ORIGINAL ARTICLE

Histopathological spectrum of lumbar disc changes in obesity: analysis of intervertebral discs in lumbar hernia patients in Zenica-Doboj Canton, Bosnia and Herzegovina

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ABSTRACT

Aim To investigate the correlation of body mass index (BMI) with severity of intervertebral disc degeneration.

Methods The study enrolled patients who had undergone surgical intervention for a herniated disc at the Department of Neurosurgery of the Cantonal Hospital Zenica. Patients underwent thorough preoperative evaluation, including medical history, neurological and physical assessments, and radiological analysis. The surgical intervention consisted of a posterior lumbar discectomy, and the excised disc material was preserved and subjected to histopathological analysis based on Histopathologic Degeneration Score (HDS). Patients were divided in two groups according to Body Mass Index (BMI): study group with BMI≥25 and control group with BMI<25.

Results Among 69 patients with herniated IVD, 26 (37.7%) were with BMI≥25 (study group), and 43 (62.3%) were with BMI<25 (controls). The study group displayed substantial increase in height, 1.80±0.06 m compared to controls, 1.74±0.06 m (p=0.001). Weight and BMI were significantly higher in the study group of patients (weight: 91.60±10.22 vs. 67.37±9.20 kg, BMI: 28±2 vs. 22±2; p<0.001). Differences were confirmed in HDS values in the study group comparing to the control group (p<0.001). The study group exhibited significant differences in chondrocyte proliferation, tears and clefts, granular changes, and mucous degeneration (p<0.05), and positive correlations were found between BMI and these alterations found in the herniated discs (p<0.05). Therefore, HDS showed positive correlations with BMI (R=0.599; p<0.001) and weight (R=0.696; p<0.001).

Conclusion The study's findings confirmed that BMI has a significant impact on intervertebral disc degeneration, emphasizing the importance of weight management in preventing disc degeneration.

Key words: chondrocyte proliferation, obesity, weight management

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INTRODUCION

Chronic low back pain (LBP) exerts a substantial impact on a significant portion of the population, and one of its primary contributors is intervertebral disc degeneration (IDD) (1). However, the progression of IDD and its manifestation in patients exhibit notable variability (2). The relationship between severe IDD cases and the degree of LBP is controversial; severe degeneration may result in mild LBP and vice versa (3). This complexity hints at potential involvement of histogenetic factors. Various factors such as age, gender, height, obesity, smoking, occupation, heredity and psychosocial elements contribute to the risk of LBP (4). Alterations in intervertebral disc (IVD) biology have been linked to lumbar disc herniation (LDH), involving diminished water retention in the *nucleus pulposus* (NP), elevated presence of type I collagen in the NP and inner *annulus fibrosis* (AF), degradation of extracellular matrix components, activation of apoptosis, expression of matrix metalloproteinases, and engagement of inflammatory pathways (5). The link between inflammatory signalling and nerve pain in LDH underscores the immunoprivileged nature of the IVD. When the NP protrudes into the epidural space, changes in vascular permeability and vasodilation lead to immune cell recruitment and the initiation of inflammatory cytokine signalling (6).

This study addresses a significant gap in the current research landscape by concentrating exclusively on histopathological analysis as a diagnostic approach for IDD in the context of LBP. Despite extensive investigations into various factors influencing IDD (2), there is a notable scarcity of studies specifically delving into the microscopic examination of disc tissues. Histopathological analysis provides a nuanced understanding of structural changes and cellular responses within the intervertebral disc, offering valuable insights into the degenerative processes (5).

The aim of this study was to investigate the correlation between body mass index (BMI) and the severity of IVD degeneration, recognizing BMI as a potentially modifiable risk factor for degenerative disc conditions. The findings from this research could not only contribute to a more comprehensive understanding of the intricate mechanisms underlying IVD, but also inform targeted interventions and preventive strategies for chronic LBP associated with IVD.

PATIENTS AND METHODS

Patients and study design

This prospective observational study enrolled 69 patients who had experienced surgical intervention for a herniated IVD at the Department of Neurosurgery, Zenica Cantonal Hospital, in the period July 2022-June 2023. Inclusion criteria encompassed: individuals necessitating surgical intervention due to LDH, aged above 18 years, residents of Zenica-Doboj Canton, and those possessing both MRI record and a consistent stream of data availability. Exclusion criteria were patients with the occurrence of trauma to the lumbar spine, the presence of spondylolisthesis, recurrent IVD prolapse, failed back surgery syndrome, or infection. Patients were divided in two groups according to Body Mass Index (BMI): study group with BMI ≥25 and control group with BMI <25 (7).

A written informed consent was obtained from all patients. The Ethics Committee of the Cantonal Hospital Zenica approved the study.

Methods

Patients underwent thorough preoperative evaluations, encompassing the collection of medical history, as well as comprehensive neurological and physical assessments, in addition to radiological analysis. Demographic data included gender and age. Prior to the surgical procedure, measurements of height (m) and weight (kg) were recorded, and BMI was calculated (kg/m^2).

The radiological evaluation involved magnetic resonance imaging (MRI; Magnetom Avanto 1.5 T, Siemens, Erlangen, Germany), with a specific emphasis on discerning the intervertebral disc (ID) level.

The surgical intervention consisted of a posterior lumbar discectomy, with extraction of extruding or sequestered disc material (DM). The excised DM was preserved and subjected to histopathological analysis. In the analysis of tissue samples, surgical specimens were swiftly immersed in formaldehyde solution (4-6%; pH 7.4) for 12-16 hours. Following this, thin sections (4 μm) were produced from the DM that had been fixed in for-

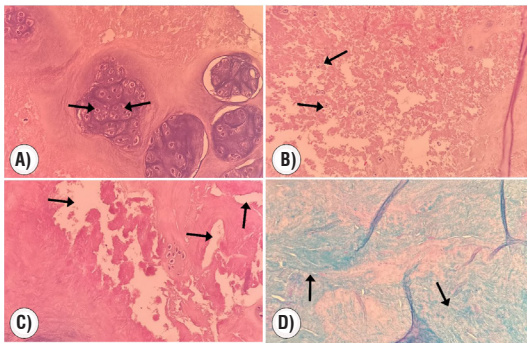

Figure 1. Histomorphological indicators of intervertebral disc degeneration. A) Elevation in cell density (indicating chondrocyte proliferation); B) a pronounced occurrence of granular alterations; C) structural modifications characterized by tears and clefts; D) severe escalation in acid mucopolysaccharides (indicative of mucous degeneration)

malin and embedded in paraffin. These sections were then placed on glass slides treated for this purpose and were subjected to haematoxylin & eosin and alcian blue staining. The main focus was on identifying alterations in the tissue's morphology based on Histologic Degeneration Score (HDS) (8). This semi-quantitative approach involved the assignment of specific subscales (Figure 1): cell density (chondrocyte proliferation): 0 - no indication of proliferation, 1 - elevated cell density, 2 - linkage between two chondrocytes, 3 - presence of small-sized chondrocyte clusters (3-7 cells), 4 - presence of moderate lysized clusters (8-15 cells), 5 - presence of substantial clusters (>15 cells); structural alterations (tears and clefts): 0 - absence, 1 - rare presence, 2 - moderate presence, 3 - significant presence, 4 - indicative of scars or tissue defects; granular changes: 0 - absence, 1 - infrequent presence, 2 - intermediate presence, 3 - pronounced presence; mucous degeneration: 0 - absence, 1 - rare presence, 2 - intermediate presence, 3 - pronounced presence. This assessment offered insights into the extent of degeneration on the HDS scale of 0-15 (8).

Statistical analysis

The evaluation of departures from a normal distribution was executed via the Kolmogorov-Smirnov test, prompting the utilization of non-parametric analyses. To ascertain noteworthy differences in categorical variables between the groups, the Pearson's χ^2 test was applied, while for continuous variables, the Mann-Whitney U test was employed. The correlation between variables was assessed employing the Spearman's Rho correlation coefficient (R). Statistical significance was acknowledged at $p \leq 0.05$.

RESULTS

Among 69 patients with herniated IVD, 26 (37.7%) were with BMI ≥25 (study group), and 43 (62.3%) were with BMI <25 (controls). In the study group males were predominated, 17 (65.4%), and in the control group there was female predomination, 24 (55.8%) (p=0.072). Significant age differences were observed in the 18-29 age group (p<0.001), no patients in the study group comparing to six (14.0%) patients in the control group. The study group displayed substantial increase in height compared to controls, 1.80±0.06 m and 1.74±0.06 m, respectively (p=0.001). The weight and BMI were significantly higher in the study group of patients, 91.60±10.22 kg vs. 67.37±9.20 kg (p<0.001), and 28±2 vs. 22±2 (p<0.001), respectively. No considerable differences were observed in the affected vertebral levels (p=0.424).

Chondrocyte proliferation was absent in both groups. Moderate size clones (8-15 cells) were noted in 6 cases (23.1%) of the study group and 2 cases (4.7%) of the controls. Large clones (>15 cells) were more prevalent in the study group, six (23.1%), than in the control group, one (2.3%) (p=0.003). Granular changes showed rare presence in 10 (38.5%) cases of the study group and 22 (51.2%) of the controls. Intermediate

Table 1. Baseline characteristics of patients

Variable		Study group (N=26)*	Control group (N=43)†	p
		No (%) of patients		
Gender	Male	17 (65.4)	19 (44.2)	0.072
	Female	9 (34.6)	24 (55.8)	
Age (years)	18-29	0	6 (14.0)	<0.001
	30-39	2 (7.7)	22 (51.2)	
	40-49	4 (15.4)	7 (16.3)	
	50-59	15 (55.7)	7 (16.3)	
	60-69	4 (15.4)	0 (0)	
	>70	1 (3.8)	1 (2.3)	
Affected vertebral level	L2/L3	0 (0)	1 (2.3)	0.424
	L3/L4	4 (15.4)	5 (11.6)	
	L4/L5	16 (61.5)	20 (46.5)	
	L5/S1	6 (23.1)	17 (39.5)	
		Mean±SD (Min. – Max.)		
Height (m)		1.80±0.06 (1.69 - 1.92)	1.74±0.06 (1.62 - 1.89)	0.001
Weight (kg)		91.60±10.22 (77.11 - 118)	67.37±9.20 (51.10- 87.42)	<0.001
BMI (kg/m^2)		28±2 (26-34)	22±2 (17-24)	<0.001

*BMI≥25; †BMI<25;
SD, standard deviation; Min, minimal value; Max, maximal value; BMI, body mass index;

Table 2. Pathohistological characteristics of disc material

Variable	Description	Study group (N=26)*	Control group (N=43)†	p
		No (%)	No (%)	
Chondrocyte proliferation	No proliferation	0 (0.0)	0 (0.0)	<0.001
	Increased cell density	0 (0.0)	8 (18.6)	
	Connection of two chondrocytes	5 (19.2)	21 (48.8)	
	Small size clones (3-7)	9 (34.6)	11 (25.6)	
	Moderate size clones (8-15)	6 (23.1)	2 (4.7)	
	Huge clones (>15)	6 (23.1)	1 (2.3)	
Tears and clefts	Absent	2 (7.7)	6 (14.0)	0.003
	Rarely presented	4 (15.4)	24 (55.8)	
	Intermediate presented (1-3)	12 (46.2)	10 (23.3)	
	Abundantly presented	7 (26.9)	3 (7.0)	
	Scar/tissue defects	1 (3.8)	0 (0.0)	
Granular changes	Absent	0 (0.0)	9 (20.9)	0.006
	Rarely presented	10 (38.5)	22 (51.2)	
	Intermediate presented	8 (30.8)	9 (20.9)	
	Abundantly presented	8 (30.8)	3 (7.0)	
Mucous degeneration	Absent	6 (23.1)	27 (62.8)	0.003
	Rarely presented	11 (42.3)	12 (27.9)	
	Intermediate presented (1-3)	9 (34.6)	3 (7.0)	
	Abundantly presented	0 (0.0)	1 (2.3)	
		Mean±SD (Min. – Max.)		
HDS		8.6±2 (4–13)	5.1±2 (1–12)	<0.001

*BMI≥25; †BMI<25;
HDS, histopathological degenerative score;

presence was more common in the study group (30.8% vs. 20.9% in controls), and abundant presence was observed in eight (30.8%) cases of the study group and three (7.0%) cases of controls (p=0.006). Mucous degeneration was less frequent in the study group (23.1%) than controls (62.8%) (p=0.003), with higher prevalence of rare (42.3% vs. 27.9%) and intermediate (34.6% vs. 7.0%) occurrences in the study group. Abundant mucous degeneration was found only in the control group (2.3%). Evident differences were confirmed in HDS values in the study (8.6±2) and control (5.1±2) group (p<0.001), indicating that there are differences in severity of disc degeneration in specific groups (Table 2).

There is a strong positive correlation between BMI and chondrocyte proliferation (R=0.530; p<0.001) (Figure 2A), indicating that higher BMI was associated with an increase of chondrocyte proliferation. Additionally, tears and clefts (R=0.459; p<0.001; Figure 2B), granular changes (R=0.401; p=0.001; Figure 2C), and mucous degeneration (R=0.330; p=0.006; Figure 2D) also showed positive correlation with BMI, implying that these pathohistological features tend to be more prevalent in patients with a higher

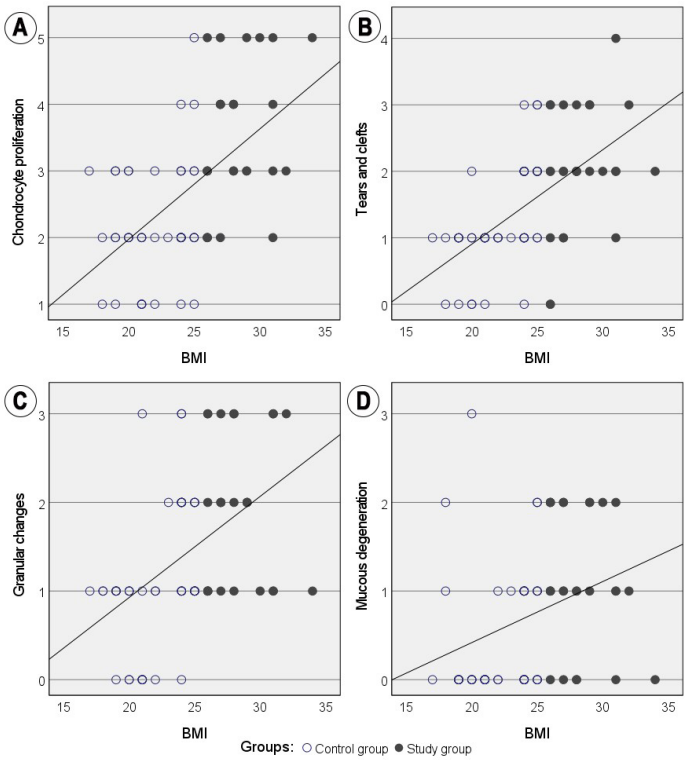

Figure 2. Correlation between body mass index (BMI) with: A) chondrocyte proliferation, B) tears and clefts occurrence, C) granular changes and D) mucous degeneration

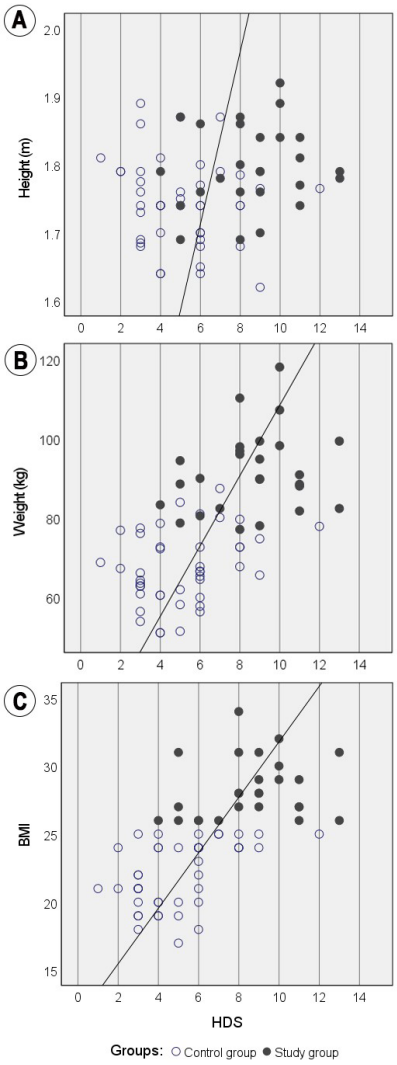

Figure 3. Correlation between histopathological score (HDS) with: A) height (m), B) weight (kg), and C) body mass index (BMI) HDS, histopathological degenerative score;

BMI. Strong positive correlation of HDS with BMI (R=0.599; p<0.001) and weight (R=0.696; p<0.001) was found (Figure 3B & 3C).

DISCUSSION

This study investigated pathohistological alterations of the lumbar IDs related to an increase of BMI in patients who required surgical intervention at the Cantonal Hospital Zenica. The distribution of patients indicated a slightly higher proportion of males in the study group. Elevated BMI has been identified as a risk factor for the development of symptomatic and clinically significant LDH and spinal canal stenosis (8,9). Also, the prevalence of LDH development was noticed to double in males than in females (ratio 2:1) (10).

Currently, investigations are focused on exploring the association between LDH and socio-epidemiological factors in an effort to mitigate their impact and, consequently, prevent the onset of LDH (11,12). In this study most of the participants were between 50-59 years old, which is in accordance with data obtained from other studies (8). The development of clinically significant LDH mostly occurs in patients 30 to 50 years old, usually at L4-L5 or L5-S1 level (13), which is in accordance of our finding.

Novel studies highlighted that obesity, especially with central distribution of fat (around the trunk), is closely related to the biomechanical changes that damage lumbar IVDs (14,15). This can affect the important functions of IVDs, such as their protective role in the transfer of loads and shock through the vertebral column and enabling the movement of the vertebrae (16,17). Obese patients often take non-physiological body positions to compensate for symptoms caused by obesity, such as dyspnoea and pain in the lumbar spine, which creates a heavy load on the bones and joints, especially in working active population (18,19).

In everyday clinical practice, LDH is diagnosed and classified using imaging techniques, such as CT or MRI scan. To our knowledge, the research regarding histopathological changes in the IVDs are scarce and insufficient. Histopathological analysis of discs removed by posterior discectomy investigated four important IDD characteristics: structural changes (tears and fissures), cell density (proliferation of chondrocytes), mucosal degeneration and granular changes. These histopathological determinants resulted with degenerative semi-quantitative score – HDS. The presence of tears and fissures was observed in 26.9% of the BMI ≥25 group and 7.0% of the study group. On the other hand, in the study by Ammar et al. (16) scar tissue and vascularization/granulation tissue were observed in a much higher prevalence in obese patients (23.8%) but were not noted in the controls. The most common changes that were noted in all patients from the study group were tears/clefts and degenerated fibrocartilaginous stroma.

Structural changes (the presence of scar tissue) were visible in 3.8% of the study group; granular changes were found in 30.8% and 7.0% in the controls, respectively. Our results also found a

strong positive correlation between BMI value and chondrocyte proliferation. This was also shown in the Weiler et al. study (10). Moreover, several studies have confirmed leptin receptors (LEPR) expression in osteoblasts and chondrocytes and reported leptin as a modulator of cartilage catabolic activity, proinflammatory joint environment (20), endochondral bone formation (21), and chondrocyte differentiation and mineralization (22).

High BMI promotes different histopathological changes, such as the initiation of chondrocyte proliferation and the formation of fissures and cracks in the affected discs (17), because of an increase of synthesis and adipokine release leptin and adiponectin, from white adipose tissue (23-26).

In clinical practice, knowing the intensity of the IVD degeneration could guide postoperative treatment in a direction that ensures the best possible outcome for patients. Histopathological analysis of the disc material does not require large economical or material resources, which makes its diagnostic importance worthy of further research, especially in low- and middle-income countries. The use of more innovative and inexpensive methods in neurosurgery, especially histopathological analysis, could additionally reduce costs of these procedures (27-29).

In conclusion, our study elucidates the association between elevated body mass index (BMI) and pathohistological alterations in the lumbar IVD necessitating surgical intervention. While existing investigations on risks associated with IDD predominantly concentrate on clinical parameters, the application of histopathological analysis to elucidate the influence of BMI and body weight on IDD severity, particularly in distinguishing between obese and non-obese individuals, has not been systematically explored. The identified structural modifications and heightened chondrocyte proliferation strongly suggest a substantive role for obesity in the manifestation of clinically relevant disc abnormalities.

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TRANSPARENCY DECLARATIONS

Competing interest: None to declare.

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