Research Article

The Relationship between the Severity of Lumbar Spinal Stenosis and Levels of Vitamin D and Parathyroid Hormone

Zeliha Cosgun[1,*], Yasar Dagistan[2], Emine Dagistan[1], Melike Elif Kalfaoglu[1], Caner Cicek[2]

[1]*Department of Radiology, Abant Izzet Baysal University Hospital, Bolu, Turkey.*
[2]*Department of Neurosurgery, Abant Izzet Baysal University Hospital, Bolu, Turkey.*

Abstract: Background: It is known that parathyroid hormone (PTH) and vitamin D have a wide variety of effects on bone metabolism. However, the levels of PTH and vitamin D in patients with lumbar spinal stenosis (LSS) have not been adequately investigated in the literature.

Objective: The objective of this study was to investigate the relationship between PTH and vitamin D levels and the severity of stenosis in patients with LSS.

Materials and Methods: This retrospective observational study included consecutive patients who presented to the Neurosurgery outpatient clinic with chronic leg pain and low back pain and were diagnosed with LSS between January 2019 and July 2022. Patients were categorized into three groups based on their vitamin D and parathyroid hormone status. Group 1: High parathyroid hormone and Low vitamin D levels; Group 2: Normal parathyroid hormone and low vitamin D levels; Group 3: Normal parathyroid hormone and vitamin D levels. There were 17 (37%), 10(22%), and 19(41%) subjects in groups I, II, and III, respectively.

Results: The mean age of the groups with a total of 46 patients I, II and III were 62.2±11, 58.3±6, and 63.2±6.4 years, respectively (p=0.553). Sex of the study groups was not statistically different, either (p=0.079). Spinal canal AP diameter (p=0.002) and ligamentous interfacet distance (p=0.008) were significantly different in study groups. Vitamin D positively correlated with Spinal canal AP diameter (r=0.56, p<0.001) and ligamentous interfacet distance (r=0.51, p=0.003), while PTH was inversely correlated with them (r=-0.33, p=0.020), (r=-0.47, p=0.007) .

Conclusion: Vitamin D is significantly correlated with the diameters of spinal canal AP and ligamentous interfacet distance. PTH is negatively correlated with the diameters of spinal canal AP and ligamentous interfacet distance.

Keywords: Lumbar spinal stenosis, Vitamin D, Parathyroid hormone, Neurogenic claudication, Low back pain, Ligamentous interfacet distance.

INTRODUCTION

The Lumbar Spinal Stenosis (LSS) is a prevalent degenerative condition among older individuals, characterized by the compression of the spinal canal due to degenerative osteophytes and ligament hypertrophy. Lumbar spinal stenosis may also be the reason of diminished maintenance in daily activities of elderly patients because of the related back pain and neurogenic claudication and LSS patients may require surgical intervention for relief the symptoms [1-3].

Vitamin D, a fat-soluble hormone, is naturally found in few food sources, added to others, and available as a dietary supplement. It is also endogenously synthesized in response to ultraviolet rays from sunlight contacting the skin. Vitamin D plays a crucial role in various physiological processes. It enhances calcium absorption in the gastrointestinal tract, maintains appropriate serum calcium and phosphate levels for normal bone mineralization, and supports bone growth and remodeling through the activity of bone-forming and remodeling cells. Inadequate vitamin D levels can lead to bone thinning, brittleness, and deformities. Sufficient vitamin D levels prevent rickets in children and Osteomalacia in adults [4]. While the precise mechanisms underlying these protective effects are not fully comprehended, potential explanations include enhanced protein synthesis in muscle via activation of the vitamin D receptor or the presence of myopathy resulting from vitamin D deficiency [5, 6]. The serum parathyroid hormone (PTH), promotes bone growth and increases bone mass, making it an anabolic hormone. However, as part of its physiological function, it also contributes to bone remodeling. PTH stimulates bone formation in a number of ways, including by encouraging mesenchymal stem cells to commit to the osteoblast lineage, facilitating osteoblast maturation and possibly extending their lifespan, and reducing sclerostin production by osteocytes [7]. A well-documented negative correlation exists between serum PTH and 25-hydroxyvitamin D levels. Until a certain threshold of 25-hydroxyvitamin D is reached, a consistent decrease in PTH levels has been observed. Optimal calcium homeostasis, proposed as an indicator of vitamin D sufficiency, may correspond to PTH levels, which are closely associated with serum 25-hydroxyvitamin D levels [8, 9].

*Address correspondence to this author at the Department of Radiology, Abant Izzet Baysal University Hospital, Bolu, Turkey.
Email: zeliha44@gmail.com

 © 2023 NIBD Publications

Patients with symptomatic LSS frequently have poor gait, high bone turnover metabolism, and co-morbid conditions such essential hypertension and diabetes mellitus, which are partly linked to vitamin D insufficiency [10-12]. As a result, it is projected that LSS patients would have a high prevalence of vitamin D insufficiency [13]. This holds clinical significance as vitamin D deficiency can have detrimental effects on falls by exacerbating functional disturbances in the lower extremity, potentially leading to fractures. Due to its crucial role in bone mineralization, vitamin D directly protects against fracture risk while also indirectly preventing falls by enhancing muscular performance and preventing myopathy [14-16]. PTH is the major hormone in bone metabolism [17]. However, there are few research in the literature examining the relationship between secondary hyperparathyroidism and vitamin D deficiency in LSS patients.

Therefore, we aimed to investigate the relationship between PTH and vitamin D levels on the severity of the stenosis in patients with LSS. We also aimed to observe the association between spinal stenosis and secondary hyperparathyroidism and vitamin D deficiency.

MATERIALS AND METHODS

This retrospective observational study was conducted with the approval of the Bolu Abant Izzet Baysal University (BAIBU) Ethics Committee for Clinical Research (Decision no. 2021/244). The study included consecutive patients who presented to the Neurosurgery outpatient clinic with chronic low back pain and leg pain, and were diagnosed with lumbar spinal stenosis (LSS) between January 2019 and July 2022. Based on the presence of radiculopathy, neurogenic claudication, and magnetic resonance imaging (MRI)-confirmed neural canal stenosis at the pertinent level, the diagnosis of LSS was made.

The following measurements were taken: spinal canal antero-posterior diameter, thecal sac transverse diameter (mm), lateral recess height (right-left, mm), and ligamentous interfacet distance (Figs. **1**, **2**). The distance between the middle of the vertebral body and the middle of the spinous process at the dural sac's border served as the antero-posterior diameter of the sac. The distance between the lateral end of the dural sac and the lateral recess served as the transverse diameter of the thecal sac. The distance between the superior process and the upper portion of the pedicle served as the measurement for the lateral recess depth. The ligamentous interfacet distance was calculated as the separation between the inner ligament portion and the facet joint space [18]. Stenotic lesions were defined as mid-sagittal diameters less than 10 mm on MRI.

Patients were ruled out if they satisfied any of the following requirements: identifiable motor weakness in both lower extremities; neurodegenerative disorders affecting walking; history of fracture within the past year; known rheumatoid arthritis or symptomatic osteoarthritis of the hip, knee, and ankle (Kellgren Lawrence grade III or higher on x-ray); any history or signs of medical comorbidities impacting vitamin D metabolism (renal failure, chronic liver disease, gastric surgery, diabetic nephropathy, intestinal malabsorption [such as celiac disease, inflammatory bowel disease, cystic fibrosis etc.], systemic infection, and neoplasms in particular); use of medications that can influence bone metabolism (hormone replacement therapies, corticosteroids, anti-osteoporotic drugs, anticonvulsants, and products containing vitamin D in particular); premenopausal women; and history of psychiatric disorders, including depression. Patients with lumbar spondylolisthesis, drug induced Osteomalacia, oncogenic Osteomalacia, obesity (BMI>30 kg/m^2), hyperthyroidism and granulomatous diseases were excluded from the study. In power analysis, for an 80% estimated power, required sample size was calculated 8 for each group. Taking into account 10% loss during study we increased the sample size to 10 in each groups.

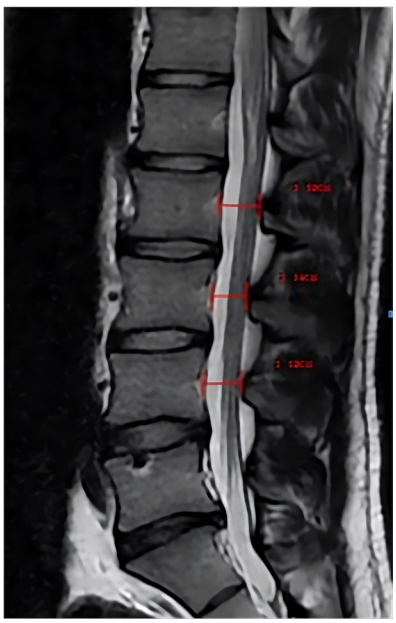

Fig. (1). Antero-posterior (AP) Spinal Canal (red line) Diameter at the Mid-Vertebral Level in the Sagittal T2w Image.

Biochemistry and Assessment of the Bone Metabolism

Following an overnight fasting, approximately 5 mL of blood samples were collected in dry tubes between 8:30 and 9:30 AM to account for circadian variation. Then blood samples were centrifuged at 1000 g for 10 minutes, after kept on hold for 30 minutes. Analyses were performed at the same day. Serum vitamin D and intact PTH concentrations were calculated with the method of electrochemiluminescence in fully automatic immune analyzers, as dictated in the directions from the manufacturer (Cobas e 601, Roche Diagnostics, Germany). Measurements of serum alkaline phosphatase, enzymatic measurements, albumin, calcium and phosphorus were completed with colorimetric methods by auto analyzers as noted in the directions from the manufacturer (Architect c 8000, Abbot Laboratories, USA).

The patients with LSS who were included in the study were classified into three groups based on their vitamin D and parathyroid hormone (PTH) levels:

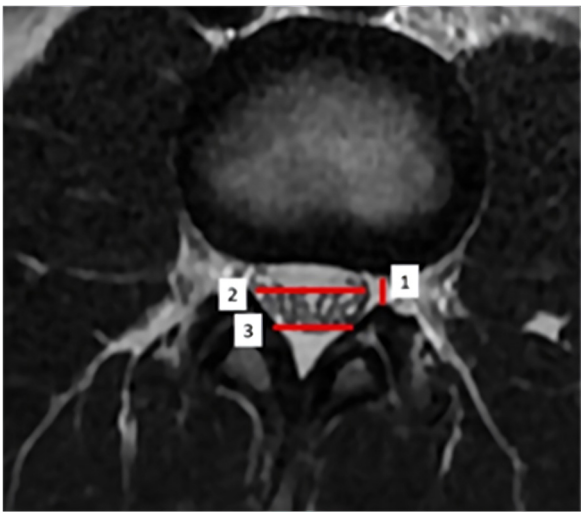

Fig. (2). Measurements of Lateral Recess Height Left (mm) (1), Thecal Sac Transverse Diameter (2), Ligamentous Interfacet Distance (3) in the Axial T2w Image.

Group 1: High parathyroid hormone and Low vitamin D levels (patients with hyperparathyroidism secondary to vitamin D deficiency).

Group 2: Normal ranged PTH and low vitamin D levels.

Group 3: Normal PTH and vitamin D levels.

Definition of vitamin D deficiency was assigned for the levels below 10 ng/mL [6]. Secondary hyperparathyroidism definition was used for the cases with vitamin D levels below 10 ng/mL and PTH levels over 70 pg/mL. The interassay variation for a serum parathyroid hormone (PTH) level of 68.0 pg/mL was 2.9%.

Magnetic resonance images of the participant were obtained by a 1.5 T MRI device (Magnetom symphony 1.5T, Siemens Co., Germany). Diagnosis of LSS were established according to the quantitative criteria of Society of Experts in Musculoskeletal Radiology [19].

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences (SPSS) software (version 15, SPSS Inc., Chicago, IL, US) for Windows was used for statistical analysis. The Kolmogorov-Smirnov test was utilized to assess the significance of differences in distributions. Continuous variables were reported as mean ± standard deviation ordinal variables as median (maximum - minimum), and categorical variables as frequency with percentages. Parametric data were compared using a one-way analysis of variance (ANOVA) test. The ANOVA test was also employed to determine significant differences between groups, as appropriate. Nonparametric data were compared using the Kruskal-Wallis test to assess significant differences between median values. To compare categorical data, the chi-square test was performed. A statistically significant p-value of less than 0.05 was evaluated.

RESULTS

Clinical and Laboratory Characteristics

There were 17, 10, and 19 subjects in groups I, II, and III, respectively. Mean age of the groups I, II and III were 62.2±11, 58.3±6, and 63.2±6.4 years, respectively (p=0.55). Sex of the study groups was not statistically different, either (p=0.08). Clinical and laboratory parameters of the groups which were included in the study are described in Table **1**.

Table 1. Clinical and Laboratory Parameters of the Patient Groups which were Included in the Study.

Parameter		Group 1 (n=17)	Group 2 (n=10)	Group 3 (n=19)	P
Gender	Men (n)	7 (41%)	1 (10%)	10 (53%)	0.081
	Women (n)	10 (59%)	9 (90%)	9 (47%)	
Mean ± SD					
Age (years)		62.2±11	58.3± 6	63.2±6.4	0.553
Ca (mg/dL)		9.3±0.7	9.25±0.4	9.3±0.5	0.619
Albumin (g/dL)		4.4±0.2	4.3±0.2	4.2±0.2	0.114
Alkaline phosphatase (U/L)		90±26	78±37	85±22	0.688
PTH (pg/mL)		94±23	44±12	42±10	<0.001
Median (Min-max)					
Vitamin D (IU/L)		6 (3-9)	4 (3-8)	15 (11-30)	<0.001
Spinal canal AP diameter (mm)		14 (10-17)	12(11-17)	16(11-19)	0.002
Thecal sac transverse diameter (mm)		14 (6-20)	14 (7-19)	14 (6-21)	0.950
Lateral recess height right (mm)		1.3 (0-3.7)	1.3(0-3.2)	1.4 (0-3)	0.871
Lateral recess height left (mm)		0.5 (0-4.1)	0.5(0-1.6)	1.4 (0-4)	0.622

No statistical difference was observed between three groups regarding age, gender, calcium, albumin, and alkaline phosphatase levels. Levels of vitamin D were significantly higher in group 3 when compared to other two groups. Also, PTH levels were significantly higher in group 1 than the other two groups (all p<0.001). In present study, approximately 58% of the patients had low vitamin D levels. In 43% of these patients, Parathyroid hormone levels were increased. In contrast, 37% of our patients have normal vitamin D and PTH levels.

Radiological Parameters

The study groups' mean spinal AP diameters differed significantly (p=0.002). The mean thecal sac transverse diameter of the groups did not differ substantially (p=0.95), nor did the mean spinal lateral recess right diameter (p=0.87). The groups' aver-

age spinal lateral recess left diameters did not differ (p=0.62). The study groups' ligamentous interfacet distances differed significantly (p=0.008).

Bivariate Correlations in Vitamin D Levels and Radiological Measurements of the Spinal Stenosis

Vitamin D was significantly and positively correlated with AP diameter of spinal canal (r=0.56, p<0.001). Similarly, PTH was inversely correlated with AP diameter of spinal canal (r=-0.33, p=0.02). Table **2** shows the correlation between study parameters.

Table 2. Correlation of Vitamin D and PTH with Spinal Canal AP Diameter and Ligamentous Interfacet Distance.

	Spinal Canal AP Diameter	**Ligamentous Interfacet Distance**
Vit D	r= 0.56, p<0.001	r=0.51, p=0.003
PTH	r=-0.33, p=0.020	r=-0.47, p=0.007

In present study, approximately 58% of the patients had low vitamin D levels. In 43% of these patients, PTH levels were increased. In contrast, 37% of our patients have normal vitamin D and PTH levels.

DISCUSSION

LSS commonly affects individuals aged 50 years and older, with a prevalence ranging from 1.7% to 10% [20, 21]. Symptoms can manifest unilaterally or bilaterally and may include pseudo-claudication, low back pain, numbness, weakness, and pain upon lumbar spine extension [16, 22, 23]. These symptoms are typically relieved by flexion of the lumbosacral spine [23]. Over the past two decades, the positive effects of vitamin D on health have surpassed musculoskeletal health to include osteoarthritis, colon and breast cancer, cardiovascular disease, essential hypertension, diabetes mellitus and osteoporosis [24, 25].

In a recent study authors found that patients with LSS had significant amount of vitamin D deficiency [26]. In another study, it was reported that pain and vitamin D deficiency were more common in subjects with LSS. They also recommended measurement of serum vitamin D level in LSS patients with severe pain [27]. According to the literature vitamin D levels were decreased in subjects with LSS compared to healthy patients in present study.

LSS patients may have vitamin D deficiency which can have additional effects on functions of the lower extremities, which may lead to increased risk of fall that can be caused by neurological claudication and radiculopathy. Therefore, LSS patients might have impaired mobility due to vitamin D deficiency; or vitamin D deficiency due to impaired daily mobilization and related falls [6]. So on, high levels of vitamin D deficiency and related (or age related) osteoporosis may cause repeating falls that can end-up with fractures, which would be the reason for low quality of life parameters due to severe pain. As noted above, it is important to point out the relationship of serum 25-hydroxyvitamin D and PTH levels, in detail. This is the result of an effort to establish the optimal balance of calcium. So; in patients with increased sense of pain, this significantly decreases the quality of life, 25-hydroxyvitamin D levels, PTH levels, and bone mineral density should be checked in routine blood studies. Also in this group of patients combining the choice of treatment with calcium, vitamin D and/or bisphosphonates should be kept in mind.

Our study evaluates the relationship between low vitamin D levels and lumbar spinal stenosis; however, there are numerous studies indicating that low vitamin D levels are not solely related to bone metabolism. Therefore, in patients with low vitamin D levels, it is necessary to investigate other factors such as the presence of elevated parameters indicative of inflammation or other reasons like diabetes or sarcopenia that may affect vitamin D levels [28, 29].

Our work has three major limitations; small study population and lack of postoperative hormonal status data, which make our results difficult to interpret with literature. Another limitation of our study is that it was conducted as a single-center study.

In this study, we have revealed two major outcomes; initially, LSS patients with low levels of vitamin D, measurements of spinal stenosis were similar.

CONCLUSION

The results of the present study indicated that vitamin D and PTH levels were associated with the parameters of the lumbar spinal stenosis. Moreover, they are significantly correlated with AP spinal canal and ligamentous interfacet distance.

AUTHORS' CONTRIBUTION

- **Zeliha Cosgun and Yasar Dagistan**: Design.
- **Zeliha Cosgun, Yasar Dagistan and Emine Dagistan**: Writing, Statistics.
- **Zeliha Cosgun, Melike Elif Kalfaoglu and Emine Dagistan**: Editing.
- **Zeliha Cosgun, Melike Elif Kalfaoglu, Emine Dagistan and Caner Cicek**: Data Interpretation.
- **Yasar Dagistan and Caner Cicek**: Translate.
- **Zeliha Cosgun and Emine Dagistan**: Supervising.

CONFLICT OF INTEREST

Declared none.

ACKNOWLEGEMENTS

Declared none.

REFERENCES

[1] Lotan R, Oron A, Anekstein Y, Shalmon E, Mirovsky Y. Lumbar stenosis and systemic diseases - Is there any relevance? J Spinal Disord Tech 2008; 21: 247-51. doi:10.1097/BSD.0b013e31813707af.

[2] Cosgun Z, Dagistan E, Dagistan Y. Effects of sagittal balance differences on spondylolisthesis. Acta Ortop Bras 2019; 27: 120-3. doi:10.1590/1413-785220192702205665.

[3] Dagistan Y, Dagistan E, Gezici AR, Cancan SE, Bilgi M, Cakir U. Effects of minimally invasive decompression surgery on quality of life in older patients with spinal stenosis. Clin Neurol Neurosurg 2015; 139: 86-90. doi:10.1016/j.clineuro.2015.09.009.

[4] Gartner LM, Greer FR, Nutr SBC. Prevention of rickets and vitamin D deficiency: New guidelines for vitamin D intake. Pediatrics 2003; 111: 908-10. doi:10.1542/peds.111.4.908.

[5] Sorensen OH, Lund BI, Saltin B, *et al*. Myopathy in bone loss of aging: Improvement by treatment with 1 alpha-hydroxycholecalciferol and calcium. Clin Sci 1979; 56: 157-61. doi:10.1042/cs0560157.

[6] Schott GD, Wills MR. Muscle weakness in Osteomalacia. Lancet 1976; 1: 626-9. doi:10.1016/S0140-6736(76)90428-1.

[7] Lane NE, Silverman SL. Anabolic therapies. Curr Osteoporos Rep 2010; 8: 23-7. doi:10.1007/s11914-010-0005-4.

[8] Dawson-Hughes B, Harris SS, Dallal GE. Plasma calcidiol, season, and serum parathyroid hormone concentrations in healthy elderly men and women. Am J Clin Nutr 1997; 65: 67-71. doi:10.1093/ajcn/65.1.67.

[9] Chapuy MC, Preziosi P, Maamer M, *et al*. Prevalence of vitamin D insufficiency in an adult normal population. Osteoporosis Int 1997; 7: 439-43. doi:10.1007/s001980050030.

[10] Amundsen T, Weber H, Lilleas F, Nordal HJ, Abdelnoor M, Magnaes B. Lumbar spinal stenosis. Clinical and radiologic features. Spine 1995; 20: 1178-86. doi:10.1097/00007632-199505150-00013.

[11] Kim HJ, Lee HM, Kim HS, *et al*. Bone metabolism in postmenopausal women with lumbar spinal stenosis analysis of bone mineral density and bone turnover markers. Spine 2008; 33: 2435-9. doi:10.1097/BRS.0b013e3181829fca.

[12] Winter CC, Brandes M, Muller C, *et al*. Walking ability during daily life in patients with osteoarthritis of the knee or the hip and lumbar spinal stenosis: a cross sectional study. Bmc Musculoskel Dis 2010; 11: 233. doi:10.1186/1471-2474-11-233.

[13] Lee BH, Moon SH, Kim HJ, Lee HM, Kim TH. Osteoporotic profiles in elderly patients with symptomatic lumbar spinal canal stenosis. Indian J Orthop 2012; 46: 279-84. doi:10.4103/0019-5413.96379.

[14] Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. N Engl J Med 1997; 337: 670-6. doi:10.1056/NEJM199709043371003.

[15] Pfeifer M, Begerow B, Minne HW, Suppan K, Fahrleitner-Pammer A, Dobnig H. Effects of a long-term vitamin D and calcium supplementation on falls and parameters of muscle function in community-dwelling older individuals. Osteoporosis Int 20 2009; 20: 315-22. doi:10.1007/s00198-008-0662-7.

[16] Porter RW. Spinal stenosis and neurogenic claudication. Spine 1996; 21: 2046-52.

[17] Qin L, Raggatt LJ, Partridge NC. Parathyroid hormone: A double-edged sword for bone metabolism. Trends Endocrin Met 2004; 15: 60-5. doi:10.1016/j.tem.2004.01.006.

[18] Steurer J, Roner S, Gnannt R, Hodler J. Quantitative radiologic criteria for the diagnosis of lumbar spinal stenosis: A systematic literature review. BMC Musculoskelet Disord 2011; 12: 1-9. doi:10.1186/1471-2474-12-175.

[19] Mamisch N, Brumann M, Hodler J, Held U, Brunner F, Steurer J. Radiologic criteria for the diagnosis of spinal stenosis: Results of a Delphi survey. Radiology 2012; 264: 174-9. doi:10.1148/radiol.12111930.

[20] Ishimoto Y, Yoshimura N, Muraki S, *et al*. Associations between radiographic lumbar spinal stenosis and clinical symptoms in the general population: The Wakayama Spine Study. Osteoarthritis Cartilage 2013; 21: 783-8. doi:10.1016/j.joca.2013.02.656.

[21] Ishimoto Y, Yoshimura N, Muraki S, *et al*. Prevalence of symptomatic lumbar spinal stenosis and its association with physical performance in a population-based cohort in Japan: The Wakayama Spine Study. Osteoarthritis Cartilage 2012; 20: 1103-8. doi:10.1016/j.joca.2012.06.018.

[22] Hall S, Bartleson JD, Onofrio BM, Baker HL, Okazaki H, Oduffy JD. Lumbar spinal stenosis - clinical-features, diagnostic procedures, and results of surgical-treatment in 68 patients. Ann Intern Med 1985; 103: 271-5. doi:10.7326/0003-4819-103-2-271.

[23] Spengler DM. Degenerative stenosis of the lumbar spine. J Bone Joint Surg Am 1987; 69: 305-8.

[24] Chlebowski RT. Vitamin D and breast cancer: Interpreting current evidence. Breast Cancer Res 2011; 13: 1-9. doi:10.1186/bcr2846.

[25] Holick MF. Vitamin D deficiency. New Engl J Med 2007; 357: 266-81. doi:10.1056/NEJMra070553.

[26] Kim TH, Yoon JY, Lee BH, *et al*. Changes in vitamin D status after surgery in female patients with lumbar spinal stenosis and its clinical significance. Spine 2012; 37: E1326-E30. doi:10.1097/BRS.0b013e318268ff05.

[27] Kim TH, Lee BH, Lee HM, *et al*. Prevalence of vitamin d deficiency in patients with lumbar spinal stenosis and its relationship

with pain. Pain Physician 2013; 16: 165-76.

[28] Erkus E, Aktas G, Atak BM, Kocak MZ, Duman TT, Savli H. Haemogram parameters in vitamin d deficiency. J Coll Physicians Surg Pak 2018; 28(10): 779-82. PMID: 30266124.

[29] Erkus E, Aktas G, Kocak MZ, Duman TT, Atak BM, Savli H. Diabetic regulation of subjects with type 2 diabetes mellitus is associated with serum vitamin D levels. Rev Assoc Med Bras (1992) 2019; 65(1): 51-5. doi: 10.1590/1806-9282.65.1.51. PMID: 30758420.)

Received: June 09, 2023 Revised: August 31, 2023 Accepted: September 01, 2023

© 2023 National Journal of Health Sciences
This is an open-access article.