Original Article

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The Relationship between Chronic Musculoskeletal Pain and Vitamin D Deficiency in the Elderly Population of Amirkola, Iran

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ABSTRACT

BACKGROUND AND OBJECTIVE: Chronic musculoskeletal pain may persist for more than three months and is often resistant to treatment. The aim of this study was to examine the relationship between chronic musculoskeletal pain and vitamin D deficiency in the elderly population of Amirkola, Iran

METHODS: This cross-sectional study was part of a health survey on the elderly population of Amirkola (AHAP=Amirkola Health and Ageing Project), including 1616 senior citizens, aged ≥ 60 years. Overall, 857 individuals without rheumatoid arthritis, cancer, depression, diabetes or osteoarthritis were enrolled in this study. Demographic data were collected and a questionnaire on chronic musculoskeletal pain was applied. The anatomical site of pain was determined by inquiring the elderly. The serum level of vitamin D was measured in two groups with and without chronic pain, using the ELISA method. Vitamin D deficiency, insufficiency and sufficiency were defined as serum vitamin D levels of < 20, 20-29.99 and ≥30 ng/ml, respectively.

FINDINGS: Among 857 participants, 599 (69.9%) and 258 (30.1%) cases were male and female, respectively. Moreover, 666 participants (77.7%) complained of chronic pain. The most common sites of pain were the knees (54%), back (40%), feet (35.7%) and shoulders (27.5%), respectively. Also, 41.9% of the elderly had vitamin D deficiency. However, vitamin D level was not significantly different between the two groups (with and without chronic pain), and frequency of chronic pain did not significantly vary between these groups. Based on the logistic regression model, gender (OR=2.73, 95%CI=1.78-4.21, p=0.001), body mass index and physical activity (OR=0.42, 95% CI=0.28-0.62, p=0.001) had significant impacts on chronic pain.

CONCLUSION: The results showed no significant relationship between vitamin D level and chronic musculoskeletal pain in the elderly population of Amirkola, Iran..

KEY WORDS: Body mass index, Chronic pain, Elderly, Physical activity, Vitamin D.

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Introduction

Chronic musculoskeletal pain is defined as pain lasting for more than three months, with the symptoms remaining even after treatment. In fact, chronic pain is a complex problem involving various biopsychosocial factors (1). Chronic musculoskeletal pain has been also defined as treatment-resistant pain, persisting beyond the expected healing period (2). The mean prevalence

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of chronic pain in adult populations has been estimated at 15%. According to World Health Organization, this rate has been reported to be 20% (3). The most common age of chronic pain is the fourth or fifth decade of life (4). The six-month incidence of chronic and persistent pain in the elderly population (60-90 years) was reported to be 67% in Iran (5). According to previous research, the prevalence of chronic pain and its consequences is related to both gender and age. In fact, chronic pain in women is twice as common as men (4).Disorders which can lead to chronic pain include muscular pain, joint pain, muscular weakness and fatigue, fibromyalgia syndrome, rheumatic disorders, osteoarthritis, hyperesthesia, chronic migraine headaches and other physical symptoms, which are all induced by vitamin D deficiency (6,7).

Vitamin D is a steroid prohormone, with its active type contributing to the metabolism of calcium phosphate. It seems that vitamin D plays a major role in the central and peripheral nervous systems (8,9). Detection of vitamin D receptors in different areas of the brain and particularly the spinal cord can verify the transition of this vitamin through the blood-brain barrier (10). In fact, vitamin D receptors are present in the bone, heart, kidneys, nervous system, skin, teeth and thyroid gland (11). Different mechanisms can be introduced to explain the role of vitamin D in chronic pain management. There is evidence indicating the effect of this vitamin on the increased level of neurotrophins (proteins involved in the growth, differentiation and maintenance of nervous tissues) such as nerve growth factor (NGF), neurotrophin-3 and glial cell line-derived neurotrophic factor (GDNF) (12, 13). As previous research has suggested, decreased level of vitamin D can reduce NGF and GDNF, resulting in a decline in pain threshold (14).

Also, NGF is among the most important neurotrophins, which can improve the function of spinal cord and nervous system following injury, mostly through the rehabilitation and maintenance of nervous tissues (12). Vitamin D can also exert different clinical effects by reducing the formation of nitric oxide synthase (NOS) in different cells, since nitric oxide affects hyperalgesic responses (increased sensitivity to pain-inducing stimuli) and many chronic neurological disorders. This vitamin leads to reduced NOS and subsequently nitric oxide. This can explain the mechanism behind pain elimination, since NOS blockers (e.g., L-nitro-arginine methyl ester) can act as analgesics (15). Also, nitric oxide is known to be responsible for opioid resistance, which appears after the prolonged administration of morphine. Therefore, vitamin D by passing through the blood-brain barrier, which is involved in pain sensation, reduces nitric oxide build-up and increases the pain threshold (16). Some common causes of vitamin D deficiency include inadequate exposure to sunlight (17), aging (17), clothing in different countries (18), smoking and multiple pregnancies (19), geographic distribution and cold climate (17), lack of outdoor activities (20), race (e.g., skin color and thickness) (20), female gender (especially in areas where women are not commonly employed) (9) and lack of training on the use of supplements and foods containing vitamin D.

According to previous research, vitamin D deficiency is more common among the elderly and has various side-effects (18). Vitamin D deficiency is described as serum levels lower than 75 nmol/L (30 nmol/ml). Vitamin D level of 75-374 nmol/L (30-150 nmol/ml) is considered to be normal, whereas levels higher than 374 nmol/L (150 ng/ml) are regarded as toxic (18). The prevalence of vitamin D deficiency has been estimated at 40-80% (21). Mcbeth et al. and Heidari et al. noticed a significant relationship between vitamin D level and chronic pain. Chronic pain, which might result in reduced physical activity and therefore, reduced exposure to sunlight, might be the main source of this deficiency (22,23). Considering the abovementioned issues, this study aimed to evaluate the association between chronic pain and vitamin D deficiency in the elderly population of Amirkola, Iran. An adequate number of male and female participants were recruited and the study was carried out in all seasons of the year in order to control the effects of seasonal variation on vitamin D level.

Methods

This cross-sectional study, which was part of a cohort project, known as "Amirkola Health and Ageing Project (AHAP)", was performed on senior citizens, aged 60 years or above (24). Two major

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health centers are located in Amirkola, which keep a record of all senior citizens and their addresses in the city. Through phone calls and home visits, the elderly were invited to enroll in this study, while providing them with the required information about the study. Out of 2,234 senior citizens, 1,616 cases participated in this study (72.3%). The required information was gathered by a trained individual through using standard questionnaires and examinations. Demographic data including age, sex, occupational status, education and marital status were collected, using a questionnaire. Volunteers with cancer, depression, osteoarthritis, rheumatoid arthritis (self-reported) or a prior history of surgery within the last three months were excluded from the study. Finally, 857 participants were enrolled in the study. Chronic musculo-skeletal pain and its site were assessed using a questionnaire. The participants were asked whether they had experienced persistent pain (lasting for at least three months) within the past six months in the following sites: hands, wrists, elbows, shoulders, face, jaw, neck, hips, knees, ankles, legs and back. All questionnaires were completed through conducting interviews with the participants. In order to determine the serum level of 25-hydroxy-vitamin D (the active form of vitamin D), blood samples were obtained from the elderly in the morning and were evaluated by ELISA method at the Cellular and Molecular Research Center of Babol University of Medical Sciences, using the enzyme immunoassay kit. A normal cut-off point was used to interpret serum vitamin D levels. Vitamin D deficiency, insufficiency and sufficiency were defined as vitamin D levels < 20 ng/ml (50 nm/L), 20-29.99 ng/ml and ≥ 30 ng/ml (75 nm/L), respectively (6). Vitamin D level was studied and compared between the participants with and without chronic pain. Data on physical activity was assessed using a standard questionnaire of physical activity in the elderly (PASE).

The total physical activity score for each individual was calculated as between 0 and 400; higher scores meant higher physical activity levels.For data analysis, descriptive statistics (mean and standard deviation), analytical tests (t-test and Chi-square), Spearman's correlation coefficient and logistic regression were performed, using SPSS version 18. $p< 0.05$ was considered statistically significant.

Results

This study was conducted on 1,616 participants in Amirkola, Iran. The mean age of the participants was 69.21±7.30 years (range: 60-92 years). Overall, 599 (69.9%) and 258 (30.1%) cases were male and female, respectively. The mean vitamin D level in the participants was 29.19±27.30. Overall, 666 participants (77.7%) complained of chronic pain and 191 subjects (22.3 %) did not describe any chronic pain. Also, 201 subjects (23.5 %) were cigarette smokers (table 1). In total, 359 participants (41.9%) had vitamin D deficiency (vitamin D level < 20 ng/ml), 295 cases (34.4%) presented with insufficient vitamin D (20-29.99 ng/ml) and 203 cases (23.7 %) had sufficient vitamin D (≥ 30 ng/ml).

Table 1. The frequency and percentage of participants in the study in terms of demographic characteristics

Variables	N (%)
Educational level	
Illiterate	543(63.4)
Primary level	229(26.7)
Secondary level	18(2.1)
High school	38(4.4)
University	29(3.4)
Occupational status	
Unemployed	40(4.7)
Housekeeper	232(27.1)
Previously employed (retired)	232(27.1)
Employee	347(40.5)
Unknown	6(0.7)
Cigarette smoking	
Yes	201(23.5)
No	656(76.5)
Body mass index (kg/m^2)	
<25	308(35.9)
25-29.99	366(42.7)
30≤	183(21.4)
Comorbidity	
Yes	712(83.1)
No	144(16.8)
Diabetes mellitus	
Yes	235(27.4)
No	622(72.6)

The subjects were divided into two groups, based on vitamin D level: ≥30 ng/ml and <30

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ng/ml. The mean vitamin D level in women with chronic pain was 28.38 ng/ml (fig 1). The mean age, calcium level, physical activity, concomitant diseases and body mass index (BMI) were not significantly different between the two groups (table 2).

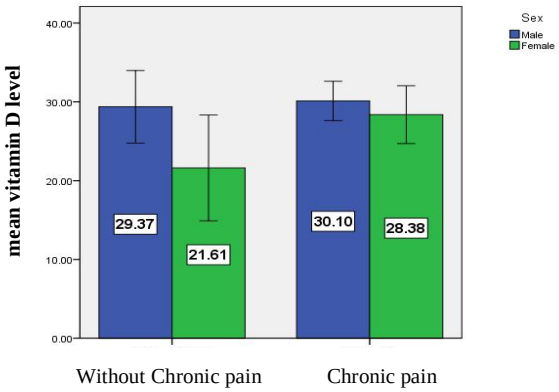


Figure 1. The mean vitamin D level in elderly men and women participating in the study with and without chronic pain

Table 2. Comparison of some variables according to chronic pain

Chronic pain / Variables	Yes (n=666) Mean±SD	No (n=191) Mean±SD	p-value
Age	69.37±7.28	68.66±7.36	0.23
Calcium	9.21±0.42	9.25±0.47	0.30
Vitamin D	29.51±27.11	28.06±28.02	0.51
Physical activity	101.35±54.88	122.18±81.27	0.001
Concomitant diseases	2.15±1.65	1.63±1.33	0.001
BMI	26.97±4.43	25.91±4.24	0.003

As the results indicated, 463 cases (54%) had chronic knee pain, 324 cases (40%) had back pain, 306 cases (35.7%) suffered from chronic pain in the legs and 236 cases (27.5%) had chronic shoulder pain. In addition, 151 (17.6%), 145 (16.9%), 142 (16.6%), 63 (7.4%), 52 (6.1%), 43 (5%) and 1 (0.1%) participant suffered from chronic pain in the hands, neck, joints, ankle, elbow, wrist and face, respectively. Table 3 compares the prevalence of chronic pain (based on the anatomical site) with regard to vitamin D level. Overall, 159 (78.3%) participants with vitamin D level >30 ng/ml and 507 cases (77.5%) with vitamin D level < 30 ng/ml suffered from chronic pain; no significant difference was observed between the two groups. The mean BMI and number of concomitant diseases were significantly higher in patients with chronic pain, compared to those without chronic pain (p=0.003).

Table 3. Comparison of the frequency of chronic pain (categorized by the anatomical site) with regard to vitamin D level

Anatomical location	Vitamin D levels	Chronic pain N(%) Yes	Chronic pain N(%) No	p-value
Hands	≥30	33(20.5)	128(79.5)	0.48
	30>	118(23.1)	392(76.9)	
Wrists	≥30	11(6.8)	150(93.2)	0.81
	>30	32(6.3)	474(93.7)	
Elbows	≥30	17(10.6)	144(89.4)	0.13
	30>	35(6.9)	472(93.1)	
Shoulders	≥30	59(36.6)	102(63.4)	0.68
	30>	177(34.9)	330(65.1)	
Face	≥30	0(0)	161(100)	0.57
	30>	1(0.2)	506(99.8)	
Neck	≥30	32(19.9)	129(80.1)	0.51
	30>	113(22.3)	394(77.7)	
Hip joints	≥30	40(24.8)	121(75.2)	0.20
	30>	102(20.1)	405(79.9)	
Knee	≥30	118(73.3)	43(26.7)	0.20
	30>	345(68)	162(32)	
Ankles	≥30	23(14.3)	138(85.7)	0.01
	30>	40(7.9)	467(92.1)	
Feet	≥30	82(50.9)	79(49.1)	0.13
	30>	224(44.2)	283(55.8)	
Back	≥30	82(51.3)	78(48.8)	0.43
	30>	242(47.7)	265(52.3)	

Moreover, the mean physical activity in subjects without chronic pain was significantly higher than participants with chronic pain (p=0.001). As the results indicated, 274 cases (76.3%) with vitamin D levels < 20 ng/ml, 233 cases (79%) with vitamin D levels of 20-29.99 ng/ml and 159 cases (78.3%) with vitamin D levels ≥ 30 ng/ml complained of chronic pain; there was no significant difference among the three groups. To determine the role of some variables influencing chronic pain, we used the logistic regression model. By using the backward method, different variables including gender, BMI and physical activity had significant effects on chronic pain (table 4).

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Table 4. Logistic regression model for determining the factors associated with chronic pain in the elderly in Amirkola, Iran

Variables		OR(95% CI)	p-value
Gender	Female-to-male ratio	2.73(1.78-4.21)	0.001
BMI(kg/m^2)	25-25.99	1.45(1.00-2.10)	0.04
	≥30	1.72(1.05-2.81)	0.03
Age	65-69	0.98(0.63-1.53)	0.94
	70-74	1.49(0.90-2.46)	0.11
	75-79	1.36(0.80-2.32)	0.25
	80-84	1.05(0.51-2.17)	0.88
	85-99	1.21(0.46-3.17)	0.69
Fracture history	Yes to no ratio	1.35(0.90-2.02)	0.13
PA150	≥150 to <150 ratio	0.42(0.28-0.62)	0.001
Vitamin D status	Lower-to-normal ratio	0.94(0.63-1.40)	0.77

Discussion

In this study, there was no significant association between vitamin D level and chronic pain, which was quite similar to the results reported by some previous studies in this area. In a study by Hicks and colleagues in Italy, the frequency of chronic pain in women was higher than men and no significant correlation was observed between low vitamin D level and chronic back pain in elderly men, whereas this association was considerable in females (25). Moreover, in a study by Atherton et al. in England, no significant association was found between vitamin D level and chronic pain in men, while the relationship was statistically significant in females (26). A study by Leveille et al. showed that chronic pain in elderly women was more common than men (27). Additionally, in a review article, Rollman and colleagues reported that pain sensitivity is higher in women than men (28). This difference might be related to the higher prevalence of osteomalacia in women (which is one of the causes of back pain) (25), differences in biological and psychological factors (27), hormonal factors such as menstruation, use of oral contraceptives, pregnancy, hysterectomy (which may increase the risk of musculoskeletal disorders in women) and higher stress in women than men (28).In addition, in our study based on the logistic regression model, gender, BMI and physical activity had significant effects on pain. In fact, subjects with BMI > 30 kg/m^2 experienced more pain than others. In this regard, Ray and colleagues in a study on American seniors over 70 years of age suggested that high BMI significantly increased chronic pain in the mentioned group (29). In addition, McCarthy et al. in USA showed that the elderly with BMI of 30-34.9 kg/m^2 are twice as likely to have chronic pain as those with normal weight (BMI=18.5-24.9) (30).

Concomitant metabolic syndromes, insulin resistance, depression and anxiety, associated with obesity (28), physical load tolerance, increased inflammatory markers and psychological factors (31) and increased sequestration of vitamin D in adipose tissues (32, 33) may be the causes of this association. In this regard, one related factor in our study may be the anatomical location. In our study, the knees were the most common anatomical location, followed by back, legs and shoulders. Physical activity in patients without pain was significantly more than the group with chronic pain. Chronic knee pain reduced physical activity and resulted in weight gain.

Therefore, weight gain in addition to weight-bearing on the knees led to the sequestration of vitamin D in fat tissues.In our study, the mean level of vitamin D in the elderly with chronic musculoskeletal pain was not significantly different from those without pain. Many studies have reported the high prevalence of vitamin D deficiency in Iran (31, 34). In the present study, 76% of the elderly with no chronic pain also had vitamin D levels < 30 ng/ml; this might have resulted in the similarity of vitamin D level between the elderly with and without chronic pain. This finding also indicates the high prevalence of vitamin D deficiency in our country. Warner and colleagues in USA showed that the mean level of vitamin D in patients with chronic pain was not significantly different from the control group (35), although the definition of chronic musculoskeletal pain in their study was similar to the present research. The present findings were in contrast with some previous studies. For instance, S. Abou-Raya et al. in a study on the elderly (≥ 65 years) in Egypt showed that patients with chronic musculoskeletal pain had significantly lower vitamin D levels, compared to patients without pain. In the mentioned study, chronic pain was defined as persistent pain over the last month or within three

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months over the past year (36). Moreover, McBeth in UK showed that the elderly with no chronic pain had lower vitamin D levels. Even after eliminating the confounding factors, e.g., physical activity, BMI, smoking and alcohol consumption, a significant relationship between chronic pain and low vitamin D level was found (22). A study by Heidari et al. showed a significant association between vitamin D deficiency and chronic pain, which was in contrast with the results of the present research. In their study, vitamin D level < 20 ng/ml was considered as vitamin D deficiency and only patients with bone pain were included in the experiment (23).

It seems that bone pain was associated with osteomalacia and vitamin D deficiency; however, in our study, patients with musculoskeletal pain were studied.In our study, the mean level of vitamin D in the elderly was 19.29 ng/ml in Amirkola, which was much lower than the value reported by Najafipour et al. in Tabriz, Iran (37). Their study population consisted of healthy senior citizens without chronic pain and the mean age of the participants was lower than the present research. Moreover, Ettehad et al. performed a study in Guilan, Iran on patients with chronic pain. Serum vitamin D levels in their study were lower than our research (38). The participants in the mentioned study were mostly women, while in our research, 69% of the subjects were male. In this study, despite the age similarity of men and women, vitamin D level was significantly lower in women than men; however, the lowest levels of vitamin D were reported in women without chronic pain. Maggio and colleagues in Italy introduced advancing age as a risk factor for vitamin D deficiency. Decline in vitamin D level in women begins after 50 years of age, while men tend to experience deficiency after 70 years of age (39). In our study, 41% of the elderly had vitamin D levels lower than 20 ng/ml. In a study on Arab adults (90% female), Al Faraj et al. reported this rate to be 83%, which was much higher than the figure reported in our study (40). As previous studies have indicated, due to limited natural vitamin D resources in nature, diet alone is not a reliable source of vitamin D (41). Therefore, one alternative is exposure to sunlight to stimulate the production of vitamin D in the skin as the primary mechanism. In this research, the elderly spent their time outside the house most of the days and were in good condition. Moreover, high rates of vitamin D deficiency may be related to cultural factors such as clothing which prevents the skin to be exposed to sunlight. Also, in our study, none of the participants mentioned a history of sunbathing. One of the strengths of this study was the population-based sample of the elderly and high participation rate of the elderly in Amirkola. One of the limitations of this study was its cross-sectional nature, which hinders the evaluation of causality. In this study, no significant association was found between vitamin D level and chronic pain in the elderly. This may be due to the influence of some factors such as insufficient information about the use of opium and high prevalence of vitamin D deficiency in the country, which led to the inclusion of study and control groups with low vitamin D levels. Further prospective studies are required to investigate this relationship

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