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Original Research

Significance of Relationship Between Lumbar Disc Degeneration and Modic Changes in Acute Disc Herniation

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ABSTRACT

Objective: To determine the significance of the relationship between lumbar disc degeneration and Modic changes in acute disc herniation.

Materials and Methods: This study included 323 patients 25 to 42 years of age having acute symptoms of acute single-level lumbar disc herniation. A simple random sampling technique was used to enroll these patients. MRI lumbosacral spine 1.5 tesla was done on all patients. The patients and MRIs were evaluated by a consultant neurosurgeon and anesthetist both having more than five years of clinical experience. The disc herniations, their types, disc degeneration by Pfirrmann grading, Modic changes in end plates, their types, and location were assessed.

Results: The mean age was 34.2±3 years. Males were 185 and females were 138. A total of 1615 discs from L1 to S1 of 323 patients were evaluated. 785 (48.6%) discs had degeneration, 356(22.0%) discs had herniation, 339(20.9%) discs had Modic changes. Out of the 356 herniated discs, 347(97.4%) discs had disc degeneration while 9(2.5%) discs did not have degeneration with a p-value <0.001. Out of the 356 herniated discs, 66(18.5%) discs had Modic changes while 290(81.4%) discs did not have Modic changes with a p-value <0.001.

Conclusion: We conclude that disc degeneration and Modic changes had a significant association with acute disc herniation.

Keywords: Modic changes (MC), Annulus fibrosis (AF), Nucleus pulposus (NP), Pfirrmanns grading system, MRI (Magnetic resonance imaging), Disc degeneration, Lumbar disc herniation(LDH).

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INTRODUCTION

The spine intervertebral disc is an important component of the spine. The functional spine unit consists of two vertebrae and one intervening disc. These intervertebral discs show changes in their architecture with age. This degeneration is a leading cause of low back pain and neck pain.[1] There is disc herniation in which there is displacement of disc material from its boundary into the spinal canal. This leads to compression of the neural components including nerve roots and spinal cord and causes neurological manifestations. The etiopathogenesis of the disc disease had been extensively studied but the exact mechanisms are still not clear.[2]

The normal anatomy of the intervertebral disc consists of annulus fibrosis and nucleus pulposus. Biomechanically the function of the nucleus pulposus and annulus are very different but the components of both are similar including water, proteoglycan, and collagen. Water makes up 80% of the nucleus and 70% of the annulus. Annulus fibrosis consists of lamella of collagen fibers which are right to left oriented with an angle of 60 degrees.[3] In between them, there are elastin fibers. There are fibroblast-like cells in between these lamellae. Nucleus pulposus is a gelatinous material. It has randomly oriented collagen and elastin fibers. Along with this, it has proteoglycan-like gel and chondroitin cells. Annulus is mainly responsible for meeting the high tensile loads. The nucleus plays a role in resisting the compressive loads by applying hydrostatic pressure. The disc is the largest anural and avascular structure of the human body. Its nutrition supply and drainage of waste products depend on the process of diffusion from the adjacent capillary beds of the vertebrae. This leads to an acidic environment with low levels of oxygen, glucose, and high levels of lactic acid in the inner portion of the disc. The cartilaginous end plates are a thin layer of hyaline cartilage that demarcates between the disc and bone of the vertebral body. It has no blood vessels or nerves. Its role is in the mechanical load and nutrition of the intervertebral disc.[4,5]

Macroscopically in disc degeneration, there is a loss of demarcation between the annulus and nucleus which later on leads to cartilage degeneration, disruption of the annulus, sclerosis of endplates, and loss of disc height. Microscopically the changes in intervertebral discs are chondrocyte proliferation, mucous degeneration, tears, and granulation tissue formation. In cartilaginous endplates, there is disorganization, cracks, microfractures, and bony sclerosis. The etiology of disc degeneration is poorly understood but the three factors have been identified including nutritional, genetic, and mechanical. Nutritional factors are the insufficient nutritional supply and accumulation of degradation products including lactic acid which leads to low pH. This affects proteoglycan metabolism. Among genetic factors, polymorphism in genes predisposes to disc degeneration.[6,7] The third factor is the environmental contribution which has a modest contribution to disc degeneration. The role of mechanical overloading in disc degeneration is secondary. End plate degeneration starts with the fissures, cracks, and clefts formation. This causes vascular infiltration, disruption of endplates, and sclerosis. The disc herniation is due to the weakening of annulus fibrosis leading to rupture and herniation of disc material. Predisposing risk factors are heavy weight lifting, twisting, and a sedentary lifestyle. This causes the radiculopathy due to nerve root compression. Disc herniation may be median (in the midline of the spinal canal), paramedian(posterolateral into the lateral recess), or foraminal (into the intervertebral foramina). Herniation types are disc bulge, protrusion, extrusion, or sequestration. The disc bulge is a state when the intervertebral disc begins to protrude from the annulus. In disc protrusion, the base of the protruded disc material is wider than its tip. In extrusion, the base of the disc material is narrower than its tip. In

sequestration, the disc material detaches itself from the parent disc and is present in the spinal canal.[8]

The herniation of disc material into the spinal canal may be caused by two types. One is disc degeneration and end plate damage leading to the slip of the disc material into the canal while the other is annular tear formation leading to disc herniation. It means that the herniation of disc material is not always a pure annulus rupture. It means that there are two pathophysiological processes to disc herniation. One is degeneration of the nucleus with end plate damage and the other one is without end plate damage.[9,10]

Multiple studies have been done on this topic. One was done by Rajasakeran et al in 2017. He studied that end plate failure was an important contributor to single-level disc herniation as compared to tear in annulus fibrosis. End plate damage was evident on MRI of the spine with avulsion of upper or lower or both end plates. Mohd Isa et al studied disc degeneration, its pathophysiology, and treatment options. They studied that the disc herniation was caused by degeneration in annulus fibrosis which causes the clefts and tears in it. This leads to the rupture of the annulus and herniation of disc material from it.[11]

Disc degeneration was assessed by Pfirrmanns grading system[20] (Table 1). Modic changes are described as the changes in the end plates of adjacent intervertebral discs observed via MRI. These changes were first observed by Dr Micheal Modic and divided into three types. In Modic I type there are usually signal intensities such as Low T1 signal, High T2 signal, and contrast enhancement. The changes observed in MRI have an association with the edematous condition of the end plate.[10,11,13] Type II is the one in which high intensity is seen in both T1 and T2 images. The changes have an association with fat replacement of bone marrow. These are linked to the chronic phase of degeneration very commonly. Type III is characterized by both T1 & T2 low signal changes. These changes are associated with sclerosis in inter-vertebral end plates[14,16,19] (Table 2).

The rationale of this study was that we daily come across patients in our OPD clinic and indoors with disc herniation and disc degeneration. We want to know whether there was any association between disc degeneration disc herniation and end plate damage. Because MRI was done in patients with low back pain having sciatic symptoms. In these, we saw disc herniations. Along with this, there was the disc

Table 1: Pfirrmanns grading system for disc degeneration.[20]

Severity	Radiological Features	Pathologic Features
Grade 1	Low signal in AF and high signal in NP on T2 images	Normal disc
Grade 2	Linear decreased T2 signal in NP	Decreased water content
Grade 3	High signal in AF and loss of signal in NP on T2 images	Radial tear in AF and Np dehydration
Grade 4	Loss of T2 signal in both AF and NP	Complete dehydration
Grade 5	Grade 4 along with disc space lost	Dehydration and fibrosis.

Table 2: Modic changes (MC) in end plates.[17]

Severity	Radiological Features	Pathological Features
Type I	Low T1 signal, High T2 signal, and contrast enhancement	Inflammation and fibrovascular changes in end plates.
Type II	Both T1 and T2 have high signals with no enhancement	Fatty changes in end plates
Type III	Both T1 &T2 low signal changes	Sclerosis

degeneration, and end plate changes were also visible in the disc. The question arises is whether there is any association between these parameters. This will help to assess the pathophysiological mechanism of disc herniation. No local study is available on this topic so this will add to the local data of the patients.

MATERIALS AND METHODS

Study Design and Setting

This study was cross-sectional research that was done in the Department of Neurosurgery at Bakhtawar Amin Hospital Multan from August 2021 to September 2023.

Inclusion Criterion

323 patients 25 to 42 years of age having acute symptoms of acute lumbar disc herniation less than 6 weeks of duration were enrolled in this study.

Exclusion Criterion

Patients with spine diseases like recurrent disc herniation, lumbar spinal stenosis, spondylolisthesis, spinal instability, spinal trauma, spinal tumors, spine infections, spine deformities like kyphoscoliosis, chronic low back pain patients, patients having neurological deficits, bedridden patients were not included in this study.

Sampling Technique and Sample Size

A simple random sampling technique was used to enroll 323 patients in this study. G-Power version 3.1.9.4 software was used to calculate the sample size. Alpha was taken as 0.05, effect size 0.3, and power of the test as 80%, sample size of 303 was calculated. However, a sample size of 323 patients was taken in the study.

Clinical and Radiological Management

All patient data was collected. All patients having single-level disc herniation were enrolled in this study. All patients were examined by a consultant neurosurgeon having more than 5 years of clinical experience. The duration of symptoms was less than 6 weeks. We took the patients with acute symptoms because the disc degeneration or end plate damage could have occurred after the herniation of the disc material. MRI lumbosacral spine 1.5 tesla was done on all patients.[6,]. This was evaluated by a consultant radiologist having more than five years of clinical experience (Figure 1).

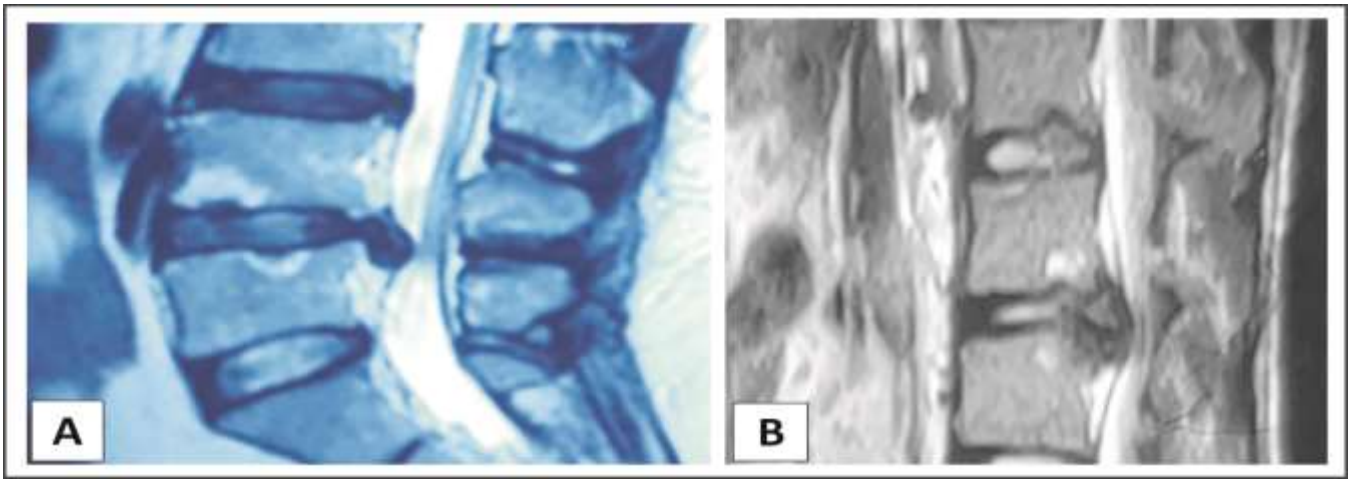

Figure 1: A= Disc herniation with degeneration of nucleus pulposus and annulus rupture, **B**= Disc herniation with Modic changes in end plates.

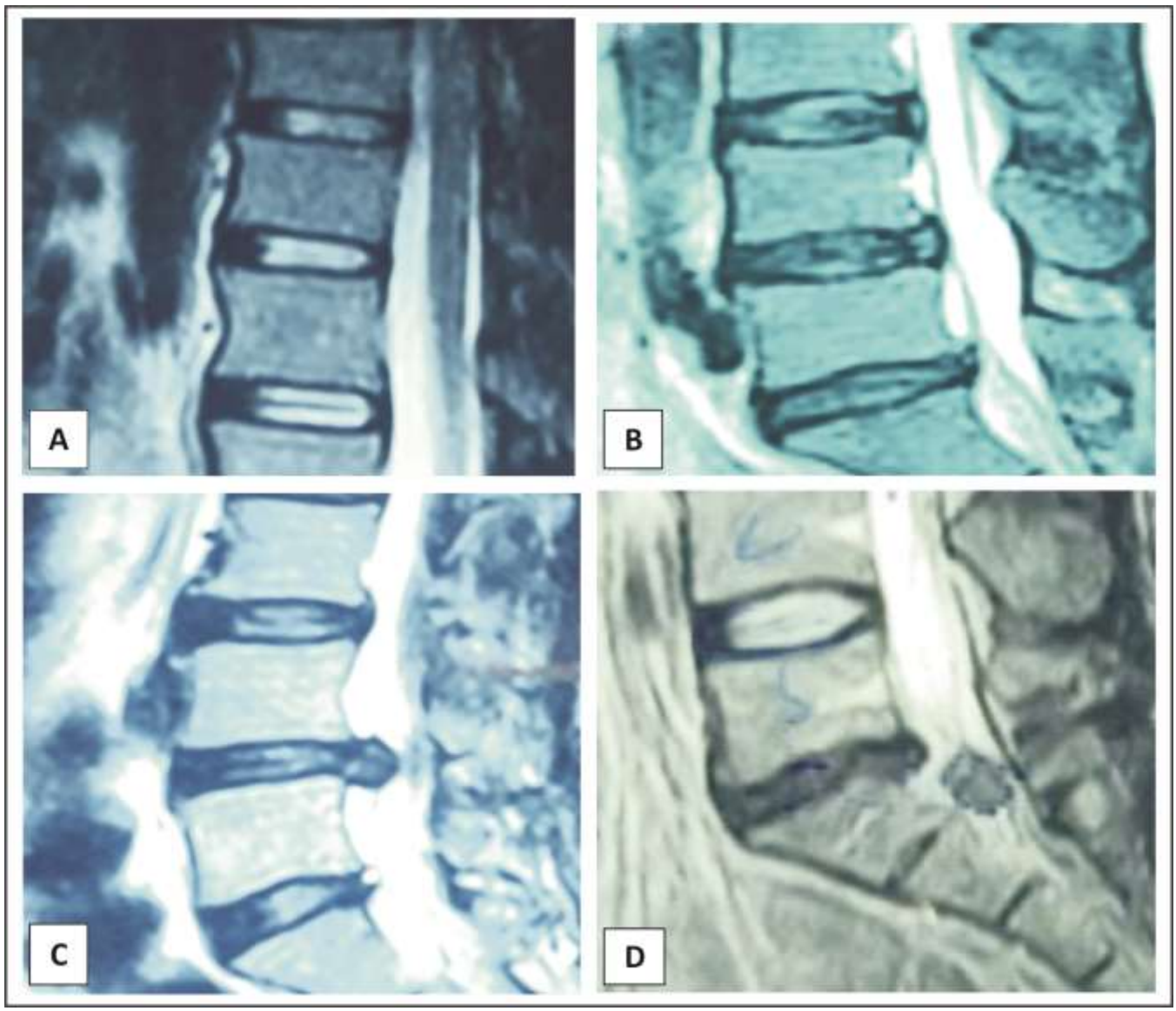

Figure 2: Different types of disc herniation. **A**= Normal disc, **B**= Disc bulge, **C**= Disc protrusion and **D**= Disc sequestration.

Data Collection

Lumbar levels from L1 to S1 intervertebral spaces were evaluated. 1615 intervertebral discs were evaluated for disc herniation types, end plate Modic changes, and disc degeneration at each level. Disc herniation types were evaluated by the anatomy of herniation disc material into 4 types: Disc bulge, disc protrusion, extrusion, and sequestration. The disc bulge was a state when the intervertebral disc began to protrude from the annulus. In disc protrusion, the base of the protruded disc was wider than its tip. In extrusion, the base of the disc material was narrower than its tip. In sequestration, the disc material detached itself from the parent disc and was present in the spinal canal (Figure 2).

Disc degeneration was assessed by Pfirrmanns grading system[20] (Table 3). Grade more than 3 was regarded as degenerated this was assessed on sagittal T2 MRI images. End plate changes were assessed by Modic changes. It was further classified into types 1, 2, and 3 grades.[17] The details are mentioned in the following Table. The presence of MC was studied based on the

location of the plate whether upper or lower-end plate (Table 4). It was further assessed by location whether it was anterior, middle, posterior third, or the whole of the endplate. To determine the location of MC, three sagittal images were studied. One midsagittal image was taken and the other 2 parasagittal images were taken on the right and left sides. The study was approved by the hospital's ethical committee. Written informed consent was taken from all participants. They were properly explained the purpose of the study and their privacy was maintained. The MRI images of the patients were taken with written permission from the patients. The privacy of the patients and MRI was fully maintained.

Statistical Analysis

SPSS version 26.0 was used for statistical results. Qualitative variables were analyzed by frequencies and a chi-square test was used to determine the association of these 2 groups. Quantitative variables were analyzed by mean and Standard deviation. An Independent sample t-test was used to assess the difference in the mean of the numeric variables. P-value< 0.05 was taken as significant with 5% taken as significance level.

RESULTS

Age and Gender Distribution

The demographic analysis was done on 323 patients. The age range of patients was from 25 to 42 years with a mean age of 34.2 ± 3.185 (57.2%) patients were males and 138 (42.7%) patients were females.

Disc Degeneration, Modic Changes, and Disc Herniation

A total of 1615 discs were studied in this study. The levels from L1 to S1 were taken. In this study. In the total of 1615 (lumber) discs of 323 patients, disc degeneration was observed in 785 (48.6%) discs and absent in 830 (51.3%) discs. Out of the total 1615 discs, 356 (22.0%) disc herniation was observed while in 1259 (77.9%) discs there was no herniation. Modic changes were observed in end plates. MC was present in 339 (20.9%) discs and absent in 1276 (79.0%) discs (Table 5).

Disc Herniation Levels

Herniation at different levels of the vertebra was seen as follows. Out of the 56 herniated discs, L1-L2 1(0.2%), L2-L3 11(3.0%), L3-L4 23 (6.4%), L4-L5 170 (47.7%) and L5-S1 151(42.4%) (Table 6).

Table 2: Pfirrmanns grading system for disc degeneration[20]

Severity	Radiological Features	Pathologic Features
Grade 1	Low signal in AF and high signal in NP on T2 images	Normal disc
Grade 2	Linear decreased T2 signal in NP	Decreased water content
Grade 3	High signal in AF and loss of signal in NP on T2 images	Radial tear in AF and Np dehydration
Grade 4	Loss of T2 signal in both AF and NP	Complete dehydration
Grade 5	Grade 4 along with disc space lost	Dehydration and fibrosis.

Table 3: Modic changes(MC) in end plates[17].

Severity	Radiological Features	Pathological Features
Type I	Low T1 signal, High T2 signal, and contrast enhancement	Inflammation and fibrovascular changes in end plates.
Type II	Both T1 and T2 have high signals with no enhancement	Fatty changes in end plates
Type III	Both T1&T2 low signal changes	Sclerosis

Table 5: Demography of disc degeneration, herniation, and MC.

Disc Degeneration Presents Pfirrmann Grade ≥3	Disc Degeneration Absent Pfirrmann Grade ≥3	Disc Herniation Present	Disc Herniation Absent	MC Present	MC Absent
785 (48.6 %)	830 (51.3%)	356(22.0%)	1259(77.9%)	339(20.9%)	1276(79.0%)

Herniation Types

The herniation was also seen concerning its types mainly disc bulge 148(9.1%), disc protrusion and extrusion 192 (11.8%), and finally, disc sequestration 16(0.9%) while normal discs were 1259(77.9%) of the total 1615 discs (Table 7).

Table 6: Herniation levels

L1-L2	L2-L3	L3-L4	L4-L5	L5-S1	Total
1(0.2%)	11(3.0%)	23 (6.4%)	170 (47.7%)	151(42.4%)	356

Table 7: Herniation Types.

Normal Disc	Disc Bulge	Disc Protrusion & Extrusion	Disc Sequestration
1259(77.9%)	148(9.1%)	192 (11.8%)	16(0.9%)

End plate MC Type

As previously mentioned, MC changes were seen in 339 discs out of 1615 discs. Now further types of MC were studied. Type I 22 (6.4%), Type II 292 (86.1%), and Type III 25 (7.3%) were observed (Table 8).

Table 8: Type of Modic changes

Type I	Type II	Type III	Total
22 (6.4%)	292 (86.1%)	25 (7.3%)	339

Location of MC in End Plates

Out of the total 1615 discs, upper-end plate Modic changes were seen in 165 (10.2%) while 1450 (89.7%) discs did not have Modic changes in upper-end plates. Modic changes were seen in lower-end plates in 56 (3.4%) discs and not seen in the rest of the 1559 (96.5%) discs. Modic changes were also seen in both end plates of the same disc. These were seen in 118(7.3%) discs and 1497(92.6%) of the discs did not have end plate damage (Table 9).

Location of MC within a Plate

Upper-end plate MC was seen depending on the location within a plate. Anterior 1/3 133 (8.2%), middle 1/3 18 (1.1%), posterior 1/3 84(5.2%), whole 64(3.9%) and 1316(81.4%) patients did not have upper endplate Modic changes (Table 8). Lower-end plate MC were seen depending on location within a plate. Anterior 1/3 74 (4.5%), middle 1/3 12 (0.7%), posterior 1/3 58 (3.5%), whole 49(3.03%), and 1442(89.2%) patients did not have lower endplate Modic changes of 1615 discs (Table 10).

ANALYTICAL ANALYSIS

Disc Degeneration and Disc Herniation

The relationship between disc degeneration and disc herniation was assessed. Out of the 356 herniated discs, 347(97.4%) discs had disc degeneration while 9(2.5%) discs did not have degeneration. Out of the 1259 non-herniated discs, 438(34.7%) discs had degeneration while 821(65.2%) discs did not have degeneration. The p-value was <0.001. It showed that there was a significant relationship between disc herniation and disc degeneration (Table 12).

Table 9: Location of MC in end plates.

Modic changes in upper endplates		Modic changes in lower-end plates		Modic changes in both end plates	
Yes	No	Yes	No	Yes	No
165 (10.2%)	1450 (89.7%)	56 (3.4%)	1559 (96.5%)	118 (7.3%)	1497 (92.6%)

Table 10: Upper endplate Modic changes.

Nil	Anterior 1/3	Middle 1/3	Posterior 1/3	Whole	Total
1316(81.4%)	133(8.2%)	18(1.1%)	84(5.2%)	64(3.9%)	1615

Table 11: Lower endplate Modic changes.

Nil	Anterior 1/3	Middle 1/3	Posterior 1/3	Whole	Total
1442(89.2%)	74(4.5%)	12(0.7%)	58(3.5%)	49(3.03%)	1615

Table 12: Disc Degeneration and Disc Herniation.

	Disc Herniation Present	Disc Herniation Absent	Total	P- value
Degeneration Present	347(97.4%)	438 (34.7%)	785	<0.001 (Significant Result)
Degeneration absent	9(2.5%)	821(65.2%)	830	
Total	356	1259	1615	

End plate MC and Disc Herniation

The relationship between end plate MC and disc herniation was assessed. Out of the 356 herniated discs, 66(18.5%) discs had Modic changes while 290(81.4%) discs did not have Modic changes. Out of the 1259 non-herniated discs, 273(21.6%) discs had MC while 986(78.3%) discs did not have Modic changes. The p-value was <0.001. It showed that there was a significant relationship between disc herniation and MC in end plates (table 13).

Location of end Plate MC and Disc Herniation

The location of end plate MC was observed whether it was in the upper, lower, or in both end plates. Out of the 356 herniated discs, 71(19.9%) discs had Modic changes in upper end plates while 285(80.0%) discs did not have Modic changes in upper end plates. Out of the 1259 non-herniated discs, 94(7.4%) discs had Modic changes in the upper-end plates while 1165(92.5%) discs did not have changes in the upper-end plate. The p-value was <0.001 making the relationship between upper end plate MC and disc herniation significant. Out of the 356 herniated discs, 23(6.4%) discs had Modic

Table 13: End plate MC and Disc Herniation

	Disc Herniation Present	Disc Herniation Absent	Total	P- value
MC Present	66(18.5%)	273(21.6%)	339	<0.001 (Significant Result)
MC Absent	290(81.4%)	986(78.3%)	1276	
Total	356	1259	1615	

changes in lower-end plates while 333(93.5%) discs did not have Modic changes in lower-end plates. Out of the 1259 non-herniated discs, 33(2.6%) had Modic changes in lower-end plates while 1226(97.5%) did not have Modic changes in lower-end plates. The p-value was 0.064 making the relationship between lower end plate MC and disc herniation non-significant. Out of the 356 herniated discs, 83(23.3%) discs had Modic changes in both end plates while 273(76.6%) discs did not have Modic changes in both end plates. Out of the 1259 non-herniated discs, 35(2.7% discs had Modic changes in both end plates while 1224(97.2%) discs did not have Modic changes in both end plates. The p-value was <0.001 making the relationship between both end plate MC and disc herniation significant (Table 14).

End Plate MC and Herniation Type

The relationship between the end plate MC and herniation type was studied. Out of the 339 discs with MC present, disc bulge was present in 78(23.0%), disc extrusion cases were 113(33.3%) and disc sequestration was present in 13(3.8%) discs and 135(39.8%) discs were normal. Out of the 1276 discs with MC absent, disc bulge was present in 70(5.4%), disc extrusion cases were 79(6.1%) and disc sequestration was present in 3(0.2%) discs and 1124(88.0%) discs were normal. The p-value was 0.12 making the relationship between MC and herniation type non-significant (Table 15).

End Plate MC Type and Disc Herniation:

The relationship between the type of MC in end plates were assessed and their correlation with disc herniation was assessed. Out of the 356 herniated discs, 7(1.9%) discs had MC type I while 349(98.3%) discs did not have MC type I. Out of the 1259 non-herniated discs, 15(1.1%) discs had MC type I while 1244(98.8%) discs did not have MC type I. The p-value was 0.46 making the relationship between MC type I and disc herniation non-significant. Out of the 356 herniated discs, 215(60.3%) had MC type II while

Table 14: Location of end Plate MC and Disc Herniation.

	Disc Herniation Yes	Disc Herniation No	Total	p-value
MC upper Yes	71(19.9%)	94(7.4%)	165	<0.001
MC upper No	285 (80.0%)	1165 (92.5%)	1450	
Total	356	1259	1615	
MC lower Yes	23(6.4%)	33(2.6%)	56	0.064
MC lower No	333(93.5%)	1226(97.5%)	1559	
Total	356	1259	1615	
MC both Yes	83(23.3%)	35(2.7%)	118	<0.001
MC both No	273(76.6%)	1224(97.2%)	1497	
Total	356	1259	1615	

Table 15: End Plate MC and herniation Type.

	MC Yes	MC No	Total	p-value
Normal	135(39.8%)	1124 (88.0%)	1259	0.12
Bulge	78 (23.0%)	70 (5.4%)	148	
Extrusion	113 (33.3%)	79 (6.1%)	192	
Sequestration	13(3.8%)	3 (0.2%)	16	
Total	339	1276	1615	

Table 16: End Plate MC Type and Disc Herniation.

	Herniation Yes	Herniation No	Total	p-value
MC Type I Yes	7 (1.9%)	15 (1.1%)	22	0.46
MC Type I No	349 (98.03%)	1244 (98.8%)	1593	
Total	356	1259	1615	
MC Type II Yes	215 (60.3%)	77 (6.1%)	292	0.04
MC Type II No	141 (39.6%)	1182 (93.8%)	1323	
Total	356	1259	1615	
MC Type III Yes	9 (2.5%)	16 (1.2%)	25	0.21
MC Type III No	347 (97.4%)	1243 (98.7%)	1590	
Total	356	1259	1615	

Table 17: MC location Within an End Plate and Disc Herniation.

	Herniation Yes	Herniation No	Total	p-value
Upper-end Plate				
Nil	224(17.0%)	1092(82.9%)	1316 (100%)	
Anterior	43(32.3%)	90(67.6%)	133 (100%)	
Middle	6(33.3%)	12(66.6%)	18 (100%)	<0.001
Posterior	55(65.4%)	29(34.5%)	84 (100%)	(Significant Result)
Whole	28(43.7%)	36(56.2%)	64 (100%)	
Total	356 (22.0%)	1259 (77.9%)	1615 (100%)	
Lower End Plate				
Nil	254(17.8%)	1168(82.1%)	1422	
Anterior	33(44.5%)	41(55.4%)	74	
Middle	3(25%)	9(75%)	12	<0.001
Posterior	39(67.2%)	19(32.7%)	58	(Significant Result)
Whole	27(55.1%)	22(44.8%)	49	
Total	356(22%)	1259	1615	

141(39.6%) discs did not have MC type II. Out of the 1259 non-herniated discs, 77(6.1%) discs had MC type II while 1182(93.8%) discs did not have MC type II. The p-value was 0.04 making the relationship between MC type II and disc herniation significant. Out of the 356 herniated discs, 9(2.5%) discs had MC type III while 347(97.4%) discs did not have MC type III. Out of the 1259 non-herniated discs, 16(1.2%) had MC type III while 1243(98.7%) did not have MC type III. The p-value was 0.21 making the relationship between MC type III and disc herniation non-significant (Table 16).

MC location Within an End Plate and Disc Herniation

End plate Modic changes were observed within an end plate whether it is upper or lower. It was noted that the end plate changes were in the anterior, middle, posterior, or whole of the plate. Out of the 356 herniated discs, 43(32.3%) discs had MC changes in the anterior 1/3 location, 6(33.3%) discs in the middle 1/3, 55(65.4%) discs in posterior 1/3, 28(43.7%) discs had whole and 224(17.0%) disc did not have MC change at the upper-end plate. Out of the 1259 non-herniated discs, 90(67.6%) disc had MC at anterior 1/3, 12(66.6%) at middle 1/3, 29(34.5%) at posterior 1/3 location, 36(56.2%) whole and 1092(82.9%) did not have MC at upper end plate. The association of the anterior location was assessed with a posterior location in the upper-end plate. The anterior location MC was 43(32.3%) the posterior location was 55(65.4%) and the

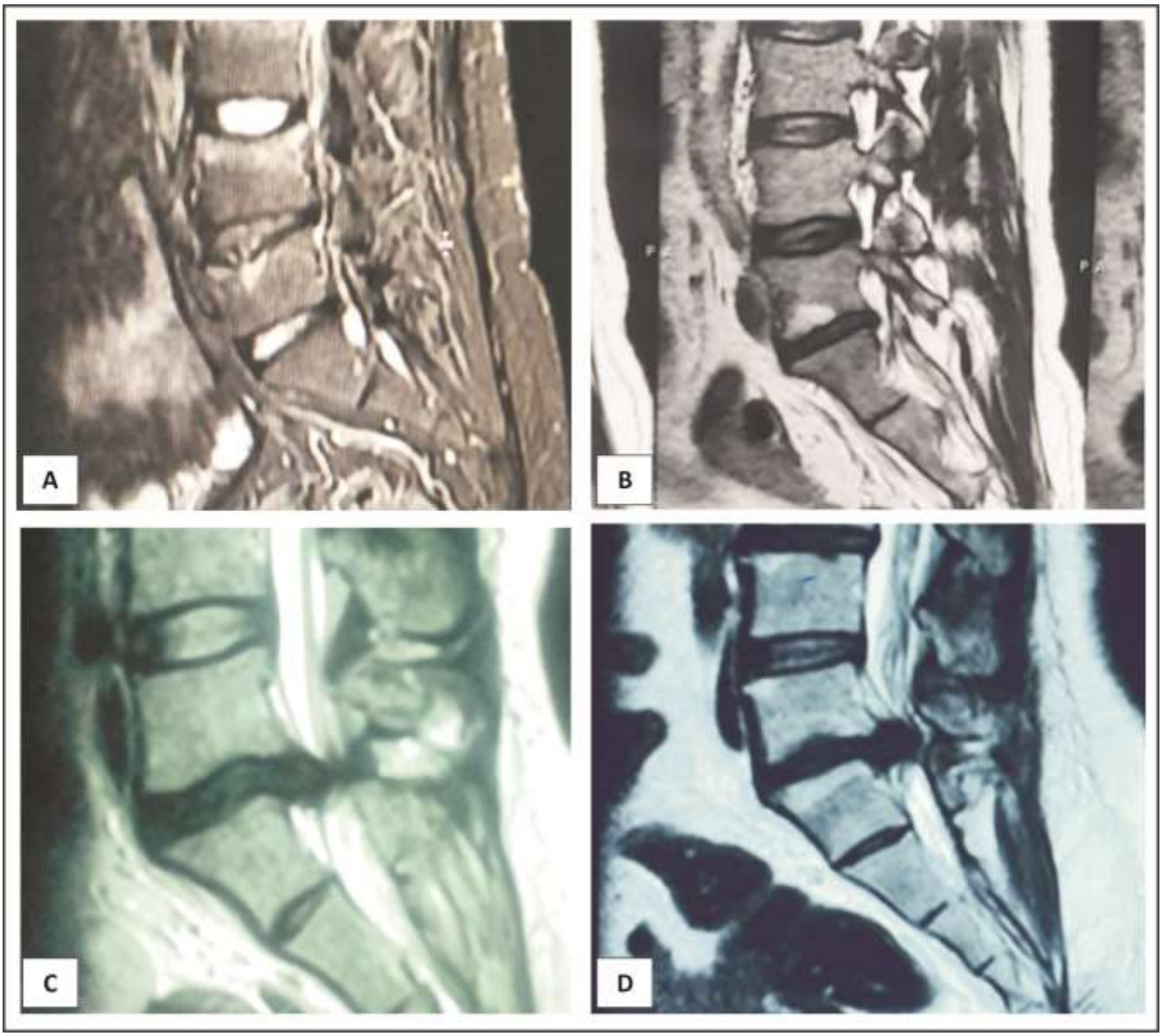

Figure 3: Various locations of Modic changes in end plates. **A =** Modic changes at the anterior 1/3 location, **B =** Modic changes in the middle of end plates, **C =** Modic changes at the posterior end of the end plate, **D =** modic changes in the whole of the end plate.

p-value was < 0.001 which showed that there was a significant association between the MC location within the upper-end plate and disc herniation. Out of the 356 herniated discs, 33(44.5%)had MC location at anterior 1/3 location, 3(25%) at middle 1/3, 39(67.2%) discs at posterior 1/3 location, 27(55.1%) disc at whole and 254(17.8%) did not have MC at lower end plate. Out of the 1259 non-herniated discs, 41(55.4%) discs had MC at anterior location 1/3, 9(75%) at middle 1/3, 19(32.7%) at posterior 1/3, 22(44.8%) at whole and 1168(82.1%) did not have MC at lower end plate (Figure 3). The association of the anterior location was assessed with the posterior location in the lower-end plate. Anterior location MC was 33(44.5%) posterior location was 39(67.2%) and the p-value was < 0.001 which showed that there was a significant association between the MC

location within the lower end plate and disc herniation (Table 17).

DISCUSSION

The intervertebral discs are jelly-like cushions present in between the vertebrae. These serve as shock absorbers to the spine.[1,2] This helps in the mobility of the spine. It consists of annulus fibrosis which is the outer layer and inner gelatinous nucleus pulposus. The annulus is the fibrous layer that provides support to the nucleus and is the structural framework of the disc. The nucleus is the spongy material to dissipates the pressure during activities of daily living.[3] Discs continue to wear and tear with time which leads to degeneration or disc herniations. Factors involved are trauma, age-related changes, and excessive stress during activities. The patients present with low back pain, leg pain, weakness of limbs, or numbness and tingling sensation in discs. Disc degeneration is the gradual degradation of disc material with time.[4] It occurs with aging. The key features of degeneration are decreased water content, the decreased structure of the disc, and elasticity of the disc. Later on, this leads to bony osteophyte formation which causes compression of the neural elements and causes limb pains and back pain. Though aging is one of the factors causing degeneration, other factors genetics, lifestyle, and environment play a crucial role in degeneration.[5] Disc herniation is a condition in which there is a slip of the inner core of disc material through the outer part. This process starts with the degeneration of disc material. This causes strain on the outer layer causing a tear in it which pushes the inner material out from it.[6] Disc degeneration may be discussed concerning the degree of this prolapse of the inner material. The types are disc bulge in which the annulus remains intact but the disc moves beyond its boundary. Disc herniation in which there is the break of the outer annulus and slip of disc material outside the boundary.[7,8] Disc herniation may be in the form of disc protrusion, extrusion, or sequestration. Causative factors are the same as disc degeneration as discussed above.

Disc herniation and degeneration are related to each other and one of these processes can accelerate the other. Disc degeneration has been often considered to be a factor in disc herniation as the decrease in water content in the nucleus and tears in the annulus lead to herniation. Like this disc herniation accelerates disc degeneration. Linhardt et al, 2016 performed MRIs of patients with disc degeneration and disc herniation. He reported that 67% of the disc patients had degenerative changes before the herniation while 33% of discs had herniation before degeneration.[3] Yamada et al, 2022 did a study on using knowledge of cell regeneration therapy for disc degeneration with a focus on functionally repairing for disc herniation treatment. He found that the relation between disc degeneration and disc herniation is significant.[4] Nehru et al, 2023 performed MRIs of the patients of acute lumber disc herniation sequentially. He found out disc degeneration was present in 98.8% of the herniated discs meaning only 1.2% of the herniated discs had no degeneration.[5] The p-value was <0.001 making the relationship significant. In this study, the relationship between disc degeneration and disc herniation was assessed. Out of the 356 herniated discs, 347(97.4%) discs had disc degeneration while 9(2.5%) discs did not have degeneration. The p-value was <0.001. It showed that there was a significant relationship between disc herniation and disc degeneration. This showed that our results matched the results of previous studies.

Modic changes had a complex relationship with disc herniation as this was still a subject of research by scientists.[18,20] Modic changes especially type I might have a distinct role in acute disc degeneration and inflammation of the end plate. Type II Modic changes had been associated with chronic stages of herniation.

Kumarasamy et al, 2022 studied the relationship between lumber disc herniation and Modic changes before microdiscectomy and found that out of 309 patients, 86 had Modic changes and 223 did not have Modic changes.[6] This showed a non-significant association between Modic changes and disc herniation. Xu et al, 2019 did a study on discs both pre-operatively and post-operatively. Out of 276 patients, 44 patients showed Modic type 1 signals,50 patients showed Modic type II signals and 182 patients did not have Modic changes before surgery was performed.[10] Like Albert and Manniche et al,[8] studied MC in disc prolapse and found MC in 23% of patients. Another study was done by Kanna
et al,[9] in 2014 found that 25% of patients had MC of disc herniation. In this study, the relationship between end plate MC and disc herniation was assessed. Out of the 356 herniated discs, 66(18.5%) discs had Modic changes while 290(81.4%) discs did not have Modic changes. Out of the 1259 non-herniated discs, 273(21.6%) discs had MC while 986(78.3%) discs did not have Modic changes. The p-value was <0.001. It showed that there is a significant relationship between disc herniation and MC in end plates. This showed that our results matched with the literature.

The relationship between Modic changes and herniation types involved the associations between types of herniation and different types of Modic changes. Type I Modic changes were associated with acute disc degeneration while type II was associated with chronic disc degeneration.[17,21] Type I Modic changes had a role in the acute stages of the disc herniation. Wei et al,[11] in 2023 studied lumbar Modic changes in patients with lumbar degeneration diseases and found that out of 500 patients, Modic changes were present in 56-disc bulges, 45-disc protrusion, 57-disc extrusion, and sequestration. In this study, the relationship between the end plate MC and herniation type was studied. Out of the 339 discs with MC present, disc bulge was present in 78(23.0%), disc extrusion cases were 113(33.3%) and disc sequestration was present in 13(3.8%) discs and 135(39.8%) discs were normal. Out of the 1276 discs with MC absent, disc bulge was present in 70(5.4%), disc extrusion cases were 79(6.1%) and disc sequestration was present in 3(0.2%) discs and 1124(88.0%) discs were normal. The p-value was 0.12 making the relationship between MC and herniation type non-significant. These results matched the results of the previous studies.

The relationship between the types of MC in end plates and their correlation with disc herniation was assessed. Type I Modic changes were associated with acute phases of disc herniation while type II Modic changes with chronic stages of degeneration and type III changes were associated with more advanced phases of degeneration.[7,13,22] Hao et al,[14] studied 2020 the relationship between herniation and MC types in postoperative follow-up of 91 patients. He operated via percutaneous endoscopic lumbar discectomy (PELD) in 99 discs. Out of those, 28(28.3%) had MC in them. Type I MC were 9(9.1%), type II was 19 (19.2%) and no type III MC were observed. Figa et al,[12] 2018 studied the prediction value of type II changes for choosing the end surgical method for disc herniation. He took 165 patients out of which 80 had type II Modic changes. In this study, out of 356 herniated discs, 7(1.9%) discs had MC type I while 349(98.3%) discs did not have MC type I. Out of the 1259 non-herniated discs, 15(1.1%) discs had MC type I while 1244(98.8%) discs did not have MC type I. The p-value was 0.46 making the relationship between MC type I and disc herniation non-significant. Out of the 356 herniated discs, 215(60.3%) had MC type II while 141(39.6%) discs did not have MC type II. Out of the 1259 non-herniated discs, 77(6.1%) discs had MC type II while 1182(93.8%) discs did not have MC type II. The p-value was 0.04 making the relationship between MC type II and disc

herniation significant. Out of the 356 herniated discs, 9(2.5%) discs had MC type III while 347(97.4%) discs did not have MC type III. Out of the 1259 non-herniated discs, 16(1.2%) had MC type III while 1243(98.7%) did not have MC type III. The p-value was 0.21 making the relationship between MC type III and disc herniation non-significant. This showed that type II MC had a significant correlation with disc herniation which matched the international results.

The specific association between the location of MC and herniation was yet not clear and was based on speculations and attempts to understand the problem entirely. Nehru et al[5] 2023 studied the interaction between the location of end plates MC and herniation in 308 cases. 43 discs had MC in the upper-end plate,13 discs at the lower-end plate, and 62 discs at both end plates. and found that the relationship between herniation and the upper-end plate was significant but with the lower-end plate MC was non-significant and with both end plates MC was significant. Eksi et al,[15] also studied lumbar disc degeneration, and end plates MC in adolescents with low back pain. In this study, the location of end plate MC was observed whether it is in the upper, lower, or both end plates. Out of the 356 herniated discs, 71(19.9%) discs had Modic changes in upper end plates while 285(80.0%) discs did not have Modic changes in upper end plates. Out of the 1259 non-herniated discs, 94(7.4%) discs had Modic changes in the upper-end plates while 1165(92.5%) discs did not have changes in the upper-end plate. The p-value was <0.001 making the relationship between upper end plate MC and disc herniation significant which matched with the previous studies. Out of the 356 herniated discs, 23(6.4%) discs had Modic changes in lower-end plates while 333(93.5%) discs did not have Modic changes in lower-end plates. Out of the 1259 non-herniated discs, 33(2.6%) had Modic changes in lower-end plates while 1226(97.5%) did not have Modic changes in lower-end plates. The p-value was 0.064 making the relationship between lower end plate MC and disc herniation nonsignificant. Out of the 356 herniated discs, 83(23.3%) discs had Modic changes in both end plates while 273(76.6%) discs did not have Modic changes in both end plates. Out of the 1259 non-herniated discs, 35(2.7% discs had Modic changes in both end plates while 1224(97.2%) discs did not have Modic changes in both end plates. The p-value was <0.001 making the relationship between both end plate MC and disc herniation significant.

MCs can also be located anywhere in the end plate it could be in the anterior, middle, or posterior thirds of the disc or it may involve a whole end plate.[4,15] The presence of MC in these locations of the disc had a relationship with LDH. Although anterior MC was commonly observed in both herniated and normal discs, the presence of posterior zone MC was positively associated with LDH. Rajasekaran et al,[21] studied end plate MC location in 181 patients with single disc prolapse. He noted that in 65% of cases, this was due to end plate failure as compared to annulus rupture. He noted rim avulsions, and corner defects in both anterior, middle, and posterior locations of end plates. Like this Peterson et al,[16] studied the location of MC in end plates in 346 patients and Huang et al,[22] did a meta-analysis on the location of MC in the lumbar spine in 2346 patients. In this study, end plate Modic changes were observed within an end plate whether it is upper or lower. It was noted that the end plate changes were in the anterior, middle, posterior, or whole of the plate. Out of the 356 herniated discs, 43(32.3%) discs had MC changes in anterior location, 6(33.3%) discs in the middle, 55(65.4%) discs in the posterior, 28(43.7%) discs had whole and 224(17.0%) disc did not have MC changes at the upper-end plate. Out of the 1259 non-herniated discs, 90(67.6%) disc had MC at anterior, 12(66.6%) at middle, 29(34.5%) at posterior location, 36(56.2%) whole and 1092(82.9%) did not have MC at upper end plate. The association of the anterior location was

assessed with a posterior location in the upper-end plate. The anterior location MC was 43(32.3%) the posterior location was 55(65.4%) and the p-value was < 0.001 which showed that there was a significant association between the MC location within the upper-end plate and disc herniation. Out of the 356 herniated discs, 33(44.5%) had MC location at anterior location, 3(25%) at middle, 39(67.2%) discs at posterior location, 27(55.1%) disc at whole and 254(17.8%) did not have M at lower end plate. Out of the 1259 non-herniated discs, 41(55.4%) disc had MC at anterior location, 9(75%) at middle, 19(32.7%) at posterior, 22(44.8%) at whole and 1168(82.1%) did not have MC at lower end plate. The association of the anterior location was assessed with the posterior location in the lower-end plate. The anterior location MC was 33(44.5%) the posterior location was 39(67.2%) and the p-value was < 0.001 which showed that there was a significant association between the MC location within the lower-end plate and disc herniation.

LIMITATIONS

One limitation of this study was that it was a cross-sectional study. So long-term effects of Modic changes a disc degeneration on disc herniation could not be assessed. To reduce this problem, we selected only patients having less than 6 weeks of duration. There was no clinical correlation done in the study concerning low back pain, leg pain, and neurology. The histopathological analysis was also not done in this study.

CONCLUSION

We conclude that disc herniation which is a very common problem can be annulus driven or end plate driven. In annulus-driven, there is degeneration of the annulus and nucleus leading to herniation of disc material. In end plate driven there is end plate damage which culminates in disc herniation. So disc degeneration and Modic changes had a significant association with acute disc herniation.

REFERENCES

1. Kushchayev SV, Glushko T, Jarraya M, Schuleri KH, Preul MC, Brooks ML, Teytelboym OM. ABCs of the degenerative spine. Insights Imaging. 2018;9(2):253-274.
2. Mohd Isa IL, Teoh SL, Mohd Nor NH, Mokhtar SA. Discogenic Low Back Pain: Anatomy, Pathophysiology and Treatments of Intervertebral Disc Degeneration. Int J Mol Sci. 2022;24(1):208.
3. Linhardt O, Grifka J, Benditz A. Bestehtein Zusammenhangzwischen der degenerativen Bandscheibenveränderung und dem Auftreten von lumbalen Bandscheibenvorfällen? [Are There Correlations Between Disc Degeneration and the Appearance of Lumbar Disc Herniations?]. Z Orthop Unfall. 2016;154(6):595-600.
4. Yamada K, Iwasaki N, Sudo H. Biomaterials and Cell-Based Regenerative Therapies for Intervertebral Disc Degeneration with a Focus on Biological and Biomechanical Functional Repair: Targeting Treatments for Disc Herniation. Cells. 2022;11(4):602.
5. Nehru, Arul P; Kanna, Rishi M; Shetty, Ajoy P; Shanmuganathan, Rajasekaran. Intervertebral disc degeneration and vertebral end plate damage in acute lumbar disc herniation. Indian Spine Journal 6(2):p 118-124, 2023.
6. Kumarasamy D, Rajasekaran S, Anand K S SV, Soundararajan DCR, Shetty T AP, Kanna P RM, Pushpa BT. Lumbar Disc Herniation and Preoperative Modic Changes: A Prospective Analysis of the Clinical Outcomes After Microdiscectomy. Global Spine J. 2022;12(5):940-951.
7. Li G, Zhang W, Liang H, Yang C. Epigenetic regulation in intervertebral disc degeneration. Trends Mol Med. 2022;28(10):803-805.
8. Albert HB, Manniche C. Modic changes following lumbar disc herniation. Eur Spine J. 2007;16(7):977-82.
9. Kanna RM, Shetty AP, Rajasekaran S. Patterns of lumbar disc degeneration are different in degenerative disc disease and disc prolapse

magnetic resonance imaging analysis of 224 patients. Spine J. 2014;14(2):300-7.
10. Xu J, Li Y, Wang B, Lv GH, Wu P, Dai Y, Jiang B, Zheng Z, Xiao S. Percutaneous Endoscopic Lumbar Discectomy for Lumbar Disc Herniation with Modic Changes via a Transforaminal Approach: A Retrospective Study. Pain Physician. 2019;22(6):E601-E608. PMID: 31775413.
11. Wei B, Wu H. Study of the Distribution of Lumbar Modic Changes in Patients with Low Back Pain and Correlation with Lumbar Degeneration Diseases. J Pain Res. 2023;16:3725-3733.
12. Figa R, Morera-Dominguez C. Predictive value of Modic type II changes in the choice of surgical treatment of lumbar disc herniation. Rev Esp Cir Ortop Traumatol (Engl Ed). 2018;62(4):297-301. English, Spanish.
13. Xin J, Wang Y, Zheng Z, Wang S, Na S, Zhang S. Treatment of Intervertebral Disc Degeneration. Orthop Surg. 2022;14(7):1271-1280.
14. Hao L, Li S, Liu J, Shan Z, Fan S, Zhao F. Recurrent disc herniation following percutaneous endoscopic lumbar discectomy preferentially occurs when Modic changes are present. J Orthop Surg Res. 2020;15(1):176.
15. Ekşi MŞ, Özcan-Ekşi EE, Özmen BB, Turgut VU, Huet SE, Dinç T, Kara M, Özgen S, Özek MM, Pamir MN. Lumbar intervertebral disc degeneration, end-plates and paraspinal muscle changes in children and adolescents with low-back pain. J Pediatr Orthop B. 2022;31(1):93-102.
16. Peterson CK, Pfirrmann CW, Hodler J. Are Modic changes related to outcomes in lumbar disc herniation patients treated with imaging-guided lumbar nerve root blocks? Eur J Radiol. 2014;83(10):1786-92.
17. Modic MT, Steinberg PM, Ross JS, Masaryk TJ, Carter JR. Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. Radiology. 1988;166(1 Pt 1):193-9.
18. Linhardt O, Benditz A, Grifka J. Einflüsse der Bandscheibendegenerationbei der Entwicklungeineslumbalen Bandscheibenvorfalls [Influence of disc degeneration on the development of disc prolapse]. Z Orthop Unfall. 2014;152(6):558-64. German.
19. Cazzanelli P, Wuertz-Kozak K. MicroRNAs in Intervertebral Disc Degeneration, Apoptosis, Inflammation, and Mechanobiology. Int J Mol Sci. 2020;21(10):3601.
20. Pfirrmann CW, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic resonance classification of lumbar intervertebral disc degeneration. Spine (Phila Pa 1976). 2001;26(17):1873-8.
21. Rajasekaran S, Tangavel C, Aiyer SN, Nayagam SM, Raveendran M, Demonte NL, Subbaiah P, Kanna R, Shetty AP, Dharmalingam K. ISSLS PRIZE IN CLINICAL SCIENCE 2017: Is infection the possible initiator of disc disease? An insight from proteomic analysis. Eur Spine J. 2017;26(5):1384-1400.
22. Huang ZY, Xu HC, Lei T, Li QL, Wu AM, Ni WF. The location of Modic changes in the lumbar spine: a meta-analysis. Eur Spine J. 2016;25(11):3746-3759.

Additional Information

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Human Subjects: Consent was obtained by all patients/participants in this study.
Conflicts of Interest:
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AUTHOR CONTRIBUTION

Author's Full Name	Intellectual/Contribution to Paper in Terms of:
1. Waqas Noor Chughtai	1. Study design and methodology.
2. Muhammad Umar Jamal	2. Data collection and calculations
3. Saeed Ahmad	3. Paper writing
4. Nauman Ahmed	4. Analysis of data and interpretation of results etc.
5. Tahira Fatima	5. Analysis of data and quality insurer
6. Zain Ali	6. Referencing and data calculations