,43}. As a result, vitamin D deficiency is typically accompanied by normal calcium blood levels and secondary hyperparathyroidism.

In the current study, most patients with MSP had normal serum calcium, while 50% exhibited hyperparathyroidism. PTH levels were significantly and inversely correlated with serum vitamin D level ($r^2 = -0.306$, $p < 0.001$).

Measuring vitamin D levels along with assessing symptoms of vitamin D deficiency, neck pain and hand numbness could serve as a reliable approach to avoid unnecessary differential diagnoses and to recommend vitamin D supplementation as a targeted intervention for these symptoms. The findings of this study provide evidence of an association between vitamin D status and neck pain, one of the most common musculoskeletal disorders with a significant economic diagnosis, and management of hand numbness among patients with MSP.

Although the findings of the current study are reported for the first time, it has some limitations. Some of the data are self-reported, despite the study's case-control design, appropriate sample size, and use of validated tools to assess its variables. Additionally, the study did not investigate the effect of vitamin D supplementation on neck pain and hand numbness. While previous studies have shown that vitamin D supplementation significantly reduces MSP^{24,25,26}, including neck pain, large clinically controlled trials are needed to further explore the link between vitamin D status, MSP, neck pain, and hand numbness, particularly with supplementation over various durations.



CONCLUSIONS

Vitamin D deficiency, neck pain and arm numbness are prevalent among patients with MSP. Arm numbness was found to be associated with neck pain, while neck pain emerged as the sole predictor of hand numbness. These findings underscore the importance of screening for vitamin D deficiency and associated symptoms in patients with MSP, particularly those presenting with neck pain and hand numbness. Future research should explore targeted interventions, including vitamin D supplementation, to alleviate these symptoms and reduce unnecessary differential diagnoses.

AUTHOR'S CONTRIBUTION

MAYA: Formal analysis, validation, and manuscript writing - original draft, review & editing. KA: Conceptualization; data curation; formal analysis; validation, methodology, project administration, and manuscript writing- original draft, review & editing. All authors approved the manuscript and agreed to be accountable for all aspects of the work.

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