Journal of Pain Research

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ORIGINAL RESEARCH

Racial Differences in 25-Hydroxy Vitamin D and Self-Reported Pain Severity in a Sample of Individuals Living with Non-Specific Chronic Low Back Pain

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Introduction: Considerable evidence suggests that there are significant ethnic/racial differences in the experience of pain among individuals suffering from chronic musculoskeletal conditions. Additionally, low levels of vitamin D have been associated with pain severity. Further, vitamin D deficiency is more prevalent in Non-Hispanic Black (NHB) individuals compared to Non-Hispanic Whites (NHW).

Objective: The aim of this study was to investigate the associations among race, pain severity, and serum levels of vitamin D in a sample of patients with chronic low back pain (cLBP).

Methods: All study participants (n = 155) self-identified their race/ethnicity as either NHB or NHW. Blood samples were collected to assess circulating levels of serum 25- hydroxy vitamin D. Vitamin D levels were categorized as optimal (≥20 ng/mL), insufficient (12–19 ng/mL) or deficient (<12 ng/mL). Participants then self-reported their pain severity using the Brief Pain Inventory – Short Form.

Results: Results showed that a greater proportion of NHB versus NHW participants were categorized as Vitamin D deficient (χ^2 (2, N = 155) = 16.79, p < 0.001). An analysis of covariance (ANCOVA) revealed that NHBs reported significantly greater pain severity relative to NHWs (F(1150) = 6.45) p = 0.012. Further, self-reported pain severity significantly differed according to Vitamin D clinical categories (F(2150) = 4.19, p = 0.013). Participants with deficient vitamin D reported significantly greater pain severity in comparison to participants with optimal vitamin D (F(1101) = 7.28, p = 0.008).

Conclusion: The findings suggest that Vitamin D deficiency may be linked to greater pain severity in a sample of individuals with cLBP, especially for those who identify as NHB.

Keywords: race, pain, vitamin D, disparities

Introduction

Chronic pain is one of the most prominent health concerns in the Western world.[1] While pain is often a symptom of other diseases, it has recently been classified as a disease in its own right.[2] Additionally, disparate burdens of pain are common among different groups of individuals based on ethnicity/race, age, sex and gender across a multitude of painful conditions.[3,4] One of the most prevalent among these conditions is chronic low back pain (cLBP). This condition can present with either specific (15% of cases) or idiopathic (85%) pathologies.[5,6] Despite the prevalence of cLBP, its biological underpinnings remain poorly understood.

Received: 17 August 2022
Accepted: 17 November 2022
Published: 7 December 2022

Vitamin D deficiency is common worldwide issue, with the prevalence estimated at 24%, 37%, and 40% in the United States, Canada, and Europe, respectively.[7,8] An emerging body of literature suggests that vitamin D status may be influencing the clinical pain experience of patients with chronic musculoskeletal conditions.[8–10] Further, there have been other investigations noting vitamin D deficiency in patients presenting predominantly with low back pain.[11] Prior research suggests that less than sufficient levels of vitamin D may cause bone and muscle pain based on its role in mineral absorption and cellular activities,[12] increasing pain sensitization,[9] and exaggerated inflammation.[13] Additionally, deficiencies in vitamin D have been consistently correlated with worse outcomes for chronic pain, as well as diabetes, cancer, immune system dysfunction, and cognitive impairment.[14]

As stated, vitamin D deficiencies and insufficiencies are common across populations. Unfortunately, racial minorities who identify as non-Hispanic Black (NHB) tend to present with less circulating vitamin D compared to their non-Hispanic white (NHW) counterparts.[15,16] Dietary quality leading to micronutrient deficiency is thought to contribute substantially to the unequal burden of various health outcomes in the NHB community.[17,18] Dietary quality has also been linked to mortality and worse health outcomes, including an increase in chronic pain prevalence.[19] It is likely that multiple factors are contributing to the insufficiency/deficiency of vitamin D in individuals who identify as NHB. Aside from racial differences in diet, it is well known that melanin reduces the ability of skin to convert cholesterol to vitamin D.[20] For individuals with greater amounts of melanin in the skin, synthesis of vitamin D requires considerably more sunlight exposure than their less-pigmented counterparts.[20] These factors may contribute significantly to the increased prevalence of Vitamin D deficiency among NHB populations. Current estimates indicate that ~40% of the deficient population are NHB, compared to only ~20% of the deficient population being NHW.[21] The vitamin D deficiency in NHBs might also underlie racial the observed racial disparities in chronic pain conditions such as cLBP. Despite the disproportionate burden of chronic low back pain severity and disability on the NHB community, the mechanisms remain understudied.[22] Thus, the purpose of this cross-sectional study was to investigate the associations among ethnicity/race, self-reported pain severity, and circulating levels of vitamin D in a sample of individuals living with cLBP.

Methods

Participants

The present study is part of an ongoing and more comprehensive project conducted at The University of Alabama at Birmingham (UAB) that aims to ethnic/racial and socioeconomic differences in cLBP severity and disability (Examining Racial And SocioEconomic Disparities in cLBP, ERASED study); R01MD010441; ClinicalTrials.gov Identifier: NCT03338192. All study participants were recruited via fliers posted at UAB affiliated pain treatment clinics and the surrounding community. The procedures and measures described below are limited to those involved in the current analyses. The study sample consisted of community-dwelling individuals living with cLBP. A comprehensive description of the stringent inclusion/exclusion criteria has been cited in a previous publication.[23] In short, potential participants were first evaluated via telephone screening and medical record review. Individuals were included in the study if low back pain had reportedly persisted for at least three consecutive months and was present for at least half the days in the past 6 months.[27] The primary pain complaint had to be low back pain with non-specific origin (idiopathic). In order to examine the full range of cLBP severity, there was no minimum threshold of self-reported pain intensity for inclusion in this study. Additionally, participants were deemed eligible only if they had not undergone a surgical intervention or experienced an accident/trauma within the past 12 months. Data collection was completed in accordance with the cLBP research standards established by the Research Task Force of the National Institutes of Health Pain Consortium.[24] This study and all procedures were reviewed and approved by the University of Alabama at Birmingham (UAB) Institutional Review Board (approval # IRB-000531566), and carried out in a manner consistent with ethical research guidelines as outlined in the Declaration of Helsinki. All participants provided written informed consent prior to enrollment in the study.

Ethnic/Racial Group Ascertainment

All participants included in this study indicated, via self-report, that their ethnicity was non-Hispanic and that their racial background was either African American/Black or Caucasian/White.

Center for Epidemiological Studies-Depression Scale (CES-D)

Due to the previously reported relationship between depression and primary variables of interest (vitamin D, chronic pain, race), all participants completed the CES-D.[25] This 20-item measure was employed in the current study to evaluate the degree of participants' depressive symptomatology. The CES-D assesses the frequency in which each participant experienced the following symptoms in the past week: negative mood, guilt/worthlessness, helplessness/hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance. Response options for each item range from (0-never or rarely to 3-most of the time/all of the time). Responses (range 0–60) are then summed with higher total scores denoting greater severity of depression.

Brief Pain Inventory-Short Form (BPI-SF)

The BPI-SF is a well validated pain scale used to measure self-reported pain severity as well as pain interference.[26] The BPI-SF pain severity subscale examines 4 aspects of pain (worst pain, least pain, average pain, and pain right now) over the past 24 hours. The pain interference subscale examines the extent to which pain has interfered with several daily activities (ie, general activity, walking, work, mood, enjoyment of life, relations with others and sleep). Individual items are scored using a scale of 0 (no pain or does not interfere) to 10 (worst imaginable pain or completely interferes) then summed to create a composite score for each subscale. Higher scores are indicative of greater pain severity and/or greater pain interference.

25-Hydroxyvitamin D

Blood samples were collected from participants' antecubital fossa at the beginning of the study session. Following collection and processing, serum was stored in a −80°C freezer. Serum 25-Hydroxyvitamin D analysis was performed by immunofluorescence, using a TOSOH Bioscience AIA 900 (South San Francisco, CA) within 6 months of the date of collection. Clinical guidelines provided by The Institute of Medicine (Health and Medicine Division of the National Academies) were used to categorize participants' Vitamin D levels as either optimal (≥20 ng/mL), insufficient (12–19 ng/mL) or deficient (<12 ng/mL).[27]

Body Mass Index (BMI)

Because of the known influence of body composition and adiposity on circulating levels of Vitamin D, BMI was calculated from height and weight measurements to be used as a covariate. Using the same stadiometer for all study participants, their height was assessed to the nearest 0.1 centimeter (cm). This instrument was calibrated prior to every use with a standardized measuring rod. Body weight was measured to the nearest 0.1 kilogram (kg). BMI was computed based on the following formula: weight in kg/height in m^2.

Data Analysis

Prior to analyses, the dataset was cleaned to case-wise remove participants who did not have complete variables of interest and covariates. All statistical analyses were performed using SPSS version 25.0 (IBM; Armonk, NY). Pearson's correlations were used to assess the strength and direction of associations among continuous variables. Analysis of covariance (ANCOVA) and chi-square statistics were employed to evaluate mean differences and associations among categorical variables, respectively. An analysis of covariance (ANCOVA) was used to explore differences in self-reported pain severity according to Vitamin D levels (optimal, insufficient, deficient). Bonferroni correction was used posthoc to account for family-wise error rate. Alpha was set as $p < 0.017$.

Results

Participant Characteristics

Prior to completion of analyses, each variable was examined to identify missing values, statistical outliers, and the violation of relevant assumptions. It must be noted that 8.23% of the overall cases (across groups) were deleted listwise due to missing data. Thus, the sample size of this study was n = 155. The mean age of the total sample was 45.4 (±13.8) years, with a greater proportion of NHB (61.9%) and female (60%) participants. There were no significant sex

Table 1 Sample Characteristics Stratified by Race

Variable	Total Sample	NHB	NHW	p-value
Total N	156	97	59	-
Age (years)	45.5 (±13.8)	45.4 (±12.8)	45.6 (±15.5)	0.947
Sex Male Female	 63 (40.4) 93 (59.6)	 38 (39.2) 59 (57.1)	 25 (42.4) 34 (57.6)	0.695
Vitamin D (ng/mL)	22.9 (±11.2)	20.5 (±11.1)	26.9 (±10.3)	<0.001*
Vitamin D Status Deficient Inadequate Adequate	 21 (13.5) 49 (31.4) 86 (55.1)	 19 (19.6) 36 (37.1) 42 (43.3)	 2 (3.4) 13 (22.0) 44 (74.6)	<0.001*
Self-Reported Pain Scores(BPI)	4.6 (±2.4)	5.0 (±2.6)	3.9 (±1.9)	<0.001*
BMI	31.3 (±7.4)	32.7 (±8.1)	29.0 (±5.8)	<0.001*

Note: *$p < 0.05$.

differences among variables of interest (ie, Vitamin D, pain severity and pain interference). Of the total sample, 21 (13.5%) were classified as Vitamin D deficient, 49 (31.6%) as insufficient, and 85 (54.8%) as optimal. A full breakdown of the sample characteristics stratified by ethnicity/race can be seen in Table 1.

Ethnic/Racial Differences in Vitamin D Status and Pain Severity

A chi-square test of independence was completed to examine the association between race and guideline concordant Vitamin D levels. As demonstrated in Figure 1, analyses revealed that a significantly greater proportion of NHB (19.6%) versus NHW (3.4%) participants were categorized as Vitamin D deficient (X^2 (2, N = 155) = 16.79, $p < 0.001$). An ANCOVA revealed that when controlling for age, sex and BMI, NHBs reported significantly greater pain severity relative to NHWs (F (1150) = 6.45) $p = 0.012$, as demonstrated in Figure 2. NHBs also reported significantly greater pain interference than their white counterparts, $p = 0.013$; however, the observed racial difference was attenuated after controlling for relevant covariates (age, sex and BMI) (F (1150) = 3.55) $p = 0.061$.

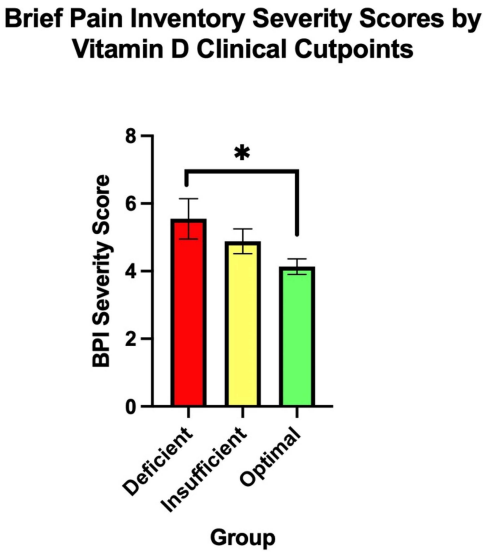

Figure 1 BPI scores of the sample categorized as deficient, insufficient, or optimal Vitamin D levels (*p < 0.05).

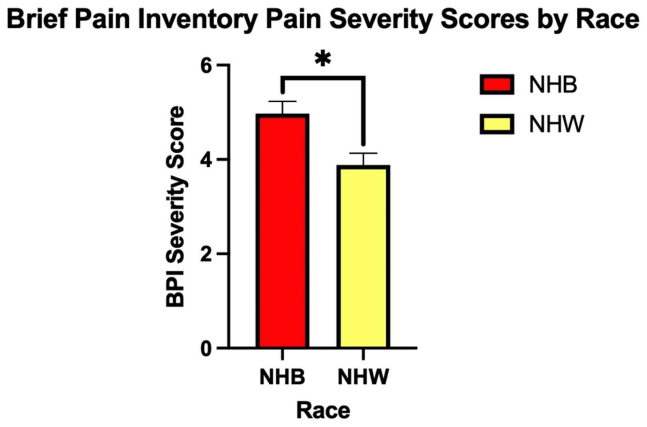

Figure 2 Self-reported pain severity scores across racial/ethnic groups (*p < 0.05).

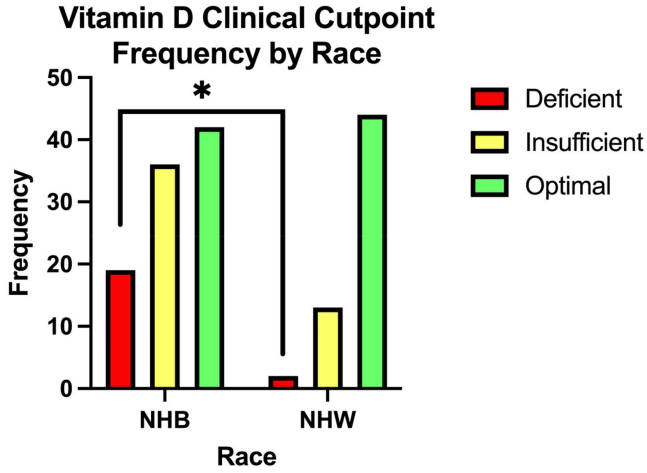

Figure 3 Differences in vitamin D status by clinical categories (deficient, insufficient, optimal Vitamin D across ethnic/racial groups (*p < 0.05).

Differences in Pain Severity According to Vitamin D Level

An ANCOVA revealed that even when controlling for age, sex and BMI, self-reported pain severity significantly differed according to Vitamin D level (F(2150) = 4.19, p = 0.013). Further, a follow-up ANCOVA with Bonferroni correction revealed that participants with deficient levels of Vitamin D reported significantly greater pain severity (F(1101) = 7.28, $p = 0.008$) in comparison to participants with optimal levels of Vitamin D. The same was observed in pain interference, however the results were no longer significant after controlling for multiple comparisons (F(2, 149) = 3.56 $p = 0.031$). Comparative results for Vitamin D categories are illustrated in Figure 3.

Discussion

In line with findings from previous studies, we found that vitamin D deficiency was significantly associated with greater self-reported pain severity in adults with cLBP.[11,28] Additionally, NHB individuals were more likely to be classified as vitamin D deficient compared to NHWs. Participants with optimal Vitamin D levels reported significantly lower pain severity compared to those classified as deficient, and the percentage of individuals reporting adequate levels of Vitamin D (55%) were on par with literature published from other southern geographical regions.[29] Findings from the current study remained significant even after controlling for covariates known to affect Vitamin D status and pain, such as age, sex, and BMI.

Current research is documenting Vitamin D as having significant associations with pain outcomes, including those with cLBP. Vitamin D is a fat-soluble secosteroid molecule that is found naturally in foods such as fish and seafood, and is also present in fortified dairy, fruit juices and other foodstuffs. Historically known for its usage in calcium regulation and bone health, advances in technology have allowed for the uncovering of the responsibilities that Vitamin D has outside of the musculoskeletal system. Upon the discovery of the VDR, which is found on many cell surfaces and DNA promoter regions, it has been documented that Vitamin D aids in the regulation of many endocrine,[30] nervous,[31] and immune system[32] processes. In terms of chronic pain, the idea of nociception and the perception of noxious stimuli within the central nervous system is historically well established. More recently, it has been noted that chronic immune system activation is essential for the development and maintenance of chronic pain.[33] Given that the immune system is responsible for inflammatory responses to allergens, pathogens, and injury, it is not bold to hypothesize that hyperalgesic priming and pronounced pain responses would be present if this system were to be chronically activated.[34] The VDR has been documented to be present on macrophages, an immune cell crucial in the peripheral immune response that is involved in the production of many inflammatory cytokines. Studies have shown that Vitamin D can dose-dependently inhibit the production of pro-inflammatory molecules mitogen activated protein kinase p38, Interleukin-6, and Tumor Necrosis Factor-α, as well as inhibit the proinflammatory nuclear factor κ-light-chain-enhancer of activated B cells (NFκB) and Interferon-γ pathways. We have previously noted differences in inflammation between those with and without cLBP,[22] and that diet-induced inflammation may contribute to greater movement evoked-pain in individuals with cLBP.[35] Moreover, a retrospective analysis examining vitamin Ds associations with cLBP noted that the relationship between the two may be mediated by these inflammatory biomarkers.[36] Additionally, bound vitamin D to the VDR has also been shown to repress genes involved in the formation of activated T cells, further reducing pro-inflammatory cytokine expression.[37] In our sample, NHBs were more likely to have sub-optimal levels of Vitamin D, so it is possible that the deficiency of this micronutrient could be contributing to immune system dysregulation, increased levels of inflammation, and increased pain prevalence and severity within this population with cLBP. Interestingly, studies aiming to look at improved pain outcomes through Vitamin D supplementation have noted significant decreases in pain severity and disability,[38,39] though results are mixed.[40,41] More research including the expansion across racial groups is necessary.

Additionally, there is evidence that nutritional intake varies substantially between NHBs and NHWs, and there are a variety of factors that are known to underlie the relationship. It should be noted that vitamin D is only naturally-occurring in foods such as fish and eggs, as well as in fortified foods such as dairy products that require refrigeration.[42] Geographic residence is thought to play a significant role in dietary behaviors. In many cities, a higher percentage of NHBs live in low-income environments compared to NHWs.[43] Research has shown that even wealthy, college-educated NHB individuals are may feel marginalized and often live in neighborhoods with 30% less income compared to NHW neighborhoods.[44] Income and neighborhood disadvantage are associated with poorer diet quality[45] and are correlated with excess meat intake, and limited consumption of fruits, vegetables and fish.[46] Food deserts – areas where residents have little to no access to healthy and affordable food options – is also more often reported in NHB neighborhoods, and these areas are more likely to report lower-quality and a limited selection of food.[47] This condition may be, in part, a by-product of racial segregation and redlining, as NHB individuals were limited in the past to food access and this injustice has not effectively been rectified to this day.[48] In one study, adherence to plant-based dietary habits (ie, vegetables of many types, fish, soups) were positively associated with socioeconomic status (SES). Additionally, it was shown that NHWs were more apt to maintain a plant-based diet, likely due to differences in average household income and access to plant-based food options between the two groups. Stronger adherence to a "Southern dietary pattern" (ie, fried food, soda, and processed meats) was reported more among NHBs.[49] It is well established that poor dietary habits can lead to a higher BMI, and in our sample, NHB participants also presented with greater BMI than their NHW counterparts. Because Vitamin D is a fat-soluble Vitamin, if there is a greater presence of adipose tissue, Vitamin D will deposit and likely remain deposited there rather than circulate in blood, resulting in decreased bioavailability of the nutrient.[50] Together, these data support the notion that there are racial differences in food intake and dietary patterns that could be influencing Vitamin D status.

Finally, the contrast of the skin pigment melanin between NHBs and NHWs likely contributes to a large percentage of the differences seen in Vitamin D levels. A large percentage of human Vitamin D is derived from the endogenous

production of 25-hydroxyvitamin D from 7-dehydroxycholesterol catalyzed by UVB radiation from the sun. Melanin, the pigment in our skin, hair and eyes that gives it color based on concentration levels, is used in the skin to physically block harmful UV rays from damaging cells. Individuals with darker skin pigmentation have more melanin present, making it more difficult for UVB rays to penetrate the layers of the epidermis to catalyze the creation of Vitamin D.[16,20] Seasonal weather shifts and the change in the angle of the sun also decreases the amount of light and subsequent UVB rays reaching the surface of the skin, especially for those who reside in geographical regions where the average amount of daylight decreases dramatically during the autumn and winter months.[51] Additionally, it is possible that NHBs, with greater cLBP severity, experience more disability. As a result, this subgroup may be more apt to staying indoors which undoubtedly would limit their exposure to sunlight.

We acknowledge that there are limitations of this study. Firstly, having only 2 NHW participants with deficient Vitamin D status, limited our ability to test whether ethnicity/race interacted with Vitamin D status in relation to pain. Thus, the hypothesis that NHBs with deficient Vitamin D will have the greatest pain severity is only indirectly supported. Our sample size was relatively small, though it yielded large effects, and future studies should aim to replicate these data in a larger sample. Additionally, the cross-sectional nature provided us with a window into the health outcomes of our sample in the present moment, but does not evaluate effects of Vitamin D over time, nor provide a temporal relationship between Vitamin D and pain experience. Additionally, the studied population is that of an area in the south with limited walkability, lack of public transportation and public services, and specific cultural beliefs when it comes to diet, stigma with pain, and treatment. However, because of the southern geography, the angle of the sun and amount of sun present will also be different compared to northern geographies. Additionally, this study did not provide any form of treatment to see if those with decreased levels of Vitamin D saw any improvement in pain sensitivity after supplementation; this would be a potential area for future research. Future research may want to also consider sun exposure and physical activity levels and its relationship to cLBP and Vitamin D levels.

Conclusion

In conclusion, findings from this study suggest that Vitamin D deficiency may be linked to greater pain severity in a sample of individuals with cLBP, especially for those who identify as NHB. Future research should consider a longitudinal design given the fluctuating nature of Vitamin D based on the variety of factors discussed, including the time of year in which the blood samples were collected. Continuing to understand the mechanisms behind the effects that Vitamin D status could have on the pain experience as a whole, and the degree by which it may be mitigating the disparities seen in cLBP is imperative in order to decrease differences seen across populations.

Data Sharing Statement

Data will be made available upon reasonable request by contacting Dr. Burel Gooding bgoodin1@uab.edu.

Ethics Approval

All protocols were reviewed and approved by the Institutional Review Board (IRB) at the University of Alabama at Birmingham.

Consent to Participate

All participants were given written informed-consent prior to study commencement as approved by the IRB at the University of Alabama at Birmingham.

Acknowledgments

The authors are grateful for the contributions to data collection by the Biobehavioral Pain Lab study team at UAB, and Greta Strath for her support in conceptualization and drafting of the manuscript. Demario S Overstreet and Larissa J Strath are co-first authors for this study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

Financial support for this research was provided by the University of Alabama at Birmingham Health Services Research Training Program award T32HS013852 (D.S.O.), the National Institute on Minority Health and Health Disparities of the National Institutes of Health under award number R01MD010441 (B.R.G.), and by Clinical and Translational Science Award number UL1TR001417, provided to the University of Alabama at Birmingham from the National Institutes of Health Center for Advancing Translational Sciences.

Disclosure

Dr D Leann Long reports grants from Amgen, Inc., outside the submitted work. The authors have no other conflicts of interest to report for this work.

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