Meta-Analysis

High Prevalence of Hypovitaminosis D in Patients with Low Back Pain: Evidence from Meta-Analysis

Dipika Bansal, MD, DM[1], Chandra Sekhar Boya, MPharm, PhD[1], Rambabu Vatte, MPharm[1], and Babita Ghai, MD, DNB[2]

From: [1]Clinical Research Unit, Department of Pharmacy Practice, National Institute of Pharmaceutical Education and Research, SAS Nagar, Punjab, India; [2]Department of Anaesthesia, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Address Correspondence: Dipika Bansal, MD, DM Clinical Research Unit, Department of Pharmacy Practice, National Institute of Pharmaceutical Education and Research, SAS Nagar Punjab, India-160062 E-mail: dipikabansal079@gmail.com

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Background: Emerging evidence suggests an association between vitamin D deficiency and low back pain (LBP).

Objective: To pool evidence on the prevalence of hypovitaminosis D in patients with LBP.

Study Design: Meta-analysis.

Methods: A comprehensive literature search was done in PubMed, Cochrane Database, and Google scholar for observational studies including cohort, cross sectional (CS), and case control (CC) evaluating the prevalence of hypovitaminosis D in LBP patients. The primary outcome assessed was a prevalence of hypovitaminosis D in patients with LBP, presented as weighted pooled prevalence ratio (WPPR) with 95% confidence interval (CI) using the random effects model. Heterogeneity and inconsistency of the measurements were identified through Cochran's Q statistic and I^2 statistic. We also performed sensitivity analysis, publication bias (using funnel plot and Begg's test), and subgroup analysis.

Results: Fourteen studies (6 were CC, 6 CS, and 2 cohort) involving 2602 patients were included in the final analysis. The WPPR (95% CI) of hypovitaminosis D in patients with LBP was found to be 0.72 (0.60–0.83). Marked heterogeneity was observed, median quality score of all studies was 7.5 interquartile range (IQR) (6.2 - 8.7) on a scale of 0 to 11. Sensitivity analysis showed robustness of the results. The WPPR of hypovitaminosis D was lower in CS at 0.60 (0.35–0.85) as compared to CC studies at 0.81 (0.72–0.90) ($P < 0.01$). The WPPR was lower in men at 0.74 (0.63–0.86) as compared to women at 0.84 (0.78–0.89) ($P < 0.01$). No publication bias was observed.

Limitations: Heterogeneity in the cut off level of vitamin D to classify the included patients as vitamin D deficient.

Conclusions: The high prevalence of hypovitaminosis D was observed in patients with LBP. This provides a chance to screen the deficiency and correct it by supplementation, which can be therapeutic adjunct in the management of LBP patients.

Key words: Low back pain, hypovitaminosis D, meta-analysis, pooled prevalence, systematic review

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Evidence has linked low levels of vitamin D with higher incidence of chronic pain (1). It is well established that low vitamin D levels lead to osteomalacia resulting in bony pains (2). However, no clear biological mechanism is postulated for causally relating its low levels with other varieties of chronic pain. Low back pain (LBP) is a major public health concern leading to enormous disability and reduced health related quality of life (HRQOL) (3-5). Evidence suggests a link between vitamin D deficiency and LBP (6).

Vitamin D refers to a group of fat-soluble steroids of which vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol) are the most important active compounds of the vitamin D group in human. 25-hydroxyvitamin D (25(OH)D) is the most commonly measured metabolite because of its 1000-fold higher serum concentrations and greater half-life of around 3 weeks as compared to the physiologically active metabolite 1,25-dihydroxyvitamin D having half-life of few hours (7). Vitamin D controls calcium homeostasis and metabolism (8). Additionally, it is involved in bone formation, resorption and mineralization, and maintains neuromuscular function (8). Vitamin D is also implicated in regulating inflammatory cytokine synthesis (8).

Vitamin D deficiency is reported in various disorders like chronic musculoskeletal pain such as osteoporosis, rheumatoid arthritis, osteoarthritis, soft tissue rheumatism, LBP, and arthralgia (2). Its deficiency is associated with muscle weakness, bone pain, and osteomalacia in adults and rickets in children (2). Although obtained from dietary sources, its main source of cutaneous production is under the direct influence of solar ultraviolet B (UVB) radiation (9). The UVB exposure varies with the geographical location and season, so average 25(OH) D concentrations of populations also vary accordingly. The patients with persistent musculoskeletal pain, especially LBP patients, are at a higher risk of developing consequences of unrecognized and untreated vitamin D deficiency. Vitamin D supplementation, together with calcium, has demonstrated its effectiveness in lowering fracture risk in osteoporotic patients (10). In recent pooled evidence involving 19 studies, vitamin D supplementation is shown to decrease pain scores in patients with chronic pain (11).

Extensive literature search revealed no published systematic review and meta-analysis that provides a comprehensive review about quantification of prevalence of vitamin D deficiency in patients with LBP. Thus, the present analysis is planned to aggregate evidence on the relationship between vitamin D deficiency and LBP. This evidence generation may provide a useful guide for the planning of future studies and public health policies for prevention and treatment of vitamin D deficiency in LBP patients.

Methods

The present analysis was conducted according to the guidelines outlined in Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The (PRISMA) Statement.

Study Eligibility

Eligible studies are observational studies including cohort, cross sectional, and case-control studies that evaluated the prevalence of hypovitaminosis D in patients with LBP, published in English language. We excluded articles if they were reviews, letters to the editor without original data, editorials, case reports, and articles containing nonhuman data.

Vitamin D deficiency is defined as a serum 25(OH)D less than 20 ng/mL; insufficiency is considered at levels between 20 to 30 ng/mL. For the purpose of the present analysis and clarity of presentation, we categorized patients with less than 30 ng/mL as hypovitaminosis D, though this definition would also include patients technically categorized as vitamin D insufficient (10,12). For uniformity, vitamin D concentrations reported in various units of measurement (nmol/L, mcg/L) were converted to ng/mL.

Information Sources and Search Strategy

A literature search was done independently by 2 authors (DB, CS) in PubMed and Google scholar for observational studies. The primary search included the Medical Subject Headings (MeSH) keywords "25-hydroxyvitamin D" OR "vitamin D" AND "low back pain" OR "backache" OR "back pain" OR "lower back pain" OR "radiculopathy" OR "radicular pain" AND "hypovitaminosis" OR "vitamin D insufficiency " OR "deficiency".

Data Collection and Extraction

The articles identified in the databases were selected independently by 2 authors (VR, CS) and then the selected article titles and abstracts were examined for eligibility to be included in the study according to the inclusion and exclusion criteria. Studies which did not meet the inclusion criteria were excluded. Studies which have divergent opinion were selected according to a consensus reached between the reviewers. In the absence of a consensus, a third reviewer (DB, BG) evaluated the eligibility of the study in question.

Afterwards, the full texts of the remaining studies were completely read to extract data on the predesigned data collection form (DCF). To minimize errors in data entry, 2 reviewers (CS, VR) independently extracted and entered data in the DCF. For each eligible study, the following information was abstracted: 1) first author's last name, year of publication, and country of the population studied; 2) study design, the number, gender, and ages of patients; 3) definitions of vitamin

D deficiency and/or insufficiency and the prevalence of each condition; 4) number and type of patients, methods used to assess hypovitaminosis D, duration of LBP, cause of LBP, and other relevant information.

Methodological Quality of Studies

Two reviewers (CS, SM) independently assessed the methodological quality of each study by using The Joanna Briggs Institute Critical Appraisal checklist tool (13), which has been developed for the critical appraisal of prevalence studies. It consists of 10 questions and each question is categorized into yes, no, unclear and not applicable. For each study, questions getting answers of "yes" were awarded a score of "1," whereas answers of "no" or "unclear" were awarded a score of "0." The summed quality score for each study was obtained by adding the total score of all the questions from the checklist tool. Studies scoring ≥ 8 were considered as a high quality whereas studies scoring < 8 were considered as low quality. Any discrepancy in quality assessment was discussed and resolved in a discussion with the third reviewer (DB).

Statistical Analysis

Outcome Measures

The primary outcome measure was the weighted pooled prevalence of hypovitaminosis D in patients with LBP in all the studies irrespective of study design and presented as prevalence ratio (PR) with 95% confidence interval (CI). The results of pooled PR with 95% CI was presented as a forest plot. Results of the continuous outcome (vitamin D level) was reported as a standardized mean difference (SMD) with 95% CI.

Heterogeneity Testing

Heterogeneity and inconsistency is used to assess the variation between the study outcomes. Heterogeneity and inconsistency of the measurements were identified through Cochran's Q statistical test and I^2 statistic. Heterogeneity was considered as significant if $P < 0.10$, $I^2 > 50\%$ for Q statistic test and I^2 statistic, respectively. If heterogeneity existed and was confirmed, then random effects model was applied with inverse variance to pool the studies, otherwise fixed effects model was chosen.

Subgroup Analysis

Subgroup analyses were performed to assess the source of heterogeneity according to the study design, gender, study country, and cut off values for vitamin D deficiency and quality of studies. We also performed sensitivity analysis to evaluate the stability of our results and to determine the influence of an individual study by estimating the pooled PR excluding one study at each time.

Publication Bias

Publication bias refers to the possibility of a systemic bias due to over-reporting of positive results. It was assessed by using a funnel plot and the Begg's test (14). If publication bias was found, we applied the Trim and Fill method to negotiate the lack of studies on a particular side of the funnel (15).

All statistical tests were 2-sided, and $P < 0.05$ was considered statistically significant, except where otherwise specified. All data analyses were performed using STATA version 11.0 (StataCorp, College Station, TX).

Results

Three hundred and ninety-nine articles were retrieved from different databases using the above described search strategy. We excluded 372 articles after analyzing the titles and abstracts. Full texts were retrieved for remaining 27 articles and were read thoroughly. After this, 13 articles (3 case reports, 3 lettrs to the editor, 4 not matching inclusion criteria, and 2 clinical trials) were excluded. Finally, we identified 14 relevant articles and included them in the present analysis (Fig. 1).

Study Characteristics

Among the 14 included studies, 6 were case-control (16-21), 6 were cross sectional (22-26), and 2 were cohort studies (27-28). Seven studies had included patients with chronic LBP (> 12 weeks) (6,17,20-22,26,28). Data on chronicity of LBP was not mentioned in the other studies. The pooled sample size was 2602 with individual sample sizes ranging from 44 to 360 in different studies. All studies were published in the English language and were conducted in a hospital setting.

The majority (12 (85.7%)) were published between the years 2011 and 2016. Ten (71%) studies were conducted in Asia (6,16-19,23,24,26-28) and 4 (39%) in non-Asian countries including Denmark (22), Morocco (20), USA (25) and southern Sweden (21). Two studies were conducted in Iran (17,24), 3 in India (6,18,26), and one each in Pakistan (28), Saudi Arabia (27), Turkey (16), Egypt (19), and South Korea (23). Four studies had recruited women only (17,19,20,24), while other studies have included patients of either gender. The age range

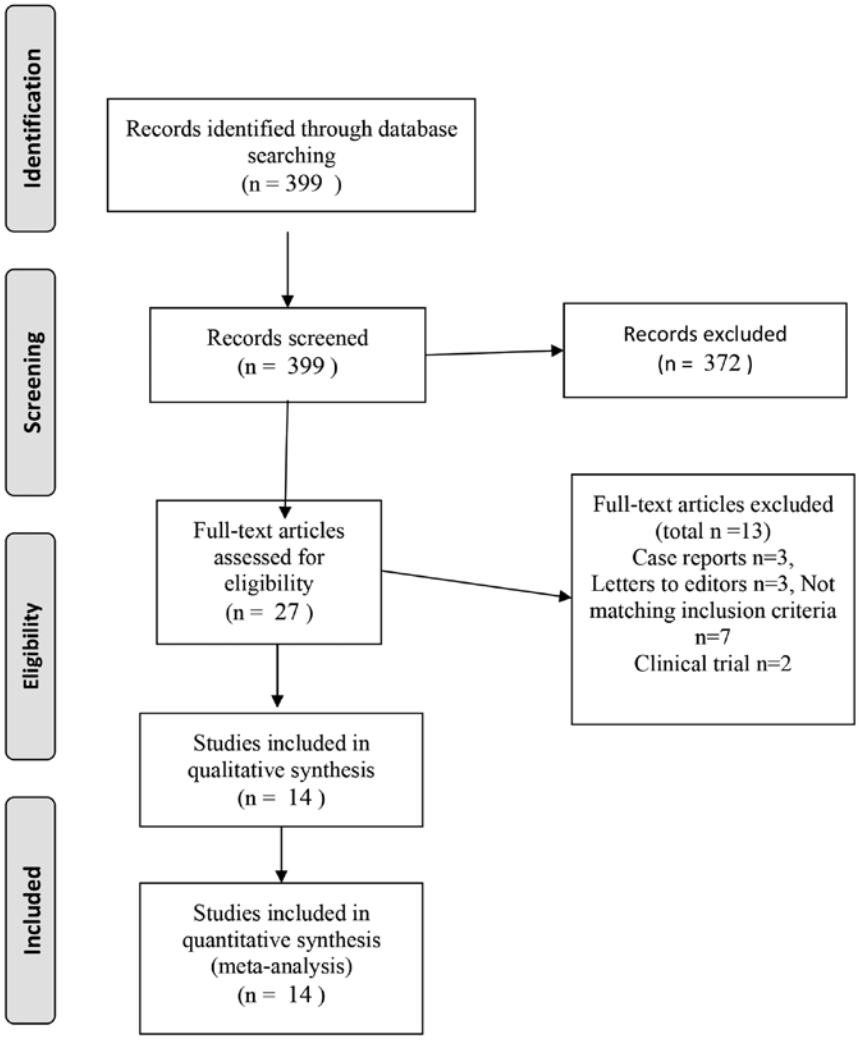

Fig. 1. *PRISMA chart showing the literature search procedure.*

in 12 studies was from 30 to 66 years, while 2 studies did not report the average age data (27,28) (Table 1).

Plasma 25(OH)D levels were measured by electro-chemi luminescence immunoassay in 5 studies (6,17,18,20,24), radioimmunoassay in 3 (19,23,27), high performance liquid chromatography in one (16), and liquid chromatography-mass spectrometry in one (21). The cut-off values for the classification of patients with vitamin D deficient were in the range of levels below 20 to 40 ng/mL and for vitamin D insufficient it was found to be less than 20 to 30 ng/mL. Only 6 studies: Ghai et al (18), Kim et al (23), Johansan et al (22), R kain et al (20), Sunny G et al (26) and Thorneby et al (21), had reported the season of 25(OH)D measurement (18,20-23,26).

Quality Assessment

The median quality score of all included studies was 7.5 (range of 6-9). Seven studies (18,20,22,23,26-28) had high quality and 7 (6,16,17,19,21,24,25) had low quality. The majority of low quality studies did report the items regarding reliability of measurements (Q7), adjustment of confounding variables (Q9), and the use of objective criteria to identify sub-populations (Q10) of the checklist (Table 2).

Table 1. *Characteristics of studies included in the analysis to assess prevalence rate of hypovitaminosis D in patients with LBP.*

Author	Baykara et al (16)	Al Faraj et al (27)	Heidari et al (17)	Johansen et al (22)	Lodh et al (6)	Kim et al (23)	Lotfi et al (19)	Madani et al (24)	Ghai et al (18)	Ravindra et al 25)	Siddique et al (28)	Rkain et al (20)	Mattam et al (26)	Thorneby et al (21)
Publication year	2014	2003	2014	2013	2014	2013	2007	2014	2015	2014	2011	2013	2016	2016
Study design	CC	Cohort	CC	CS	CS	CS	CC	CS	CC	CS	Cohort	CC	CS	CC
Location	Turkey	Saudi Arabia	Iran	Denmark	India	Korea	Egypt	Iran	India	USA	Pakistan	Morocco	India	Sweden
Season measurement	NR	NR	NR	March- May	NR	Throughout year	NR	NR	Throughout year	NR	NR	June-August	Jan-Dec	March-June, Oct-Nov
Gender	F-37 M-23	NR	F-81 M-0	F-100 M-52	F-146 M-54	F-268 M-82	F-60 M-0	F-148 M-0	F-156 M-172	NR	F-181 M-62	F-105 M-0	F-172 M-144	F-26 M-18
Age, mean (SD)	30.58 ± 7.78	NR	35.1 ± 8.14	44.6 ± 11.2	46.19 ± 15.69	66.1	32.8 ± 7.1	32.05	43.8	57 ± 13.9	NR	56.5 ± 5.6	40.9 ± 14.5	55 ± 16
Type of LBP	chronic	NR	chronic	chronic	chronic	NR	chronic	NR	chronic	NR	chronic	chronic	chronic	chronic
Method of assessment	HPLC	RIA	ECLIA	LC-MS	ELISA	RIA	RIA	ELISA	ECLIA	NR	NR	ECLIA	Chemilumin-escence	HPLC-MS
Cut off value of vitamin D (ng/mL)	N-10-60 D- < 10	N-9-37.5 D- < 9	N- > 20 D- < 20	N- > 20 D- < 20	N- > 30	N- > 30 D- < 20	N– 40 D- < 20-40	N- 30-100 D- < 30	N- > 30 D- < 20	N- > 30 D- < 20	N- > 30 D- < 30	N- > 30 D- < 20	N- > 30 D- < 20	N- > 30 D- < 10
Total number of patients	60	360	81	152	200	350	60	200	328	103	243	105	316	44
Patients with insufficiency	-	-	-	-	100	80	-	-	65	-	-	18	66	24
Patients with deficiency	53	299	57	53	-	260	49	178	217	28	197	83	190	0
hypovitaminosis D Prevalence (%)	88.3	83	70.4	34.9	50	97.1	81.7	93.2	86	27.2	81	96.1	81.01	54.54

CS = Cross sectional; CC = Case control; NR = Not reported; F = Females; SD = Standard deviation; M = Males; N = Normal level of vitamin D (ng/mL); D = Vitamin-D deficiency level (ng/mL); I = Vitamin-D insufficiency level (ng/mL); HPLC = High performance liquid chromatography; RIA = Radio immunoassay; ECLIA = Electrochemiluminescent immunoassay; LC-MS = Liquid chromatography–mass spectrometry; LBP = Low back pain.

Prevalence of Hypovitaminosis D in Patients with LBP

As significant heterogeneity was found between studies (Cochrane Q = < 0.01, I^2 = 98.82), random effects model was chosen (Table 3). The present meta-analysis included 2602 patients with LBP, of whom 1987 (76.3%) had hypovitaminosis D. The weighted pooled PR (95% CI) of hypovitaminosis D in patients with LBP in all the included studies was 0.72 (0.60–0.83) (Fig. 2). The PR of hypovitaminosis D ranged from 15–97%. None reported zero prevalence. This supports the hypothesis that a substantial amount of vitamin D deficiency (72%) is present in patients with LBP and contributes to the overall disability. The PR of hypovitaminosis D in patients with LBP for all studies are shown in Fig. 2.

Sensitivity Analysis

A sensitivity analysis was conducted to estimate the impact of any single study on the combined result. It was performed by omitting one study at a time and recalculating the pooled PR of the remaining studies. The sensitivity analysis showed robustness of the results (pooled PR value lied between 0.75 and 0.82). Thus, it is clear that no single study had a major impact on the pooled PR.

Subgroup Analysis

The weighted pooled PR of hypovitaminosis D in patients with LBP was lower in cross sectional studies (n = 6), 0.60 (0.35–0.85) as compared

Table 2. *Methodological quality assessment*.

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Total score	Quality
Johansen et al (22)	1	1	0	1	1	1	1	1	1	0	8	High
Kim et al (23)	1	1	1	1	1	1	1	1	1	0	9	High
Lodh et al (6)	1	1	1	0	1	1	1	0	1	0	7	Low
Madani et al (24)	0	1	1	1	1	1	0	1	0	1	7	Low
Mattam et al (26)	1	1	1	1	1	1	1	1	0	1	8	High
Al Faraj et al (27)	1	1	1	1	1	1	1	1	0	0	8	High
Siddique et al (28)	1	1	1	1	1	1	1	1	1	0	9	High
Baykara et al (16)	1	1	0	0	1	1	0	1	1	1	7	Low
Heidari et al (17)	1	0	1	1	1	1	0	0	1	0	6	Low
Ravindra et al (25)	1	0	1	0	1	0	0	1	1	1	6	Low
Rkain et al (20)	1	1	1	0	1	1	1	1	1	1	9	High
Thornby et al (21)	1	1	1	1	1	1	0	1	0	0	7	Low
Lotfi et al (19)	1	0	1	0	1	1	1	1	0	1	7	Low
Ghai B et al (18)	1	1	1	1	1	1	0	1	1	1	9	High

Table 3. *Subgroup analysis*.

Study characteristics	Sub groups	No. of studies	No. of patients	Hypovitaminosis D			Heterogeneity	
				No. of hypovitaminosis D patients	PR (95% CI)	*P*-value	I^2	$P_{Interaction}$
All studies		14	2602	1987	0.72 (0.60, 0.83)	< 0.01	98.82	< 0.01
Study design	Cohort	2	603	496	0.82 (0.79, 0.85)	< 0.01	0	< 0.01
	Case-control	6	678	566	0.81 (0.72, 0.90)	< 0.01	90.70	
	Cross sectional	6	1321	925	0.60 (0.35, 0.85)	< 0.01	99.52	
Gender	Male	5	352	431	0.74 (0.63, 0.86)	< 0.01	89.41	< 0.01
	Female	9	1391	1349	0.84 (0.78, 0.89)	< 0.01	89.27	
Continent	Asia	10	1918	1811	0.81 (0.74, 0.88)	< 0.01	96.47	< 0.01
	Non-Asia	4	404	206	0.53 (0.13, 0.94)	< 0.01	99.17	
Study quality	High (≥ 8 score)	7	1854	1498	0.77 (0.62, 0.93)	< 0.01	99.23	< 0.01
	Low (< 8 score)	7	748	489	0.66 (0.48, 0.84)	< 0.01	97.35	

PR: Prevalence ratio; CI: Confidence interval

to case control studies (n = 6) 0.81 (0.72–0.90) and cohort studies (n = 2) 0.82 (0.79–0.85), ($P_{interaction}$ = < 0.01) (Fig. 3). The pooled PR of hypovitaminosis D was lower in men (n = 352) 0.74 (0.63–0.86) as compared to women (n = 1391) 0.84 (0.78–0.89) ($P_{interaction}$ = < 0.01). The pooled PR of hypovitaminosis D was higher in Asians (n = 1918) 0.81 (0.74–0.88) ($P_{interaction}$ = < 0.01) as compared to non-Asians (n = 404) 0.53 (0.14–0.94) ($P_{interaction}$ = < 0.01). A significantly higher prevalence was found in high quality studies (n = 7) 0.77 (0.62–0.93) ($P_{interaction}$ = < 0.01) as compared to low quality studies (n = 7) 0.66 (0.48–0.84).

Publication Bias

No significant publication bias was observed among the included studies. Visual examination of the funnel plot revealed minimal asymmetry. Further, Duval and Tweedie's trim and fill method confirmed the absence of any missing studies. The pooled PR of hypovitaminosis D, 0.72 (0.60–0.83) was obtained using the random effects model, remains unchanged using trim and fill analysis (Fig. 4).

Vitamin D Level in Cases and Controls

Among included, 5 studies were reported vitamin

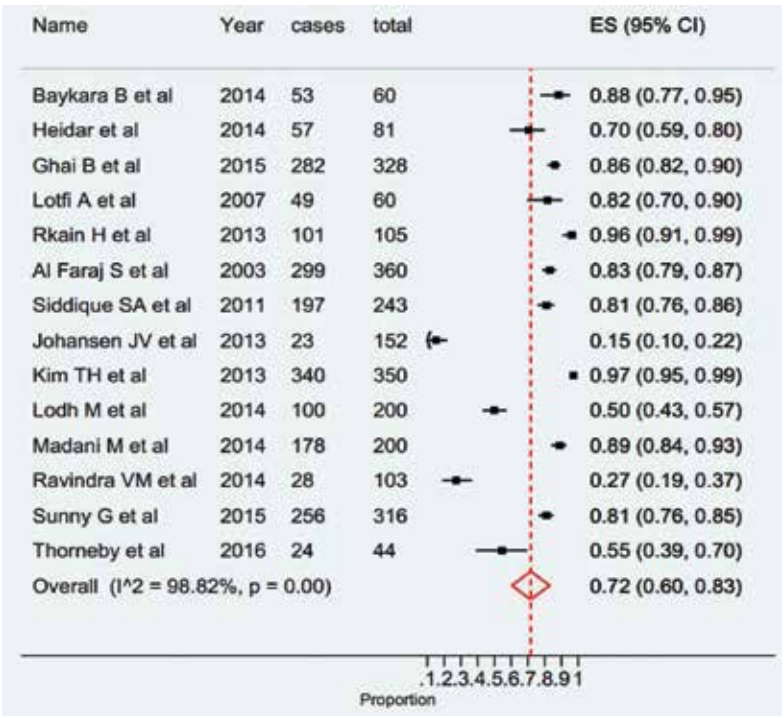

Fig. 2. *Forest plot showing a combined effect size (ES) and PR with 95% CI. The horizontal line indicates 95% CI and the diamond indicates overall pooled estimate.*

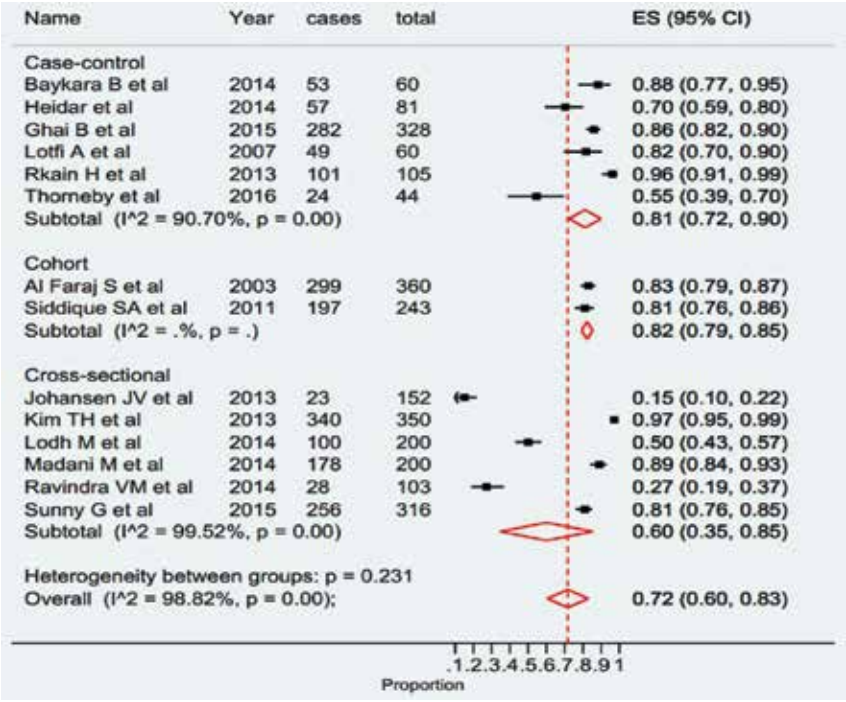

Fig. 3. *Forest plot showing subgroup analysis to assess the heterogeneity by study design. The horizontal line indicates 95% CI and the diamond indicates overall pooled estimate.*

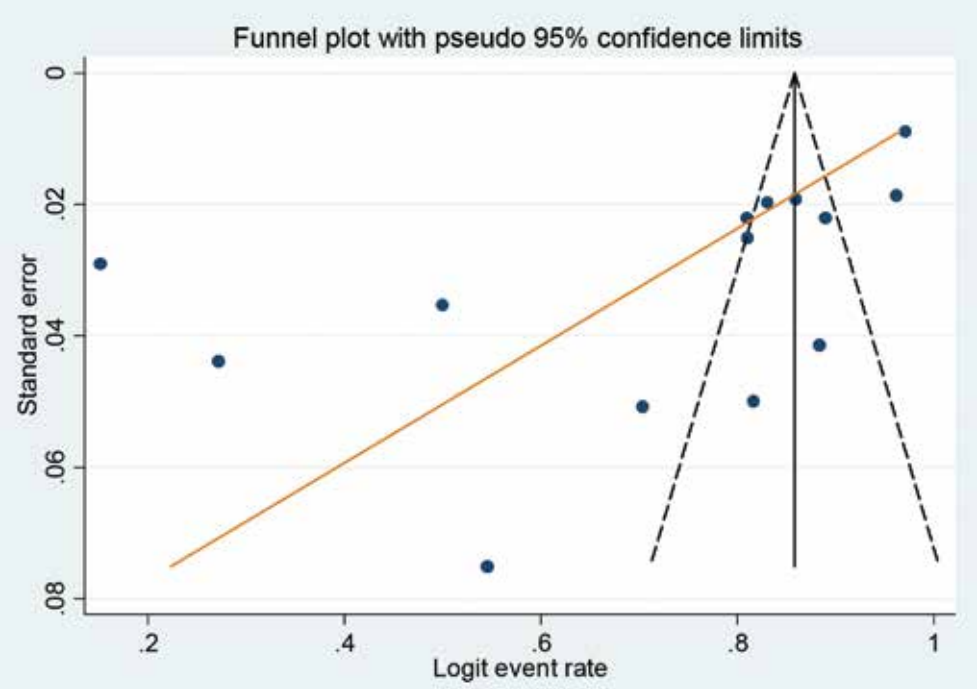

Fig. 4. *Shows the funnel plot regarding the publication bias.*

D level separately in cases and controls (6,16,17,19,20). Pooling the data from these 5 studies including 678 patients, cases (n = 502) with LBP and control (without LBP) (n = 361), the mean vitamin D levels in patients with LBP were significantly lower as compared to controls with a mean difference of -0.88 ng/mL (95% CI, -1.44 to -0.32) (Fig. 5).

Discussion

We conducted a systematic review and meta-analysis to evaluate the best available evidence regarding the prevalence of vitamin D deficiency in patients with LBP. We included 14 studies involving 2602 patients with LBP of whom 1987 (76.3%) had hypovitaminosis D and the weighted pooled PR of hypovitaminosis D was 72% (95% CI 60 - 83). This indicated the majority of the patients with LBP, irrespective of the etiology, suffer from vitamin D deficiency.

The exclusion of any single study did not have any major impact on the combined results as revealed by the sensitivity analysis (PR lied between 75–82%) showing the robustness of the results. Further, the robustness of the results and lack of publication bias was confirmed from the results of the Begg's test and Duval and Tweedie's trim and fill method. The overall quality of the included studies was fair. The included studies have reported the prevalence of hypovitaminosis D ranging from 27.2% (25) to 96.2% (20). These variations might be due to different sample sizes, which ranged from 44 (21) to 360 (27), different cut-off levels of vitamin D ranging from 10 (27) to 40 ng/mL (19), study quality (with high quality studies (77%) reporting high prevalence as compared to low quality studies (66%)), and study design with case-control studies reporting higher prevalence (81%) as compared to cross-sectional studies (60%).

Variable geographical location (Asian vs. European) might also result in a prevalence differences as this leads to variable sunlight exposure and skin color differences. Persons with lighter skin require increased UVB exposure for similar production of vitamin D as compared to persons with darker skin (29).

Studies conducted in Asian countries reported a higher prevalence (81%) as compared to non-Asian studies (53%). This might be due to high skin pigmentation and traditional clothing in Asian countries compared to other countries. One thing that could have been mentioned was the fact that sun exposure is not great in Sweden and Denmark. More sun exposure is noted in countries around the equator. Air pollution and limited outdoor activity further compounds this problem in the urban population (30,31).

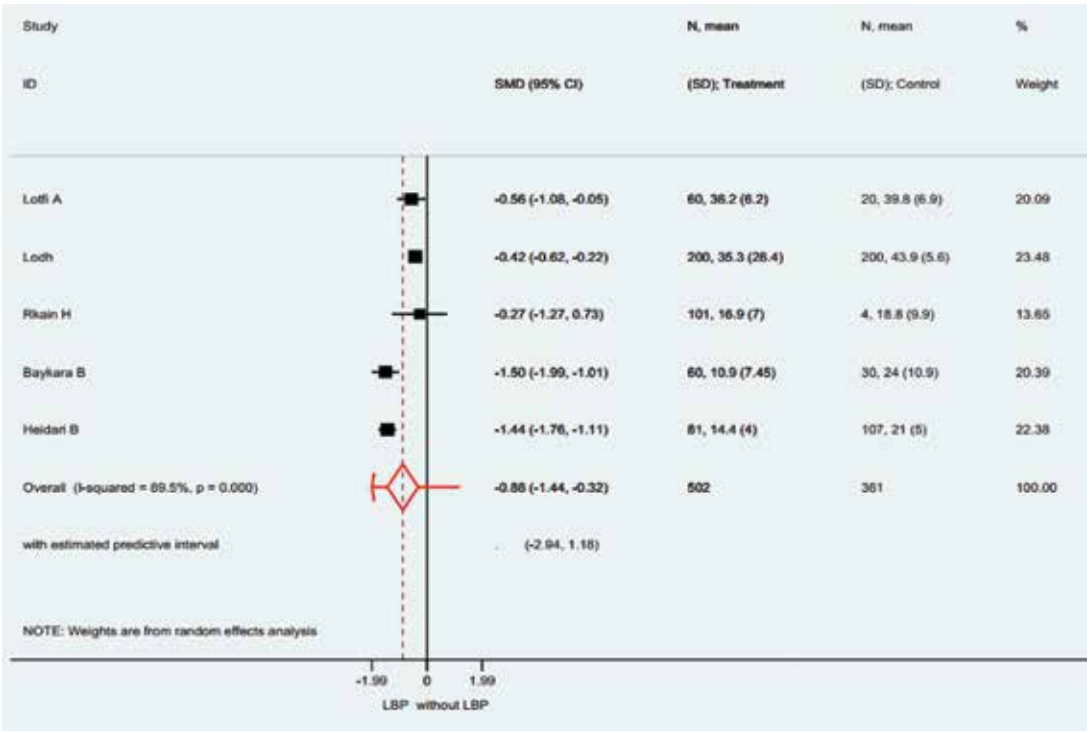

Fig. 5. *Forest plot showing the vitamin D level in cases and controls with 95% CI. The horizontal line indicates 95% CI and the diamond indicates overall pooled estimate.*

The prevalence of hypovitaminosis D was found significantly higher in women compared to men (84% vs. 74%). Evidence reports that women who wear complete coverage clothes are more prone to deficiency (32). Many women wear a hijab in some of the countries (Pakistan, Turkey, Saudi Arabia, Egypt, Morocco, and even in India). This may also contribute to low bone density in women in countries with good sun exposure. Deficiency has been found more prevalent among Muslim women wearing concealing clothes as their culture (33).

Serum vitamin D levels are strongly associated with chronic back pain of unknown etiology (6). Its deficiency may lead to enhanced nociception and impaired neuromuscular function (2). Hypovitaminosis D increases the susceptibility towards inflammation in the vertebral end plates leading to a decreased pain threshold, diffuse pain in bones and muscles, weakness, and paresthesia (8).

The prevalence of hypovitaminosis D is well documented globally in general populations with several types of chronic musculoskeletal disorders such as osteoarthritis, rheumatoid arthritis, and osteoporosis. The present analysis reports a strong association between LBP and low vitamin D levels. Recently a meta-analysis was conducted by Zadro J et al (34) to map the association between vitamin D and LBP. It reported that vitamin D deficiency is associated with LBP. This evidence strengthens the present study finding of a high prevalence of vitamin D in LBP.

The main source of vitamin D is skin exposure to solar UVB radiation. Physical factors that lead to attenuation of UVB exposure, including clothing, sunscreens, and latitudes above 37°N and below 37°S, reduce the skin production of vitamin D (30). Biological factors including skin pigmentation, medication use, body fat content, fat malabsorption, obesity, and advanced age, may also reduce cutaneous production by as much as 99.9% (12,31).

The patients in the present analysis were in the age range of 30 to 66 years, indicating that increasing age can be one of the risk factors for development of hypovitaminosis D. Studies have shown that aging is associated with decreases in 7-dehydrocholesterol, which is a cholesterol precursor found mainly in the skin, resulting in a decline of cutaneous vitamin D production in aged population (30,31).

Gendelman et al (35) assessed the impact of adding 4000 IU of vitamin D on pain intensity and serological parameters in patients with musculoskeletal pain in a randomized controlled trial (RCT). They reported that vitamin D supplementation leads to a significantly larger decline in pain intensity 48.6 (26) as compared to placebo 54.6 (28.3). This study also reported that the decrement in TNFα levels by 54.3% in vitamin D supplementation group as compared to 16.1% increment in the placebo group (35). Another study showed an improvement in pain scores by vitamin D repletion in patients with chronic back pain or failed back surgery (36). Our research group conducted an open label single group study and reported that oral vitamin D3 supplementation in a dose of 60,000 IU every week for 8 weeks resulted in an improvement of pain scores and functional ability in patients with chronic LBP (37). In a recently published pooled analysis of 19 RCTs involving 3,436 patients, the authors reported that vitamin D supplementation lead to a significantly greater decrease in pain score as compared to placebo (mean difference -0.57, 95% CI: -1.00 to -0.15, $P = 0.007$) (11). They found no difference ($P = 0.29$) in the effect of vitamin D supplementation on pain scores between studies evaluating widespread nonspecific pain (diffuse pain, fibromyalgia, musculoskeletal pain) and studies evaluating localized pain (LBP, arthritis, migraine, dysmenorrhea).

It is recommended to increase the sun exposure to correct this deficiency. It is calculated that solar exposure of as short as 11 minutes, in around 15% of the body surface in fair skin people on most days, can produce about 1000 IU/day of vitamin D3 (38). Vitamin D supplementation may be another way to ensure an adequate vitamin D status when there is no adequate sun exposure.

Limitations

The major limitation is variable cut-off for classifying patients as having vitamin D deficiency.

Conclusions

The present meta-analysis concludes a high prevalence of hypovitaminosis D was observed in patients with LBP. Significant heterogeneity is observed in reporting the prevalence of hypovitaminosis D in individual studies. Increased prevalence is associated with aging, being female, and Asians.

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