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**RESEARCH ARTICLE**

# The Role of Vitamin D3 and Trace Elements of Lumbar Spinal Degeneration in Patients Undergoing Lumbar Spinal Surgery

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**ABSTRACT**

The primary objective of this study is to investigate the levels of vitamin D3, calcium, copper, and zinc. Determine whether preoperative screening for vitamin D3 deficiency and subsequent optimization of levels can improve fusion rates, reduce postoperative complications, and enhance patient satisfaction in spinal surgery patients. The study included 120 participants, ranging in age from 18 to 70 years. Sixty of them had lumbar spine surgery and were diagnosed using MRIs or X-rays, while the other sixty were in good health and acted as a control group. The study was conducted at Ghazi Al-Hariri Hospital in Baghdad, Iraq. An enzyme-linked immunosorbent assay is used to assess blood D3, while colorimetric methods are used to measure calcium, zinc and copper levels. The study found that patients had significantly lower mean ±SD vitamin D levels compared to healthy individuals ( p-value ≤0.001). further demonstrates that the patient's calcium level was significantly lower than that of a healthy person (p-value <0.001). Moreover, the results showed that patients had significantly higher copper and Cu/Zn ratios than controls ($P < 0.001$). while copper had a significant positive correlation with the Cu/Zn ratio ($r = 0.79$, $p < 0.001$). It was shown that lower vitamin D3 and calcium levels can be used as an indicator of lumbar disc degeneration (LDD) in patients with lumbar spinal surgery. It also highlights the importance of pre-operative assessment for optimal surgical outcomes and the potential benefits of vitamin D3 supplementation in preventing osteoporosis and relieving musculoskeletal pain.

## INTRODUCTION

Degenerative disc disease (DDD) is a complicated condition that is still poorly understood. Many theories have been put forth to explain the disease such as aging and the interaction of genetic and environmental variables [1]. The lumbosacral spine is made up of five sacral vertebrae ($S_1$–$S_5$) and five lumbar vertebrae ($L_1$–$L_5$). together with the intervertebral discs, blood vessels, muscles, ligaments and nerves that connect them. Vertebral bodies, vertebral arches and discs make up each vertebra of the axial forces applied to the vertebrae, the majority are absorbed by the vertebral bodies [2].

The sympathetic chain and ganglia in the lumbar region stretch from $L_1$ to $L_5$. They are continuous with the sympathetic fibers in the pelvic area below and the sympathetic chain in the thoracic region

above. The sympathetic chain and its ganglia are located in the lumbar area close to the anterolateral surface of the vertebral body [3]. The somatic nerves are not connected to the sympathetic chain or ganglia; hence, precise lesions of these structures can be made without endangering the somatic nerves [4].

As numerous writers have demonstrated there is a close anatomical and functional relationship between the lumbar spine and the hip joint. Thus, an anomaly in one region might have an impact on another; for example, osteoarthritis in the hip joint can result in lumbar sagittal malalignment and back pain [5].

Low back pain is frequently brought on by lumbar disc degeneration (LDD), a common musculoskeletal condition (LBP) [6]. Low back pain can arise from a variety of different known or unknown pathologies or diseases; it is a symptom rather than an illness. It is identified by the site of pain, which is usually between the creases of the buttocks and the lower ribs [7]. Low back pain is frequently accompanied by discomfort in one or both legs and some persons with low back pain have accompanying neurological problems in their lower limbs [8].

Specific or non-specific low back pain (LBP) is possible. Particular LBP refers to pain that originates from a particular ailment or structural issue with the spine or when the pain travels to another area of the body **[9]**.

The aging population is more susceptible to lumbar spondylolisthesis and spondylosis, which are important causes of lower back discomfort that significantly impair everyday functioning [10]. A surgical procedure called lumbar interbody fusion (LIF) is used to treat degenerative lumber segments, their decompressed neural components and abnormalities of the facet joints that are associated with them [11].

Vitamin $D_3$ is primarily responsible for controlling the metabolism of calcium and phosphorus as well as the mineralization of the collagen matrix in human bone. One of the pathophysiological causes of osteoporosis is secondary parathyroid hormone release driven by low vitamin $D_3$ levels [12]. This condition also increases the yearly cost of surgical treatments like spinal fusion surgery and causes musculoskeletal problems**.** The researchers started by assessing the vitamin $D_3$ status of patients prior to lumbar spine surgery and observing the effects on postoperative outcomes [13] . Vitamin $D_3$ is essential for the processes involved in bone development and repair, as well as for encouraging calcium absorption in the renal and digestive systems. Thus, it stands to reason that sufficient vitamin $D_3$ level would be critical for the successful completion of spinal fusion surgery [14].

Patients with musculoskeletal disorders are commonly impacted by disc degenerative diseases. Some studies demonstrate that low back discomfort is connected with hypovitaminosis $D_3$ [15].

Vitamin $D_3$ supplementation is a successful osteoporosis prevention strategy. Numerous studies conducted in the last few years have shown that hypovitaminosis $D_3$ is linked to an increased risk of diabetes, some types of cancer and cardiovascular disease [16]. Furthermore, it has been demonstrated that a genetic variation in the vitamin $D_3$ receptor is linked to LDD [17], as well as reports of musculoskeletal pain relief with vitamin $D_3$ supplementation [18].

In addition to being essential for the processes involved in bone growth and healing, vitamin $D_3$ also plays a significant role in facilitating calcium absorption. Therefore, appropriate level of vitamin $D_3$ are hypothesized to be vital to the good outcome of spinal fusion surgery [19].

## METHOD

### Ethical consideration

Ethical approval and approval for the study were obtained from the Scientific Research Ethics Committee at the University of Baghdad / College of Medicine and Martyr Ghazi Al-Hariri Hospital

for Specialized Surgeries, according to the book number 1309 in 10/10/2023 & the book number 40681 in 25/10/2024, From 25 October 2024.

**Inclusion Criteria**

Patients scheduled for spinal surgery, aged 18-70 years without known Vitamin $D_3$ supplementation or diagnosed Vitamin $D_3$ deficiency.

**Exclusion Criteria**

Patients with a history of metabolic bone diseases, renal impairment or liver dysfunction.

**Measure**

The study questionnaire included four measurement tools: X-rays or MRI scans to test the imaging of the lumbar spine. About 3 *ml* of whole blood specimens were collected from the superficial veins of every patient and control transferred into gel tubes and left to coagulate for 15 minutes. The sample was then separated at 3000 *rpm* for 10 minutes. The acquired serum was stored in aliquots in an Eppendorf Safe-Lock at -20 ◦ C until the time of laboratory measurements. The ELISA test for $D_3$ analysis assesses vitamin $D_3$ deficiency in lumbar spinal patients. Demographic and clinical characteristics such as age and measurement of body mass index according to the classified World Health Organization were also collected [20].

**The Statistical analysis**

The data was interrupted using SPSS version 25.0 software, frequency, percentage, mean and stander deviation were used to describe data. Graphs were used to presented data. Chi-square test used to test association between qualitative variables and independent t test was used to evaluate difference of mean between two quantitative variables, Pearson correlation coefficient was used to assess correlation between two quantitative variables. With values <0.3 signifying no connection, 0.3<0.5 reflecting weak correlation, 0.5<0.7 moderate strength, and >0.7 strong correlation, the correlation coefficient value (r) can be either positive (direct correlation) or negative (inverse correlation). P-values less than 0.05 were regarded as significant at this level.

**RESULTS**

This study included 120 participants; the gender distribution was 49.2% females and 50.8% males; the age range of participants was between 18 and 70 years old; participants were divided into two groups: 60 of them were patients who underwent lumber spine surgery and 60 were used as a healthy control group.

The mean age was 40.18 ± 15.12 years. Patients had a significantly higher mean age (50.90 ± 13.76 years) in comparison to healthy controls (44.47 ± 6.21 years), p-value <0.1.

Patients had a significantly higher BMI mean (28.10 ± 3.41 $kg/m^2$) in comparison to healthy controls (24.35 ± 1.14 $kg/m^2$), p-value <0.001. Regarding BMI groups, 45.4% had a normal BMI, 41.2% were overweight, 12.6% were obese, and 0.8% were morbidly obese. Obese and morbidly obese patients belonged to the same group, as presented in Table 1.

**Table 1: demographic characterizes of participant**

| Clinical characteristics | Patients | Healthy | Total | P- value |
|---|---|---|---|---|
| **Age (years)** | 50.90 ± 13.76 (1.77) | 44.47 ± 6.21 (0.80) | 40.18 ± 15.12 | <0.001ǂ |

| | | | | | |
|---|---|---|---|---|---|
| **BMI (*kg/m²*)** | | 28.10 ± 3.41 (0.44) | 24.35 ± 1.14 | 26.24 ± 3.16 | <0.001*ǂ |
| **Sex** | Male | 28 (46.7%) | 33 (55%) | 71 (50.8%) | 0.46 |
| | Female | 32 (53.3%) | 27 (45%) | 59 (49.2%) | |
| **BMI groups** | Normal | 10 (16.7%) | | | |
| | Overweight | 34 (56.7%) | 15 (25.4%) | 49 (41.2%) | <0.001ǂ |
| | Obese | 15 (25.0%) | 0 (0.0%) | 15 (12.6%) | |
| | Morbid obesity | 1 (1.7%) | 0 (0.0%) | 1 (0.8%) | |
| Mean ± SD (SE) N (%) *p-value is significant ǂindependent t-test †chi-square | | | | | |

Patients had significantly lower vitamin $D_3$ (9.53 ± 3.94 *ng/ml*) and calcium levels (8.13 ± 0.50 *mg/dL*) in comparison to healthy controls (p-value <0.001), as presented in Table 2.

Regarding minerals, patients had a lower mean of zinc (57.3 ± 14.56 *Mmol/L*) in comparison to healthy controls (96.41 ± 17.38 *Mmol/L*), p-value 0.001, as presented in table 2.

Copper and Cu/Zn ratios were significantly higher in patients (106.60 ± 39.41 *Mmol/L*) (2.03 ± 1.06) in comparison to controls (61.03 ± 9.53 *Mmol/L*) (0.64 ± 0.12), p-value <0.001, as presented in table 2.

**Table 2: mean of vitamin $D_3$ and minerals in both groups**

| **Clinical Biomarkers** | **Patient** | **Healthy** | **p-value** |
|---|---|---|---|
| **Vitamin D (*ng/ml*)** | 9.53 ± 3.94 (0.50) | 33.79 ± 6.18 (0.79) | <0.001* |
| **$Ca^{++}$** | 8.13 ± 0.50 (0.06) | 9.80 ± 0.64 (0.08) | <0.001* |
| **Zinc (*Mmol/L*)** | 57.3 ± 14.56 (1.89) | 96.41 ± 17.38 (2.24) | 0.001* |
| **Copper (*Mmol/L*)** | 106.60 ± 39.41 (5.08) | 61.03 ± 9.53 (1.23) | <0.001* |
| **Copper/Zinc** | 2.03 ± 1.06 (0.13) | 0.64 ± 0.12 (0.01) | <0.001* |
| *p-value is significant | | | |

**Table 3: correlation between vitamin $D_3$ and minerals in patient group.**

| **Clinical Biomarkers** | **Vitamin D (*ng/ml*)** | **Zinc (*Mmol/L*)** | **Cu (*Mmol/L*)** | **$Ca^{++}$(*mg/dl*)** | **Cu/Zinc** |
|---|---|---|---|---|---|
| **Vitamin D (*ng/ml*)** | / | r= 0.14 p= 0.27 | r= -0.22 p= 0.08 | r= -0.06 p= 0.64 | r= -0.21 p= 0.10 |
| **Zinc (*Mmol/L*)** | r= 0.14 p= 0.27 | / | r= -0.11 p= 0.39 | r= 0.15 p= 0.24 | r= 0.14 p= 0.43 |
| **Copper (*Mmol/L*)** | r= -0.22 p= 0.08 | r= -0.11 p= 0.39 | / | r= 0.25* p= 0.04 | r= 0.79 p= <0.001 |
| **$Ca^{++}$(*mg/dl*)** | r= -0.06 p= 0.64 | r= 0.15 p= 0.24 | r= 0.27* p= 0.03 | / | r= 0.003 p= 0.98 |
| **Cu/Zinc** | r= -0.21 p= 0.10 | r= 0.14 p= 0.43 | r= 0.79 p= <0.001 | r= 0.003 p= 0.98 | / |

Copper had significant positive correlation with Cu/Zn ratio (r 0.79, p <0.001), as presented in table 3 and Figure 1.

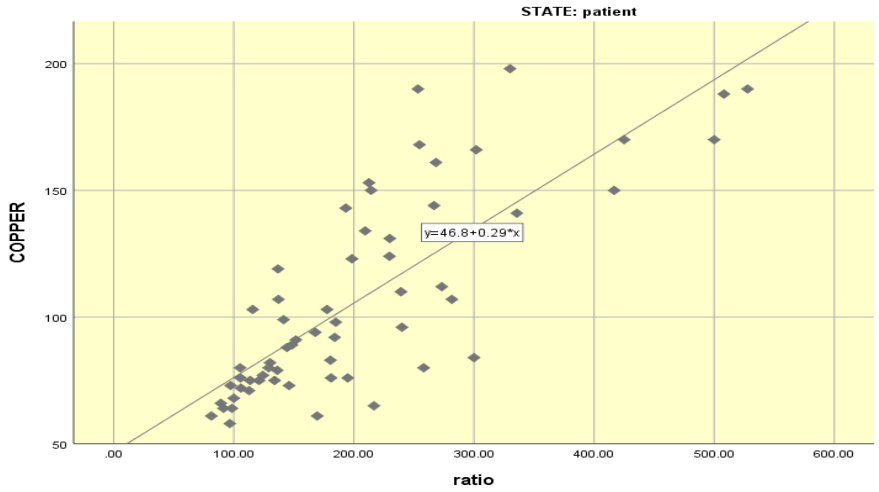


**Figure 1: correlation between copper and Cu/Zn ratio**

Copper had a significant positive correlation with calcium (r = 0.25, p< 0.04), as presented in Table 3 and Figure 2.

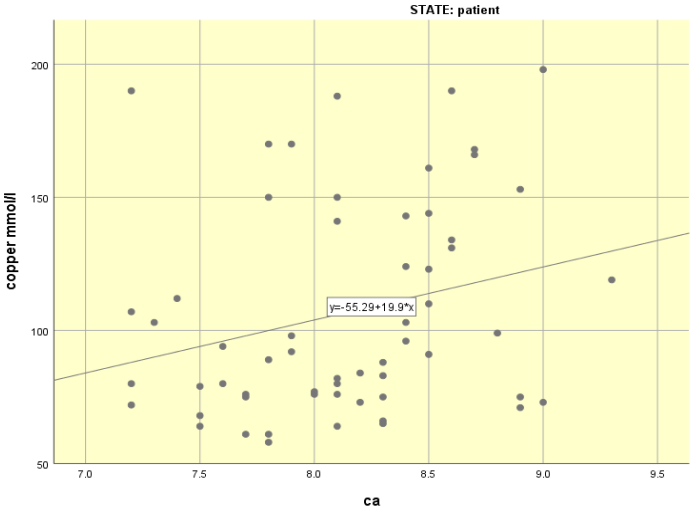


**Figure 2: correlation between calcium with copper**

## DISCUSSION

The outcomes The current study's Table 1 revealed statistically significant variations in the mean age and BMI values between the patient and control groups. The mean ±SD levels of age in patients are statistically significant compared to controls (p< 0.001). According to Lee ES, *et al*., this study is consistent. Observe that the mean in older adults is greater than in younger adults by building a

database with reference values for the lumbar vertebral bodies' concavity index, the age-dependent height of the lumbar discs and the age-dependent prevalence of vertebral osteophyte [21]. Valdez GJB., which was discovered to investigate how the musculoskeletal system requires innervating axons to form, mature and operate. It is not unexpected that skeletal muscles and bones experience adverse morphological and functional alterations when innervating axons become dysfunctional or degenerate owing to illnesses, old age and traumas [22]. People in their twenties have a more flexible upper lumbar spine than people in their sixties [23].

The mean ±SD levels of BMI in patients are statistically significant compared to controls ($p < 0.001$), as shown in Table 1. It is consistent with the Flippin M. *et al.* study, which found that obese people had a higher mean BMI than non-obese people based on data from a community-based spine registry covering a variety of diseases and that an increase in BMI was linked to a statistically significant increase in operating time [24]. Teng W. *et al*., who proved that a statistically significant increase in operating duration was shown to be correlated with an increase in BMI using data from a community-based spine registry that covers a wide range of diseases [25]. Additionally, it is consistent with a previous study that discovered that degenerative spinal pathology in the lumbar spine is also associated with obesity. This is because of a confluence of factors including fatty infiltration of paraspinal muscles, intervertebral disc degeneration and medical changes, which are bone marrow lesions visible on magnetic resonance imaging indicating low back pain [26].

Additionally, Table 2 the mean ±SD levels of vitamin $D_3$ in patients had a significantly lower level in comparison to healthy controls (p-value <0.001). This is in line with the E. Harju *et al*. study, where there was a higher incidence of low serum 25-OHD-3 concentration in the patients with hip fractures than in the controls ($P< 0.001$) [27] . Vitamin $D_3$ insufficiency is connected with LDD and LBP. Serum vitamin $D_3$ concentrations of less than 10 *ng/mL* indicate severe LDD and LBP. After surgery, poor vitamin $D_3$ level are linked to a number of unfavorable outcomes. Vitamin $D_3$ may therefore have a major impact on disc degeneration and potentially alleviate LBP [15] .Vitamin $D_3$ is also involved in the processes that lead to bone growth and repair. $D_3$ status is a predictor of extraskeletal disorders for which deficiencies should be addressed prior to surgical therapies in order to identify predispositions [28].These benefits can be achieved by supplementing with vitamin $D_3$ either before or after surgery [29].Thus, before lumbar spine surgery, preoperative vitamin D3 testing and supplementation could help patients live better. Lack of vitamin D3 has been linked to osteoporosis and can cause instrumentation failure during spine surgery or pseudoarthrosis [30] .

Current study, as shown in Table 2, patients had a significantly lower calcium level in comparison to healthy controls (p-value < 0.001). This is consistent with a French study that found a lack of calcium affects the mineralization of the lumbar vertebrae [31].The main organ responsible for storing calcium and maintaining calcium homeostasis is the bone. The bone responds mostly to calcium-dependent signals from the parathyroid and vitamin $D_3$ metabolites. Osteoblasts deposit calcium through mechanisms such as phosphate and calcium transport, whereas alkalization absorbs the acid created by mineral deposition. Passive diffusion and phosphate production are the means by which calcium mineralization in cartilage occurs. Calcium transport and calcium signaling are fundamentally important in bone cells [32] . Calcium is one of the most critical minerals in repairing bone fractures. According to these studies, the application of calcium therapy during fracture healing results in structural alterations. However, there is currently a paucity of research about the effects of calcium on spinal bone fusion and osteoporosis [33].

Calcium is necessary for appropriate skeletal growth and mineralization and it plays a crucial role in controlling bone remodeling and bone mass. This explains why calcium supplementation improves fracture repair in osteoporotic bones [34].

Also, Table 2 the patients had lower mean ±SD levels of zinc, which is statistically significant compared to the control (p-value <0.001). It is consistent with a study by Jakoniuk M. *et al*. that

showed the patients had lower mean ±SD levels of zinc in their serum compared to healthy subjects [35]. Zinc is a necessary cofactor for alkaline phosphatase, which is involved in the production of several components of the bone matrix. It is especially crucial for appropriate collagen synthesis and bone mineralization. In vitro research on osteoblast cells revealed that zinc plays an important role in bone tissue development [36]. Zinc has a crucial function in bone remodeling, regeneration and homeostasis. It does this by fostering osteoblast differentiation and proliferation and shielding osteoblasts from oxidative stress-induced apoptosis [37].

Also, Table 2, the patients had higher mean ±SD levels of copper, which is statistically significant compared to the control (p-value < 0.001). This study supports Mahmood N's., report according to these investigations patients' serum Cu concentrations were much higher than those of the control group [38]. Liu Y. *et al*. found that copper is critical for immune functioning. During infection and inflammation, serum copper concentration increases and caeruloplasmine activity also increases [39].

Increased copper levels have been found in individuals suffering from severe hip osteoarthritis, suggesting that copper is crucial for joint deterioration. In comparison to healthy persons, who found rising amounts of Cu in the degenerating intervertebral disc, people with osteoarthritis had substantially greater concentrations of Cu in their synovial fluid [40].Furthermore, a recent study shown that the decaying hip joints had larger concentrations of copper than the healthy ones. This finding may have been caused by the fact that the bone tissue had accumulated more metal than the intervertebral discs [41].

On the other hand, copper functions as a cofactor for lysyl oxidase, an enzyme that starts and controls the production of collagen and elastin. The activity of this enzyme in bone regions is significantly decreased in Cu deficiency and this results in a decrease in collagen crosslinking, which may affect the stability and synthesis of bone collagen and cause skeletal development abnormalities, ultimately resulting in osteoporosis [42]. It also revealed that persons with degenerative spine disease had much lower median Cu concentrations in their serum than healthy people. Cu's function in spinal degenerative illnesses might be attributed to its involvement in the formation of connective tissue, bone cover and nerve tissue. Low level of Cu in the blood serum may be one of the causes contributing to spine osteoarthritis, which is also seen in conditions such as osteopenia and osteoporosis [35].

The mean ±SD levels of Cu/Zn ratio were significantly higher in patients compared to controls (p <0.001). This is consistent with the Jakoniuk M. *et a*l. study, which found a statistically significant higher Cu/Zn ratio in patients compared to controls. The Cu/Zn ratio is used to detect oxidative stress and inflammation. Spinal osteoarthritis implies disc deterioration and the production of osteophytes. The development of inflammation, which is induced by among other things, oxidative stress is significant in the destruction of articular cartilage [35]. There is a relationship between high Cu/Zn ratios and lower BMD, lean mass, strength and power and lower extremity function. Several recent studies have demonstrated a clear link between increased serum Cu/Zn ratios and several progressive, degenerative diseases [43].

Table 3 shows that copper in the patient group had a significant positive correlation with the Cu/Zn ratio ($r = 0.79$, $p < 0.001$). This matches the Gaier, A. *et al.* study that found significant correlation between high Cu/Zn ratios and high serum Cu with lower BMD, lean mass, strength and power and lower extremity function [43]. Elevation of serum Cu concentration and Cu/Zn correlation in osteoarthritis patients indicate a possible connection to systemic oxidative stress [40].

In addition, as shown in Table 3 the patient had a significant positive correlation between copper and calcium ($r = 25$, p-value 0.04). Unfortunately, studying the correlation between serum calcium and copper levels and lumbar spinal surgery outcomes is not a common research focus, and during the current study, we did not find specific studies on this topic. However, both calcium and copper are essential for bone health and bone healing.

## CONCLUSIONS

It was shown that lower vitamin D3 and calcium levels can be used as indicators of lumbar disc degeneration (LDD) in patients with lumbar spinal surgery, particularly their correlation with lumbar disc degeneration. Pre-operative assessment for vitamin D3 levels is crucial for achieving optimal surgical outcomes. Additionally, the study highlights associations between vitamin D3, Ca++, BMI, and mineral levels such as copper and zinc, which have implications for spinal health. These findings underscore the relevance of considering vitamin D3 and trace elements (Zn and Cu) supplementation as a preventive measure against osteoporosis and their potential role in relieving musculoskeletal pain.

### Outcomes of the study

Deficient levels of vitamin $D_3$ and calcium in the blood in patients receiving lumbar spine surgery. Low serum level of vitamin $D_3$ have been shown to be a predictor of lumbar disc degeneration (LDD) in patients undergoing lumbar spine surgery. These findings highlight the importance of vitamin $D_3$ supplementation as a preventive measure against osteoporosis, as well as its potential involvement in alleviating musculoskeletal pain.

### Rationale of the study

The study was conducted to demonstrate that the research indicates a correlation between hypovitaminosis $D_3$ ,trace elements (Zn and Cu) and lumbar disc degeneration, emphasizing the importance of pre-operative assessment for optimal surgical outcomes.

### Limitations of the study

A bigger sample size is required to generalize the current findings on the Iraqi population, as the study's limited sample size was a drawback.

### Acknowledgment

This research received no external funding.

### Declaration of patient consent

The ethical committee of Baghdad University College of Medicine approved the study procedure. Furthermore, the study was conducted after receiving formal consent from the scientific and administrative association of Ghazi AL-Hariri Hospital in Baghdad, Iraq.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

### 6- Recommendations:

1-A study of the role of serum $D_3$ levels in the pathogenesis of pre- and postoperative lumbar disc deterioration will be needed to answer whether this role can be translated into therapeutic targets.

2-Study other biomarkers of lumbar disc deterioration such as PTH, ALP and phosphorus in a large sample size of patients with lumbar spine issues. So, this knowledge gives clinicians the ability to predict who will develop lumbar disc deterioration early and improve the prevention of this devastating disease.

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