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No association between level of vitamin D and chronic low back pain in Swedish primary care: a cross-sectional case-control study

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ABSTRACT

Objective: Assessment of vitamin D levels and deficiency status in individuals with chronic low back pain (CLBP) in a Swedish general population, compared with controls matched for sex and age.

Design: Cross-sectional case-control study.

Setting: Primary care, southern Sweden.

Subjects: Participants ($n = 44$) with self-reported low back pain for at least 3 months and individually sex- and age-matched controls without a chronic pain condition ($n = 44$), recruited from the general population by random letter of invitation.

Main outcome measure: Association between vitamin D level and CLBP when adjusting for possible confounders in a multivariate forward conditional logistic regression model.

Results: Mean S-25-hydroxyvitamin D levels were 81 and 80 nmol/L in the CLBP and control group, respectively. The prevalence of vitamin D deficiency was low and similar in the CLBP group and the control group. Vitamin D level was not associated with CLBP when potential confounders were taken into account.

Conclusions: No difference in vitamin D levels between participants with CLBP and matched controls could be demonstrated in the present sample. Assessment of vitamin D level and deficiency status may be of questionable value in the management of CLBP in primary care settings at similar latitudes, unless there are additional risk factors for deficiency or specific indicators of osteomalacia.

KEY POINTS

Vitamin D deficiency is common and reported in many chronic pain conditions, including chronic low back pain (CLBP), but evidence for an association and causality is insufficient.

- The present study found no association between vitamin D levels and CLBP in a case-control sample of 44 + 44 individuals from the Swedish general population.
- Prevalence of vitamin D deficiency was low and comparable in individuals with CLBP and controls without chronic pain, matched for sex and age.
- Assessment of vitamin D status, for the purpose of finding and treating an underlying cause of pain, may be of limited value in the management of CLBP in primary care settings at similar latitudes.

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Chronic pain; general practice; low back pain; primary health care; Sweden; vitamin D

Introduction

Low back pain is a common condition with a lifetime prevalence of up to 84%. The prevalence of chronic low back pain (CLBP), defined as pain lasting longer than 3 months, has been estimated to 23%.[1] In more than 85% of cases of low back pain no single underlying mechanism or specific cause can be identified, although the application of a bio-psycho-social perspective, including individual and work-related factors, can explain up to 50% of the variance in risk of developing chronic pain.[1,2] Authors have proposed vitamin D deficiency as a possible contributing factor in the pathogenesis and maintenance of pain conditions, including CLBP,[3–5] although there is no definitive consensus regarding optimal vitamin D levels for different clinical outcomes.

Some studies show high prevalence of suboptimal vitamin D levels in populations with musculoskeletal and/or widespread pain conditions [3–8] or co-

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variation between low vitamin D levels and indicators of pain.[9,10] Many of these studies, however, have methodological limitations such as absence of adequate control groups.[3,5,6,8] Moreover, other studies show conflicting or negative results.[11–13]

Studies have reported pain relief or other improvements with vitamin D supplementation in nonspecific musculoskeletal pain conditions including fibromyalgia,[8,10,14,15] CLBP,[3] and in rheumatology outpatients.[16] Lack of placebo control makes interpretation difficult in some of these studies,[3,8] but four studies reporting positive effect were randomised controlled trials. Arvold et al. found modest improvements in fibromyalgia symptoms and functional status with vitamin D supplementation,[10] Schreuder et al. found some positive effect on self-assessed change in pain in subjects with nonspecific recurrent or long-standing musculoskeletal pain.[14] Sakalli et al. found significant positive effect of a megadose vitamin D on muscular function and some indicators of bodily pain in a rheumatology outpatient population.[16] Wepner et al. noted a significant reduction in pain as measured by visual analogue scale, as well as improvement in some quality of life parameters, when treating patients with fibromyalgia and vitamin D deficiency to a predefined target level in a recent small trial.[15]

In contrast to these findings, no effect was seen in a randomised placebo-controlled trial on vitamin D treatment in diffuse musculoskeletal pain,[11] and a double-blind trial on vitamin D effect in nonspecific CLBP failed to show significant improvement in pain when compared with placebo.[17] A recently updated Cochrane review concludes that there is no convincing evidence for pain relief with vitamin D supplementation in most pain conditions. On the other hand, the review also recognises that study types other than double-blind randomised controlled trials may support the vitamin D hypothesis for chronic pain and the need for more work in this area.[18]

Several hypotheses for the role of insufficient vitamin D levels in the pathogenesis and maintenance of pain have been proposed. Severe vitamin D deficiency with osteomalacia is clearly associated with musculoskeletal pain including low back pain. Additional indicators of osteomalacia, i.e., proximal muscle weakness, gait abnormalities, generalised pain or local bone pain involving the rib cage, shoulder girdle or pelvis, are often present in these cases.[19] Other proposed mechanisms linking vitamin D insufficiency to chronic pain include immunoregulatory and proinflammatory effects, cytokine effects on central and peripheral pain regulation, subclinical effects on calcium homeostasis and muscular effects of secondary hyperparathyroidism.[20]

Risk factors for low vitamin D levels include low sun exposure (i.e., clothing and cultural practices that limit sunlight exposure, dark skin pigmentation, latitudes associated with oblique sun zenith angle), high age, female sex, malabsorption, chronic kidney disease, and medication including some antiepileptic agents. Seasonal variation is seen in most populations and at all latitudes.[21,22]

Thus, low levels of vitamin D can be found in many pain populations, but the causal role of mild to moderate vitamin D deficiency in pain conditions in general, as well as in CLBP, remains unclear. The aim of this study was to assess vitamin D levels and vitamin D deficiency status in individuals with CLBP in a Swedish general population, compared with controls without a chronic pain condition, matched for sex and age, and adjusting for potential confounding factors, i.e., predictors of chronic pain and factors influencing vitamin D levels.

Materials and methods

Study population and recruitment of participants

Participants were randomly recruited from the adult population listed to a primary health care centre in a rural community in southern Sweden at northern latitude 57°. Potential participants were contacted by letter with a request for participation, during March through April (batch one) and September through October (batch two) 2012. Respondents provided written consent and were asked to fill out a form for assessment of inclusion criteria.

The primary inclusion criterion was CLBP defined as self-reported pain in the low back area for more than half of the time in the past 3 months, in accordance with standardised criteria proposed by Dionne et al. [23] Individuals with a registered diagnosis of dementia, psychosis, or psychological developmental disorder were omitted. Individuals with self-reported radiologically verified spinal stenosis, spondylolisthesis, vertebral compression fracture, or other spinal fracture were excluded, as were those diagnosed with spinal malformation, osteoporosis, osteomalacia, rheumatic disorder, neurologic disorder, stroke or other brain injury, spinal cord injury, or malignancy. Individuals who had undergone spinal surgery or were diagnosed with disc herniation in the past year were also excluded.

Participants were included consecutively and additional letters were randomly sent, until the number of included participants exceeded the calculated target (see Sample size calculation, below).

To create a sex- and age-matched control group, the included participants with CLBP were individually matched with respondents who reported no pain or pain for less than half of the time in the past 4 weeks resulting in matched pairs of participants. The same exclusion criteria were applied.

Data collection

Non-fasting venous blood samples were drawn, body weight and length were measured to allow for calculation of body mass index (BMI), and additional information was collected from the participants in single visits to the primary health care centre during two separate time periods in 2012: batch one, 26 March–27 June, and batch two, 25 October–8 November.

Information was collected regarding background variables (smoking, alcohol use,[24] physical activity [25]), recent lumbar pain including pain characteristics (occurrence, frequency, duration, intensity, and impact on daily living), and factors potentially influencing vitamin D levels (diseases or use of medication associated with vitamin D insufficiency, use of vitamin supplements, recent or current pregnancy or breast feeding, skin pigmentation, use of veil, country of birth of participants and both parents, amount of outdoor activity, and solarium and sun screen use).

Pain frequency was defined as time with lumbar pain in the last four weeks, specified as some days (less than half), most days (more than half) or all days. Pain duration was defined as time since experiencing one month without lumbar pain, specified as less than 3 months, 3–6 months, 7–36 months or more than 36 months. Typical pain intensity in the last four weeks was measured by a visual numeric scale 0–10 where higher number indicated more severe pain. Impact of pain on daily living was defined as pain limiting daily activities or changing daily routines for more than one day in the last four weeks.

For pain location, participants reported by checking boxes (0–18), with corresponding predefined regions in a two-sided drawing, to allow for diagnosis of chronic widespread pain (CWP) according to the 1990 criteria of the American College of Rheumatology (ACR).[26,27]

The Örebro Musculoskeletal Pain Screening Questionnaire (ÖMPSQ) was used to collect data regarding some additional important risk factors for developing chronic pain and disability. Items intended for analyses were item 8 (heavy or monotonous work), 13 (tension/anxiety), 14 (depressive mood) and 17 (job satisfaction).[28]

Determination of vitamin D status

Serum 25-hydroxyvitamin D (S-25OHD) is to date the most widely accepted biomarker for short-term vitamin D status. However, there is no definitive consensus regarding optimal vitamin D levels.[21,22] For the purpose of the present study, three different cut-off levels for suboptimal vitamin D status were studied: S-25OHD <25, <50, and <75 nmol/L, respectively. Serum levels of 25OHD were determined using high-pressure liquid chromatography in combination with mass spectrometry (HPLC-MS).

Outcome measures

Mean difference in S-25OHD between pairs of participants with CLBP and matched controls, with the intention of adjusting for possible confounding factors.

Sample size calculation

The study was designed to detect a mean difference in levels of S-25OHD between matched participants of 10 nmol/L. Standard deviation was assumed to be 20 nmol/L based on observations in a healthy Norwegian general population.[29] With significance level set to 0.05, power to 0.80, and using a two-sided one-sample Z test, the calculated sample size was 32 matched pairs. To allow for dropouts and the possibility of a more heterogeneous population than expected, we planned to recruit a minimum of 50 matched pairs.

Statistics

Descriptive analysis was performed using means and standard deviations, median values and percentiles, or proportions and percentages, depending on data type. In the comparative analyses between the groups, the chi-square test, and, in case of small values, the Fisher's exact test, was used for nominal data, the Mann–Whitney U test was used for ordinal data and the Student's t test for independent samples was used for continuous data.

Statistical analysis of the difference in vitamin D level between the pairs of matched individuals was intended to be performed using a one-sample t-test.

Multiple logistic regression was used to analyse the association between vitamin D level and CLBP as dependent variable, and to adjust for potential confounders, i.e., available known or presumed predictors of chronic pain and additional factors potentially influencing vitamin D levels.

All the variables were evaluated for assumptions of multivariate analysis by checking the correlation matrix for the independent variables, and Spearman correlation

coefficient <0.7 was considered relevant to include in multivariate analysis. Variables were handled either as categorical data, or continuous data, without categorisation, when possible.

Separate logistic regression analyses with CLBP as dependent variable, adjusted for sex and age, were performed for each independent variable to reduce the number of independent variables of interest. Independent variables with p values <0.05 were considered relevant to enter into multivariate analysis. Multiple forward conditional logistic regression analysis was subsequently performed, entering sex, age, vitamin D level and selected independent variables in the model. The models were assessed for ''goodness of fit'' (the Omnibus test of model X^2 $p < 0.05$ and the Hosmer and Lemeshow test $p > 0.05$). Odds ratios (OR) with 95% confidence intervals (CI) were calculated.

The level of significance was $p < 0.05$. The IBM SPSS Statistics for Windows version 19 was used for all statistical analyses.

Results

Group characteristics

One hundred and two participants, i.e., 51 pairs (28 pairs in batch one, 23 pairs in batch two), were recruited. The recruitment and data collection process are illustrated in Figure 1. Re-checking of inclusion criteria at the time of data collection resulted in exclusion of seven pairs from statistical analyses. The remaining 44 matched pairs (25 pairs from batch one and 19 pairs from batch two) were analysed. Group characteristics are shown in Table 1.

Mean levels of S-25OHD were 81 and 80 nmol/L in the CLBP group and in the control group, respectively ($p = 0.85$), indicating relative vitamin D sufficiency in the sample. Vitamin D deficiency was not more common in either group, regardless of cut-off level (Table 2).

Pain characteristics in the CLBP group

A majority of the participants in the CLBP group reported low back pain for more than 6 months

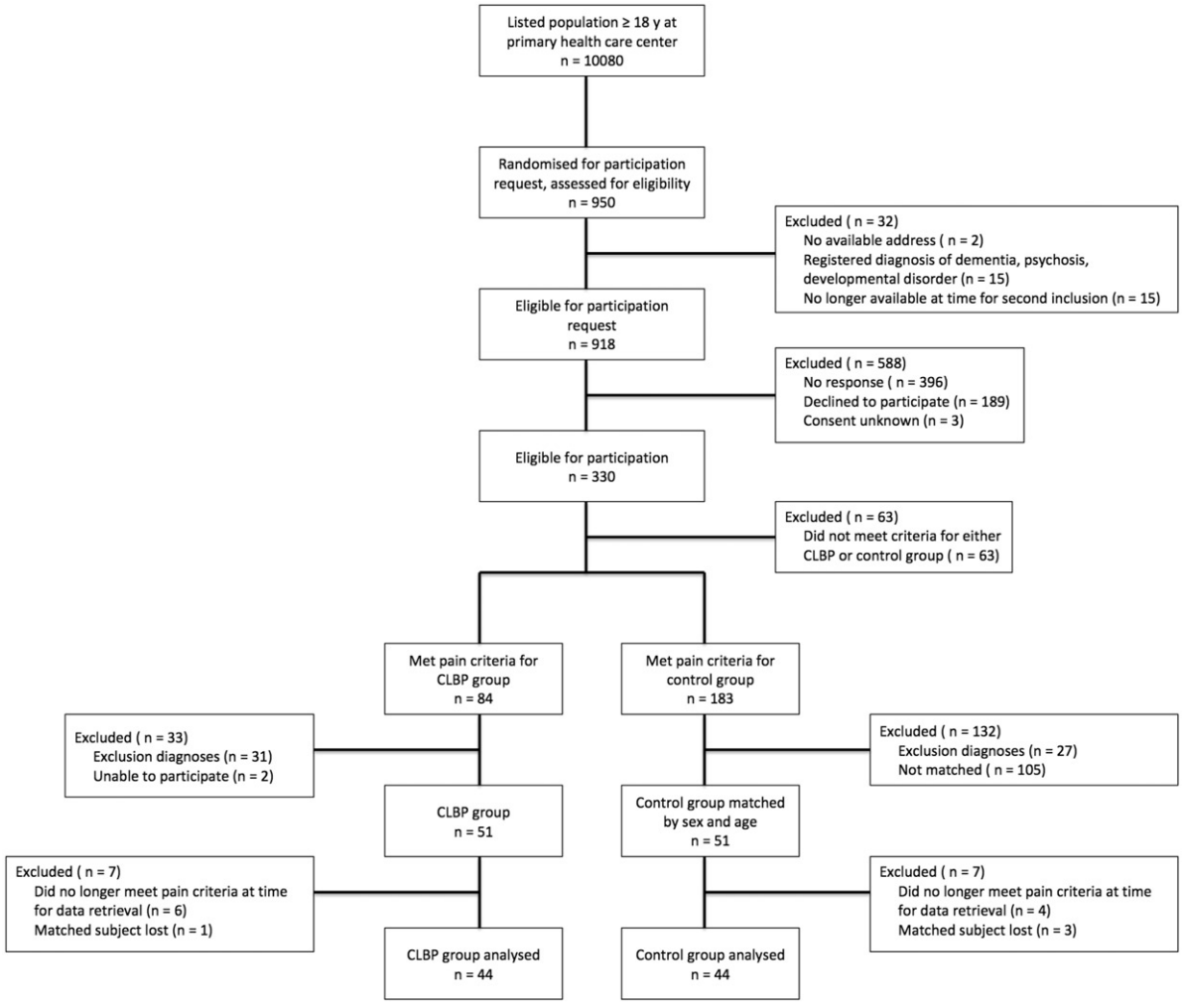

Figure 1. Recruitment and data collection process, participants' flow.

Table 1. Characteristics of the included participants in the chronic low back pain (CLBP) group and the matched control group.

	CLBP ($n = 44$)	Control ($n = 44$)	p Value[a]
Demographic data			
Sex [n (%)]			1.0
Female	26 (59)	26 (59)	
Male	18 (41)	18 (41)	
Age, years [mean (SD)]	55 (16)	55 (15)	0.87
Country of birth [n (%)]			1.0
Sweden or other Nordic countries	41 (93)	40 (91)	
Other	3 (6.8)	4 (9.1)	
Work-related variables			
Occupation [n (%)]			0.53
Employed worker	28 (64)	29 (66)	
Student	1 (2.3)	1 (2.3)	
Unpaid work	0 (0)	2 (4.5)	
Unemployed	0 (0)	0 (0)	
Retired	14 (32)	12 (27)	
Other	1 (2.3)	0 (0)	
Heavy or monotonous work ($n = 62$)[c]	5.0 (2.0–8.0)[b]	1.0 (0.0–5.0)	**0.0070**
Job satisfaction ($n = 61$)[d]	8.0 (6.8–9.3)[b]	8.0 (6.0–10)	0.92
Lifestyle factors			
Leisure time physical activity, LTPAI[e]	5.5 (3.0–8.8)[b]	6.0 (5.0–11)	0.090
Tobacco smoking [n (%)]	8 (18)	2 (4.5)	0.089
Alcohol consumption, AUDIT-C ($n = 83$)[f]	2.0 (1.5–4.0)[b]	2.0 (1.0–3.0)	0.082
Additional potential predictors of chronic pain			
Feeling tense or anxious[g]	5.0 (2.0–7.0)[b]	3.0 (1.0–6.0)	**0.038**
Feeling depressed[h]	3.0 (0.0–6.0)[b]	1.0 (0.0–2.0)	**0.018**
Factors potentially influencing vitamin D levels			
Medical conditions [n (%)]			
Cystic fibrosis	0 (0)	0 (0)	–
Celiac disease	1 (2.3)	0 (0)	1.0
Inflammatory bowel disease	0 (0)	0 (0)	–
Chronic renal failure or nephrotic syndrome	0 (0)	0 (0)	–
Hepatic failure	0 (0)	0 (0)	–
Status post gastric or intestinal surgery	0 (0)	1 (2.3)	1.0
Pregnancy during last year [n (%)]	0 (0)	0 (0)	–
Breast feeding during last year [n (%)]	1 (2.3)	0 (0)	1.0
Skin pigmentation [n (%)][i]			0.23
Type 1	1 (2.3)	1 (2.3)	
Type 2	11 (25)	13 (30)	
Type 3	22 (50)	17 (39)	
Type 4	7 (16)	13 (30)	
Type 5	3 (6.8)	0 (0)	
Type 6	0 (0)	0 (0)	
Outdoor activity[k]	3.0 (2.0–4.0)[b]	2.0 (2.0–3.0)	0.20
Use of solarium ($n = 86$)[l]	0.0 (0.0–0.0)[b]	0.0 (0.0–0.0)	0.97
Use of veil [n (%)]	0 (0)	0 (0)	–
Use of sunscreen[m]	2.0 (2.0–2.0)[b]	2.0 (2.0–2.0)	0.78
Vitamin D supplementation [n (%)]	6 (14)	5 (11)	1.0
Physical properties			
Body mass index [mean (SD)]	29 (5.1)	26 (3.7)	**0.0059**
S-25-hydroxyvitamin D, nmol/L [mean (SD)]	81 (27)	80 (25)	0.85

Bold values indicate $p < 0.05$.

[a]For nominal data the chi-square test, and, in case of small values, the Fisher's exact test, were used. For ordinal data the Mann–Whitney U test was used. For continuous data the Student's t test was used.

[b]Figures denote median value (25th–75th percentile).

[c]Örebro Musculoskeletal Pain Screening Questionnaire (ÖMPSQ) item 8 (0–10), where a higher value indicates heavier or more monotonous work.

[d]ÖMPSQ item 17 (0–10), where a higher value indicates greater job satisfaction.

[e]Leisure Time Physical Activity Index (LTPAI), total score in hours, where a higher value indicates more time in physical activity.

[f]Alcohol Use Disorder Identification Test, sum of items 1–3 (AUDIT-C), with a maximum of 12 points, where a higher value indicates greater alcohol consumption.

[g]ÖMPSQ item 13 (0–10), where a higher value indicates more severe tension or anxiety in the past week.

[h]ÖMPSQ item 14 (0–10), where a higher value indicates more severe feelings of depression in the past week.

[i]Skin pigmentation, specified as skin type 1–6 where a higher figure indicates darker skin.

[k]Self-reported time of daily outdoor activity in a 4-week period on a 5-item ordinal scale, where a higher value indicates more hours outdoors.

[l]Self-reported use of solarium in a 4-week period on a 5-item ordinal scale, where a higher value indicates more hours of solarium use.

[m]Self-reported typical use of sunscreen on a 4-item ordinal scale, where a higher value indicates less frequent use of sunscreen when spending time outdoors.

($n = 40$, 91%), and more than half had a duration of pain of more than 3 years ($n = 27$, 61%). Eighteen participants (41%) reported significant pain impact on activities or daily routines in the past 4 weeks. Reported pain intensity [median (25th–75th percentile)] in the same time span was 5.0 (4.0–6.0). Nine participants (20%) reported any number of days of sick leave because of CLBP, and three participants (6.8%)

reported sick leave for more than 30 days, in the previous year. Thirteen participants (30%) met criteria for CWP.

Main outcomes

The analysis of the association between vitamin D level and CLBP with adjustment for potential confounders was made in the multiple logistic regression (Table 3). The results of unadjusted comparative analyses are omitted because of potential confounding differences between the CLBP and control group (Table 1). The logistic regression for each independent variable, adjusted for sex and age, showed that heavy or monotonous work, higher alcohol use, tension/anxiety, depressive mood and higher BMI were relevant to enter into multivariate analysis. When vitamin D levels and selected independent variables were entered in a forward conditional logistic regression model ($n = 61$), only self-reported degree of heavy or monotonous work remained statistically significant, OR 1.2 (95% CI 1.2 to 1.5, $p = 0.011$). Depressive mood was a predictor of CLBP when work-related independent variables, i.e., heavy or monotonous work, were excluded from the analysis ($n = 83$), OR 1.2 (95% CI 1.0 to 1.4, $p = 0.021$). Vitamin D level was not associated with CLBP in the model.

Table 2. Vitamin D status in the chronic low back pain (CLBP) group and the matched control group, where S-25-hydroxyvitamin D level ≥75 nmol/L indicates vitamin D sufficiency and levels <75, <50 and <25 nmol/L indicate different cut-off values for insufficiency or deficiency.

	CLBP ($n = 44$)	Control ($n = 44$)	p Value[a]
S-25-hydroxyvitamin D, nmol/L [*n* (%)]			
≥75	23 (53)	24 (55)	0.83
<75	21 (48)	20 (45)	0.83
<50	3 (6.8)	4 (9.1)	1.0
<25	0 (0)	0 (0)	–

[a]The chi-square test, and, in case of small values, the Fisher's exact test, was used.

Discussion

This cross-sectional case-control study in a Swedish primary care setting showed no difference in vitamin D

Table 3. Logistic regression analyses of the association between vitamin D level, and potential confounding variables, and chronic low back pain (CLBP), in the present sample, showing firstly the odds ratio for CLBP for each independent variable, and secondly the odds ratio for CLBP when vitamin D levels and significant independent variables from the first step where entered into multivariate analysis.

	Logistic regression per independent variable, adjusted for sex and age			Forward conditional logistic regression, S-25-hydroxyvitamin D and selected independent variables ($p < 0.05$) entered in the model ($n = 61$)	
	n	Odds ratio (95% CI)	p Value	Odds ratio (95% CI)	p Value
Demographic data					
Country of birth Sweden or other Nordic country	88	1.4 (0.29–7.0)	0.67	–	
Work-related variables					
Heavy or monotonous work[a]	62	1.4 (1.1–1.8)	**0.0020**	1.2 (1.2–1.5)	**0.011**
Job satisfaction[b]	61	1.1 (0.87–1.3)	0.55	–	
Lifestyle factors					
Leisure time physical activity, LTPAI[c]	87	0.96 (0.89–1.0)	0.26	–	
Tobacco smoking	88	4.7 (0.93–24)	0.061	–	
Alcohol consumption, AUDIT-C[d]	83	1.4 (1.0–1.9)	**0.038**	–	
Additional potential predictors of chronic pain					
Feeling tense or anxious[e]	88	1.2 (1.0–1.4)	**0.037**	–	
Feeling depressed[f]	88	1.3 (1.1–1.5)	**0.011**	–	
Factors potentially influencing vitamin D levels					
Skin pigmentation[g]	88	1.1 (0.65–1.8)	0.76	–	
Outdoor activity[h]	88	1.3 (0.86–2.1)	0.20	–	
Use of sunscreen[i]	88	1.0 (0.59–1.7)	0.98	–	
Vitamin D supplementation	88	1.3 (0.35–4.6)	0.72	–	
Physical properties					
Body mass index	88	1.2 (1.0–1.4)	**0.0074**	–	
S-25-hydroxyvitamin D	88	1.0 (0.98–1.0)	0.87	–	

Bold values indicate $p < 0.05$.
[a]Örebro Musculoskeletal Pain Screening Questionnaire (ÖMPSQ) item 8 (0–10), where a higher value indicates heavier or more monotonous work.
[b]ÖMPSQ item 17 (0–10), where a higher value indicates greater job satisfaction.
[c]Leisure Time Physical Activity Index (LTPAI), total score in hours, where a higher value indicates more time in physical activity.
[d]Alcohol Use Disorder Identification Test, sum of items 1–3 (AUDIT-C), with a maximum of 12 points, where a higher value indicates greater alcohol consumption.
[e]ÖMPSQ item 13 (0–10), where a higher value indicates more severe tension or anxiety in the past week.
[f]ÖMPSQ item 14 (0–10), where a higher value indicates more severe feelings of depression in the past week.
[g]Skin pigmentation, specified as skin type 1–6 where a higher figure indicates darker skin.
[h]Self-reported time of daily outdoor activity in a 4-week period on a 5-item ordinal scale, where a higher value indicates more hours outdoors.
[i]Self-reported typical use of sunscreen on a 4-item ordinal scale, where a higher value indicates less frequent use of sunscreen when spending time outdoors.

levels between participants with CLBP ($n = 44$, mean S-25OHD 81 nmol/L) and matched control participants ($n = 44$, mean S-25OHD 80 nmol/L). No association between vitamin D level and CLBP was found when potential confounders were taken into account. Vitamin D deficiency was not more common in either group, regardless of cut-off level. The prevalence of relative insufficiency defined as S-25OHD <75 nmol/L was 48% in the CLBP group and 45% in the control group. No participants had severe vitamin D deficiency (S-25OHD <25 nmol/L).

Strengths and weaknesses of the study

Participants were recruited from a general population and included adults of all ages and both sexes. Wide inclusion criteria and few exclusion criteria were used. This strategy reflects the clinical situation in primary care better, and is less prone to bias, than selective recruitment from secondary or tertiary care. The CLBP group comprised individuals with clinically significant pain intensity and duration, and the prevalence of CWP was comparable with that in other reported CLBP populations.[30] Furthermore, the groups were comparable regarding risk factors for vitamin D deficiency, and adjustment for possible confounders was made. We estimate that the sample represents a population relevant to the primary care clinical context at similar latitudes.

The present sample demonstrated a somewhat unexpectedly high degree of vitamin D sufficiency and few participants had severe or even moderate deficiency. Routine HPLC-MS methods may show higher S-25OHD than other methods, and further standardisation is needed before uniform clinical cut-off levels can be used.[22] It has been shown that genetic polymorphism of the vitamin D binding protein (DBP) influences the level of bioavailable vitamin D and dynamic changes in DBP concentration may also have to be taken into account when assessing vitamin D status.[31] Furthermore, the amount of non-European immigrants in the sample was relatively low, and the findings may not be relevant to populations where vitamin D deficiency is more common, including primary care populations at other latitudes.

The study design did not allow for all possible confounding factors, i.e., risk factors for low vitamin D levels and known or potential predictors of CLBP, to be accounted for in both groups. However, the collection of background variables including the use of the ÖMPSQ allowed for a relatively comprehensive set of predictors of chronic pain to be taken into consideration in both the groups.

A sample size calculation was made, and the use of sex- and age-matched controls is an advantage in comparison with some studies on vitamin D status in pain conditions.[3,5,6,8] However, since CLBP is a diverse condition, the sample size may be considered small, and it is possible that an association between vitamin D levels and pain exists in subsets of CLBP patients. This hypothesis could warrant further studies.

Findings in relation to other studies

High prevalence of vitamin deficiency has been reported in large parts of the world, both in general populations and in specific subpopulations, including pain populations.[3–8,22] However, the presence of vitamin D deficiency in populations in uncontrolled studies may be explained by background prevalence and should not be confused with presence of causal or other association with the specific condition at hand.

Vitamin D levels in the present sample varied between individuals, but were remarkably similar for the CLBP and control groups and no association with CLBP was demonstrated. This finding is in contrast to some previous findings and does not support the hypothesis of mild to moderate vitamin D deficiency as an important factor in the pathogenesis and maintenance of CLBP. Vitamin D deficiency, defined as S-25OHD <22.5 nmol/L, was identified in a majority of 360 subjects with CLBP attending secondary care in Saudi Arabia.[3] The absence of adequate controls makes interpretation difficult, even if the findings were somewhat supported in an Egyptian secondary care setting with 60 female pain subjects and 20 healthy controls.[4] The cut-off level used for vitamin D deficiency in the latter study was 40 ng/mL (i.e., 100 nmol/L). Unfortunately, the control subjects were not described which complicates assessment of systematic bias. High prevalence of insufficient vitamin D levels was recently confirmed in an Indian observational study on 328 individuals with CLBP in tertiary care.[5] An association between vitamin D deficiency and functional disability, but no association with pain severity, was found. In an Italian population-based study of 958 participants, low vitamin D levels were associated with occurrence of isolated back pain, not specified as chronic, in elderly women but not in men.[9]

The non-association demonstrated in the present study supports the findings in the study by Heidari et al. of 276 subjects with nonspecific skeletal pain and 202 control subjects in northern Iran.[7] They found a significant positive association between vitamin D deficiency and pain in general, but not for the 54 subjects with back pain. A Danish study of subjects with CLBP

in a secondary care setting found vitamin D levels comparable with those of the general Danish population, but there was no control group.[13]

Vitamin D supplementation showed no effect on pain parameters compared with placebo in participants with CLBP in the randomized controlled trial by Sandoughi et al.[17] The prevalence of deficiency, defined as S-25OHD <50 nmol/L, was 42% and 52% in the active treatment ($n = 26$) and in the placebo group ($n = 27$), respectively. In comparison, the prevalence of vitamin D deficiency, using the same cut-off level, in the CLBP group in the present study was only 6.8%, and this did not differ from the prevalence of deficiency in the control group.

The identified independent variables associated with CLBP, i.e., heavy or monotonous work, high BMI, depressive mood, tension/anxiety and higher alcohol use, are in concordance with previous studies [2] and support the multifactorial bio-psycho-social explanatory model for chronic pain. However, heavy or monotonous work was the only significant predictor of CLBP in the multiple logistic regression model.

Unanswered questions and future research

Justification of recommendations and guidelines regarding assessment of vitamin D levels and deficiency status in the management of chronic pain requires additional studies in different pain populations, on different levels of care, in different geographic and ethnic contexts including populations were deficiency is more common, and, importantly, with adequate control groups.

There appears to be relative consensus on S-25OHD >50–75 nmol/L as cut-off level for biochemical vitamin D sufficiency and possibly for some long-term skeletal and non-skeletal outcomes. This consensus needs to be supplemented with the establishment of cut-off levels for relevant short- and mid-term clinical outcomes, possibly taking into account additional factors such as analysis method, DBP polymorphism and varying DBP levels.

As has previously been pointed out,[18] randomised controlled treatment trials in well-defined pain populations with different baseline vitamin D levels, with relevant endpoints and using different treatment regimes, are needed to find the place, if any, for vitamin D supplementation in chronic pain conditions.

Conclusion

The present study found no association between vitamin D level and CLBP. This finding suggests that routine assessment of vitamin D status, for the purpose of finding and treating an underlying cause of pain, is of limited value in the management of CLBP in primary care settings at similar latitudes. Vitamin D measurement in selected cases might still be justified where additional risk factors for deficiency or where additional indicators of osteomalacia are present.

The results should be extrapolated with caution, and we emphasise that the findings do not allow conclusions regarding the potential association between moderate or severe vitamin D deficiency and CLBP because of low prevalence of insufficient levels in the present sample.

Some skeletal and non-skeletal health benefits may be expected with treatment of vitamin D insufficiency even if no effect on back pain has been shown, but this notion is presently primarily supported by epidemiological studies. High quality evidence in this regard is still insufficient and the place for vitamin D supplementation in the management of chronic pain remains to be established.

Ethical approval

The study was approved by the Regional Ethical Review Board in Gothenburg.

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Disclosure statement

A Thörneby MD, L Nordeman PhD RPT and EH Johanson PhD RD declare having no competing interests.

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