

Original Research Article

Clinical Correlation between Back Pain and Schmorl's Node – Modic's ChangesHalil İbrahim SERİN¹, Iskender Samet DALTABAN², Sinan KARACABEY³, Aylin OKUR⁴, Ayşe Yeşim GÖÇMEN⁵, Hakan AK⁶¹Assistant Professor Bozok University, School of Medicine, Department of Radiology, Yozgat, TURKEY²Assistant Professor, Bozok University, School of Medicine, Department of Neurosurgery, Yozgat, TURKEY³Assistant Professor, Bozok University, School of Medicine, Department of Emergency Medicine, Yozgat, TURKEY⁴Associate Professor Bozok University, School of Medicine, Department of Radiology, Yozgat, TURKEY⁵Associate Professor, Bozok University, School of Medicine, Department of Biochemistry, Yozgat, TURKEY⁶Assistant Professor, Bozok University, School of Medicine, Department of Neurosurgery, Yozgat, TURKEY***Corresponding author**

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Abstract: In this study, we aimed to evaluate correlation of back pain and osteomalacia with Schmorl nodules and endplate degeneration in vertebrates observed on MR imaging. This study was prospective case control study. First group composed of 135 patients with back and/or low back pain. In this group, visual analog scale scores, body mass index and tender point counts were recorded. In the second group, 119 patients were enrolled into the study. In all patients, complete blood count, vitamin D, vitamin C, calcium, phosphate, magnesium, aspartate aminotransferase, *alanine transaminase*, blood urea nitrogen, creatinine, estradiol, testosterone, parathyroid hormone, thyroid stimulating hormone levels were measured and MR imaging was performed. This prospective study included 254 patients. Modic degeneration was observed in 123 (91.1%) of 135 patients with back pain. Vitamin D, total testosterone, calcium, phosphate, magnesium, TSH, parathyroid hormone and vitamin C values were found to be significantly lower in the first group. VAS scores, tender point count, Schmorl's node and Modic's degeneration values were higher in the first group. There is a significant relationship between abnormal values that may cause osteomalacia and Modic's changes and Schmorl's node formation in the patients with back pain.

Keywords: Schmorl's node, Modic's change, lumbar spine, back pain, magnetic resonance imaging

INTRODUCTION

Schmorl's node (SN) is a specific type of vertebral lesion, seen primarily in the thoracolumbar spine. It is the herniation of nucleus pulposus (NP) through the cartilaginous and bony end plate into the body of an adjacent vertebra [1]. Although it is generally considered to be an asymptomatic incidental radiological finding, in rare circumstances it may present with acute onset of pain [2-4]. The pathogenesis of SN is still in debate. However, trauma and stress transmitted through a weakened endplate are considered to be suspected pathogenetic mechanisms [2, 5]. This could be due to intrinsic factors in the endplate (indentations, ossification gaps, vascular channels, Scheuermann's disease) or acquired factors (infection, malignancy, osteoporosis or osteomalacia, hyperparathyroidism, Paget's disease) [2,5,6].

A formal classification of degenerative vertebral endplate and subchondral bone marrow changes were performed by Modic *et al.* in 1988, based on a study of 474 patients. Most of them had chronic low back pain [7]. Modic's changes are uncommon in asymptomatic individuals without degenerative disk disease [7-9]. Weishaupt *et al.* reported a prevalence of 3%-10% among 60 asymptomatic volunteers 20-50 years of age [9].

The causal relationship between Vitamin D deficiency and musculoskeletal pain has been reported by Hollick *et al.* [10]. Vitamin D plays crucial roles in calcium hemostasis, inflammatory cascades by increasing anti-inflammatory and decreasing pro-inflammatory cytokines and optimization of muscular and neurological functions (11,12). The correlation between Vitamin D deficiency and Modic's changes were showed in a recent study [12].

In our prospective study we aimed to evaluate the relationship between back pain and Schmorl's node and end-plate degeneration in spine observed on MR imaging.

MATERIALS AND METHOD

This prospective case-control study was conducted in a tertiary care hospital via collaboration of the departments of radiology, neurosurgery, and biochemistry.

All conditions and procedures of the study were approved by the local ethics committee (24.03.2014/41).

Study groups and patient selection

Two groups were performed for this study.

Randomly selected 135 patients with back and/or low back pain attended to the neurosurgery clinic were enrolled in to the first group of the study (painful group). Patients with congenital skeletal anomaly, osteoarthritis, and osteoporosis, history of antecedent trauma, cardiovascular disease, and drug usage were excluded. Patients younger than 18 years of old age were also excluded from the study. In the patient group, visual analog scale (VAS) scores, body mass index (BMI) and tender point counts were recorded. The pain was assessed by VAS. The patients were asked to mark mean severity of pain within prior week. Tender point count was performed in back region at 17 vertebral levels (12 thoracic and 5 lumbar).

In the second group, 119 randomly selected patients were enrolled into the study. In this group, MRI were taken for other reasons other than back and or low back pain (control group).

Radiological assessment

MR imaging was performed at radiology department by using 1.5 Tesla Inginia MR Device (Philips Medical Systems, Tilburg, Netherlands). The sagittal T1- and T2-weighted sequences were obtained by using following parameters: FOV, 180; TR, 2300-6000; and section thickness, 4-mm. All images were assessed by a single radiologist to avoid subjective assessment.

In all subjects, Schmorl nodules and endplate degeneration which are the findings of osteomalacia were assessed by obtaining thoracolumbar sagittal MR imaging. In all patients, number of Schmorl nodules and type 1, type 2 and type 3 Modic's degenerations were determined.

Biochemical assessment

In all patients, complete blood count (CBC), vitamin D, vitamin C, Ca, P, Mg, AST, ALT, blood urea nitrogen, creatinine, PTH, TSH levels were measured. Vitamin D, vitamin C, Ca, P, Mg and PTH levels and CBC were studied to investigate potential causes of osteomalacia. AST and ALT levels were examined for probable hepatic insufficiency. TSH, estradiol, and testosterone levels were measured to investigate the presence of any pathology related with thyroid gland, ovarium, and testicle.

All the blood samples were centrifuged for 10 min at 3000 RPM, and the serum samples were frozen at -80°C until the assays were performed by an investigator who was blind to each patient's status. Commercial enzyme-linked immunosorbent assay (ELISA) kits were used for the measurement of human Vitamin C levels (Elabscience, Wuhan, PRC) using appropriate wavelengths on a micro-plate reader (BioTech Instruments, EL \times 800 TM, Winooski, USA) following the assay instructions. Serum levels of routine biochemistry parameters were measured using an Architect ci2800 integrated system (Abbott Diagnostics, Abbott Park, IL).

Statistical analysis

Statistical analysis was performed using SPSS package program (Version 18.0 for Windows, SPSS Inc., Chicago, IL, USA). An analysis of normality of the continuous variables was performed with the Kolmogorov-Smirnov test for multivariate analysis; only variables with a P-value < 0.05 were entered into the model and selected using a stepwise selection procedure.

Continuous variables were expressed as a mean \pm standard deviation (SD) or median, and categorical variables were expressed as a percentage. A P-value < 0.05 was considered statistically significant. The χ^2 -test was used to compare proportions. Continuous variables were compared using an independent-groups Student's t-test if normality assumptions were met; otherwise, groups were compared using the Wilcoxon rank-sum test. Pearson correlation analysis was performed.

RESULTS

This prospective study included 254 patients. 135 of them were in the painful group. 103 of them (76.3%) were female and 32 (23.7%) were male. Mean age was 44.43 ± 14.9 in this group.

119 patients were enrolled in the second group. 73 (61.3%) of them were female. Mean age was 43.10 ± 15.1 in the control group. The demographic properties of the patients summarized in Table 1.

Table-1: Demographic and laboratory data of the patients.

Parameters	25-OH-D3 >20 ng/ml N=84	25-OH-D3 <20 ng/ml N=170	P value
Height	169.02 ± 7.31	168.18 ± 6.64	0.372
Weight	85.19 ± 10.34	83.70 ± 9.05	0.262
Age (Years)	42.38 ± 15.78	44.51 ± 14.05	0.296
VAS scoring	0.00 ± 0.00	2.50 ± 2.34	0.001
Tender point count	0.00 ± 0.00	3.44 ± 2.72	0.001
Schmorl nodule	0.11 ± 0.31	3.55 ± 2.74	0.001
Modic degeneration	0.26 ± 0.44	4.48 ± 3.07	0.001
Vitamin D (ng/ml)	29.91 ± 8.66	11.64 ± 4.74	0.001
Estradiol (pg/ml)	67.21 ± 98.86	54.20 ± 64.54	0.275
T. Testosterone (ng/ml)	2.79 ± 3.41	1.44 ± 2.24	0.001
Calcium (mg/dl)	10.00 ± 2.16	8.77 ± 1.63	0.001
Phosphate (mg/dl)	4.01 ± 2.56	2.77 ± 1.88	0.001
Magnesium (mg/dl)	1.90 ± 0.39	1.49 ± 0.29	0.001
ALT (U/L)	21.88 ± 19.93	18.05 ± 11.98	0.108
AST (U/L)	31.65 ± 26.25	25.97 ± 15.59	0.070
Creatinine (mg/dl)	0.72 ± 0.29	0.67 ± 0.18	0.138
TSH (U/ml)	2.27 ± 3.06	1.17 ± 1.46	0.001
Parathormone (pg/ml)	55.34 ± 12.21	30.23 ± 7.12	0.001
Vitamin C (µmol/L)	55.33 ± 15.42	47.38 ± 16.12	0.001
HB (g/dl)	15.02 ± 1.73	14.26 ± 1.88	0.002
WBC (K/µL)	8.56 ± 0.74	8.33 ± 0.89	0.042
PLT (K/µL)	244.44 ± 21.91	244.31 ± 28.38	0.968
RBC (K/µL)	5.60 ± 0.26	5.46 ± 0.36	0.001

Schmorl's node was observed in 116 (85.9%) of 135 patients with back pain and in only one of 119 subjects in the control group. A significant correlation was detected between back pain and Schmorl's node ($p=0.001$).

Modic's degeneration was observed in 123 (91.1%) of 135 patients with back pain and in 20 (16.8%) of 119 subjects in the control group. A significant correlation was detected between back pain and Modic degeneration ($p=0.001$).

Vitamin D (ng/mL) ($p=0.001$), total testosterone (ng/mL) ($p=0.029$), calcium (mg/dL) ($p=0.006$), phosphate (mg/dL) ($p=0.009$), magnesium (mg/dL) ($p=0.001$), TSH (U/mL) ($p=0.001$), parathyroid hormone (pg/mL) ($p=0.001$) and vitamin C

(µmol/L) ($p=0.003$) values were found to be significantly lower in the patient group when compared to controls. PLT value (K/µL) ($p=0.020$) was found to be higher in painful group.

VAS scores ($p=0.001$), tender point count ($p=0.001$), Schmorl nodule ($p=0.001$) and Modic degeneration ($p=0.001$) values were higher in the painful group. Vitamin D (ng/mL) ($p=0.001$), total testosterone (ng/mL) ($p=0.001$), calcium (mg/dL) ($p=0.001$), phosphate (mg/dL) ($p=0.001$), magnesium (mg/dL) ($p=0.001$), TSH (U/mL) ($p=0.001$), parathyroid hormone (pg/mL) ($p=0.001$), vitamin C (µmol/L) ($p=0.001$), Hb (g/dL), WBC (K/µL) ($p=0.042$) and RBC (K/µL) ($p=0.001$) values were found to be significantly lower in the painful group when compared to control group. (Table 2)

Table-2: Comparison of the demographic and laboratory data according to the 25-OH-D3 levels.

Parameters	25-OH-D3 >20 ng/ml N=84	25-OH-D3 <20 ng/ml N=170	P value
Height	169.02 ± 7.31	168.18 ± 6.64	0.372
Weight	85.19 ± 10.34	83.70 ± 9.05	0.262
Age (Years)	42.38 ± 15.78	44.51 ± 14.05	0.296
VAS scoring	0.00 ± 0.00	2.50 ± 2.34	0.001
Tender point count	0.00 ± 0.00	3.44 ± 2.72	0.001
Schmorl nodule	0.11 ± 0.31	3.55 ± 2.74	0.001
Modic degeneration	0.26 ± 0.44	4.48 ± 3.07	0.001
Vitamin D (ng/ml)	29.91 ± 8.66	11.64 ± 4.74	0.001
Estradiol (pg/ml)	67.21 ± 98.86	54.20 ± 64.54	0.275
T. Testosterone (ng/ml)	2.79 ± 3.41	1.44 ± 2.24	0.001
Calcium (mg/dl)	10.00 ± 2.16	8.77 ± 1.63	0.001
Phosphate (mg/dl)	4.01 ± 2.56	2.77 ± 1.88	0.001
Magnesium (mg/dl)	1.90 ± 0.39	1.49 ± 0.29	0.001
ALT (U/L)	21.88 ± 19.93	18.05 ± 11.98	0.108
AST (U/L)	31.65 ± 26.25	25.97 ± 15.59	0.070
Creatinine (mg/dl)	0.72 ± 0.29	0.67 ± 0.18	0.138
TSH (U/ml)	2.27 ± 3.06	1.17 ± 1.46	0.001
Parathormone (pg/ml)	55.34 ± 12.21	30.23 ± 7.12	0.001
Vitamin C (µmol/L)	55.33 ± 15.42	47.38 ± 16.12	0.001
HB (g/dl)	15.02 ± 1.73	14.26 ± 1.88	0.002
WBC (K/µL)	8.56 ± 0.74	8.33 ± 0.89	0.042
PLT (K/µL)	244.44 ± 21.91	244.31 ± 28.38	0.968
RBC (K/µL)	5.60 ± 0.26	5.46 ± 0.36	0.001

Results are given as mean ±STD. The abbreviations are as in the text. *P* value for Back pain *versus* Control

DISCUSSION

The results of this study showed a strong association between the presence of Schmorl nodules and Modic degeneration with low back pain. Moreover, Vitamin D (ng/mL) ($p=0.001$), total testosterone (ng/mL) ($p=0.029$), calcium (mg/dL) ($p=0.006$), phosphate (mg/dL) ($p=0.009$), magnesium (mg/dL) ($p=0.000$), TSH (U/mL) ($p=0.001$), parathyroid hormone (pg/mL) ($p=0.001$) and vitamin C (µmol/L) ($p=0.003$) values were found to be significantly lower in patients with back pain when compared to controls.

The causes of osteomalacia include many conditions such as vitamin D deficiency, inadequate exposure to sunlight, glucocorticoid and anticonvulsant drug use, tumor-related osteomalacia, hepatic failure, hypothyroidism, estrogen and androgen deficiencies, gastrectomy, hypophosphatemia, chronic renal failure, proximal renal tubular acidosis (type 2), use of mineralization inhibitors such as bisphosphonates, idiopathic disorders including fibrogenesis imperfecta ossium, genetic disorders including hypophosphatemic Rickets and insufficient calcium intake [13]. In our study, vitamin D insufficiency/deficiency was found as most common cause of osteomalacia.

Thyroid hormones are essential for normal skeletal growth and maintenance of bone mass, while

hypothyroidism causes growth retardation and impaired bone formation. It was also suggested that hyperthyroidism leads reduction in bone mass, advanced bone age, accelerated growth and increased risk for osteoporotic fracture. In a study on patients with thyroid disease, Mackawy *et al.* reported that there was a correlation between vitamin D insufficiency and autoimmune thyroid Diseases, thyroid dysfunction, thyroid antibodies and demographic characteristics [14]. In a study by Zhang *et al.*, it was shown that TSH levels were inversely correlated to vitamin D levels regardless of thyroid hormones [15]. All these studies confirm association between D hypovitaminosis and hypothyroidism. In this study increased TSH level was found in vitamin D deficiency independent from age, gender and potential confounders. In our study, the subjects were stratified into 2 groups according to vitamin D (25-OH-D3) levels as follows: vitamin D>20 ng/mL and vitamin D<20 ng/mL.

In patients with high vitamin D levels, VAS scores (0.001), tender point count (0.001), Schmorl nodule (0.001) and Modic degeneration (0.001) values were significantly higher patients with low Vitamin D levels. Vitamin D (ng/mL) (0.001), total testosterone (ng/mL) (0.001), calcium (mg/dL) (0.001), phosphate (mg/dL) (0.001), magnesium (mg/dL) (0.001), TSH (U/mL) (0.001), parathyroid hormone (pg/mL) (0.001),

vitamin C ($\mu\text{mol/L}$) (0.001), Hb (g/dL), WBC ($\text{K}/\mu\text{L}$) (0.042) and RBC ($\text{K}/\mu\text{L}$) (0.001) values were found to be significantly lower in patients with back pain. In our study, we didn't observe anticipated TSH elevation in patients with low vitamin D levels.

Studies have shown that androgens, estrogens or both have significant role in bone turnover in adult men and women [16]. In recent studies, Lerchbaum and Obermayer-Pietsch reported that vitamin D regulates sex hormones [17]. In a study reported Wehr *et al.*, it was reported that vitamin D affects risk for diseases related to sex hormone levels such as insulin resistance, polycystic ovarian syndrome and visceral obesity or prostate cancer [18]. Parikh *et al.*, it was reported that active vitamin D stimulates synthesis of testosterone, progesterone, estrone and estradiol [19]. In our study we detected significantly lower testosterone levels with back pain, however, we didn't observe any significant relationship between estradiol levels and patient groups.

In some epidemiological studies, it was shown that back pain incidence was significantly higher in patients with Schmorl nodule when compared to normal individuals. In the majority of preliminary studies on Schmorl nodules, authors addressed potential relationship with predisposing factors and other disorders as well as lesions on imaging studies such as X-ray, CT scan and MR imaging [1,20,21,22]. In addition, histopathological samples were compared to radiological findings in some anatomic-pathological studies. Schmorl nodules and end-plate degenerations can be due to either internal factors such as Scheuermann disease or acquired causes such as infection, malignancy, osteoporosis or osteomalacia, hyperparathyroidism, trauma and Paget's disease [19]. Many studies have shown that there is a strong relationship between Modic endplate changes and back pain. It has been emphasized that pain in axial skeleton results from bone inflammation and instability in the presence of Modic endplate changes. Some authors linked Schmorl nodules to degenerative disk disorder, back pain and Modic changes. There is a consensus on presence of a relationship between Modic changes and Schmorl nodules; thus, edema and pathological bone marrow changes observed in the presence of herniated nucleus pulposus content can be explained [2,5,6,20]. In our study population, Schmorl nodule was observed in 116 (85.9%) of 135 patients with back pain and in one of 119 subjects in the control group, indicating a significant correlation between back pain and Schmorl nodule (0.000). In addition, Modic degeneration was observed in 123 (91.1%) of 135 patients with back pain and in 20 (16.8%) of 119 subjects in the control group, indicating a significant correlation between back pain and Modic degeneration (0.000).

In a study by Matsumoto *et al.*, it was shown that back pain incidence was higher in patients with Schmorl nodule when compared to normal population. In a study, it was suggested that pain observed in the presence of Schmorl nodule might be associated to cellular infiltration and inflammatory changes induced by intra-spongious disk component which comes into contact with vertebral bone marrow. As a result, many patients with symptomatic Schmorl nodule suffer from axial back pain alone [23].

Interestingly, it was observed that asymptomatic Schmorl nodule was developed on subsequent MR imaging in 43% of patients having edema at endplate bone marrow but not Schmorl nodule. In a study by Mok *et al.*, MRI findings were analyzed in patients with symptomatic and asymptomatic Schmorl nodules [21]. Bone marrow was hypointense on T1-weighted images while hypointense on T2-weighted images, indicating edema and inflammation in bone marrow at vertebral corpus. Lack of these findings in asymptomatic patients suggests that Schmorl nodules are asymptomatic when inflammation is relieved [21].

Osteomalacia develops due to vitamin, mineral and hormone deficiencies, particularly vitamin D deficiency, and organ dysfunction, manifesting with Modic's degeneration and Schmorl nodules at varying degrees in thoracic and lumbar vertebrates. In the present study, we aimed to emphasize that there might be vitamin and mineral deficiency as well thyroid, parathyroid, gonad, liver and kidney dysfunction, all which can cause osteomalacia, in patients with back pain.

CONCLUSION

We found a significant relationship between abnormal values that may cause osteomalacia and endplate degenerations and Schmorl node formation in the patients with back pain. We recommend to perform thoracolumbar MR imaging and to evaluate blood chemistry for vitamin D deficiency and other osteomalacia risk factors in patients presenting with back pain and to re-design treatment based on results obtained.

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