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Comparison of T2-weighted Magnetic Resonance Imaging findings with histological findings in degenerated lumbar discs in patients with lumbar disc herniation

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ABSTRACT

Diagnosis of disc degeneration and herniation largely depends on Magnetic Resonance Imaging (MRI) and X-rays which fails to detect early disc degeneration. This study was conducted to compare the degenerative changes seen in histological assessment with T2-weighted MRI findings. The study recruited 104 patients with lumbar disc herniation undergoing lumbar discectomy. Excised lumbar disc fragments were taken for histology and T2-weighted MRI was conducted prior to the surgery. Excised disc fragments were subjected to routine histology procedure and van Gieson stain for collagen was performed on each specimen. Disc degeneration was assessed by histological parameters and T2-weighted MRI findings. The majority of subjects (94.2%) showed degenerative changes of the excised portion of the lumbar discs in histological assessment of the disc. However, T2-weighted MRI findings of degenerative changes of the discs were comparatively less (35.6%). According to the histological assessment, higher percentage (61.5 %) of discs were moderately degenerated while 7.7 % had severely degenerated discs. All patients who were confirmed for disc degeneration with T2-weighted MRI (n=37) had confirmed degenerative changes in the histological assessment as well. Histological degenerative alterations were observed in the majority of patients when compared to detectable degenerative changes in T2-weighted MRI suggesting the importance of histological assessment of degeneration in the excised intervertebral disc fragments. As early degenerative changes are not detected by the standard T2weighted MRI technique, if neglected, can progress to severe stages resulting in more discomfort and pain to the patients.

KEYWORDS: *Disc degeneration, Histology, Magnetic Resonance Imaging*

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1 INTRODUCTION

Lower back pain (LBP) is one of the commonest problems among subjects who require medical treatments not only globally but also in Sri Lanka. The majority of the affected people are in the 3rd - 4th decades of their lives (Chirste *et al.*, 2005; Paul *et al.*, 2018). LBP is a common clinical entity that causes major disability in patients affecting their quality of life and also contribute to the socio-economic burden in the country. Among the many factors that contribute to LBP, lumbar disc degeneration and herniation (LDHD) is suggested as the leading cause for the development of LBP in majority of the affected individuals (Pietri *et al.*, 1992). Intervertebral disc (IVD) degeneration is regarded as a natural process. Studies have reported that degeneration associated with LDHD begins at the third decade of life (Zhang *et al.*, 2009), whilst some have reported it beginning even in early stages of life. Although degeneration is pronounced in the third decade of life, it starts a few years after birth (Antoniou *et al.*, 1996). According to the available data, there is 72% disc degeneration in people between the ages 39 - 70 years whilst annular tears can be seen during the fourth decade of life, and nuclear clefts appear at the age of 40 years (Zhang *et al.*, 2009; Antoniou *et al.*, 1996).

IVD is a cartilaginous structure which articulates the vertebral bodies and permit movements between vertebral bodies and also acts as "shock absorbers" between vertebra (Le Maitre *et al.*, 2007). They prevent spinal nerve compression while allowing limited movements of the vertebral column such as bending, torsion and flexion. It also plays a mechanical role, as IVD transmits the weight arising from muscles through the spinal column (Le Maitre *et al.*, 2007; Urban & Roberts 2003). The normal IVD comprises of three distinct components: cartilage end plate which is located superiorly and inferiorly, outer annulus fibrosus (AF) and inner gelatinous nucleus pulposus (NP) (Roberts *et al.*, 2006). According to reported medical explanations, with advanced age, there will be a reduction of the elasticity of the IVD and the content of proteoglycans within the disc thus leading to a decrease in water retention by the IVDs (Roberts *et al.*, 2006, Jarman *et al.*, 2015, Martin *et al.*, 2002). Usually the integrity and stability of the IVDs depend on these factors. Reduction in water and proteoglycan content leads to decrease in elasticity of the IVD causing IVD to resists the mechanical compression and also lead to reduction in disc height which causes reduction in its mechanical integrity (Jarman *et al.*, 2015). It is evident that sequela of these events leads to disc degeneration and its clinical symptoms manifest as LBP.

Magnetic Resonance Imaging (MRI) is widely used as a valuable diagnostic tool in assessing disc degeneration and also aids in the grading of degeneration in the clinical setting (Jarman *et al.*, 2015; Metalloproteinaz, 2013; Samartzis *et al.*, 2012; Griffith *et al.*, 2007). It provides information regarding the water content, disc height and biochemical environment of the IVD. In addition, MRI also grades the degree of disc degeneration. The gold standard 5-grade system of disc

degeneration grading was introduced by Pifirmann et al (Jarman *et al.*, 2015). Apart from the reduction in disc height and water content, disc degeneration also shows tearing of the AF and the NP in the events of disc degeneration (Osti *et al.*, 1992). Currently, in the clinical setting, T1 weighted and T2 weighted MRI techniques are being used in the assessments where loss or reduced signal intensity is regarded as the hall mark of disc degeneration. However, some authors have indicated that early degenerative changes of the IVD, especially quantitative degeneration measurements could not be identified using standard T1-and T2-weighted MRI technique (Wang *et al.*, 2007). They have further proposed that standard T1-and T2-weighted MRI provide limited findings on the structural changes and it is difficult to determine whether water reduction is due to loss of proteoglycan content or due to reduction in diurnal water content of the disc. In some instances, such as inflammation and infections, there can be accumulation of fluid in the disc which can obscure the T2-weighted findings (Paul *et al.*, 2018). Therefore, there is a need for another advanced imaging technique or histological affirmation on the degeneration as there is a possibility of missing early degenerative changes of the disc as degeneration may be the cause for LBP, and if not treated, the LBP associated with LDHD will persist even after surgical intervention. Further, early disc degeneration may be benefited or improved by introducing alternative treatments such as, replacement of nucleus pulpous, cell therapy, total disc arthroplasty and growth factor replacement (Wang *et al.*, 2007) if identified in the early stages.

Hence, the present study was conducted to compare the degenerative changes appearing on histology with the degenerative findings of the T2-weighted MRI of the excised lumbar disc tissue fragments in patients with lumbar disc herniation.

2 MATERIALS AND METHODS

2.1 Study design and setting

Study design was a descriptive cross sectional study where patients were recruited from a selected hospital in the capital of Sri Lanka which drains patients all over the island and thereby representing almost all the districts of Sri Lanka. All patients underwent lumbar discectomy as the surgical treatment for lumbar disc herniation. The analysis was carried out at the University of Sri Jayewardenepura, Sri Lanka. Ethical approval was obtained from the Ethics Review Committee of Faculty of Medical Sciences, University of Sri Jayewardenepura, Colombo, Sri Lanka (29/14). After detailing out the study protocol, informed written consent was obtained from all participants.

2.2 Study population

Study consisted of 104 patients who had low back pain with lumbar disc herniation which was confirmed by a T2-weighted Magnetic Resonance Image (MRI) by a consultant neurosurgeon and consultant radiologist. The concomitant presence of other bone disorders such as osteoarthritis, osteoporosis and pregnancy, malignancies, trauma and accidents related LDH were excluded for patient selection.

2.3 T2-weighted MRI investigation

All subjects underwent T2-weighted MRI and images were evaluated for degenerative changes by a consultant radiologists and a consultant neurosurgeon.

2.4 Histological evaluation

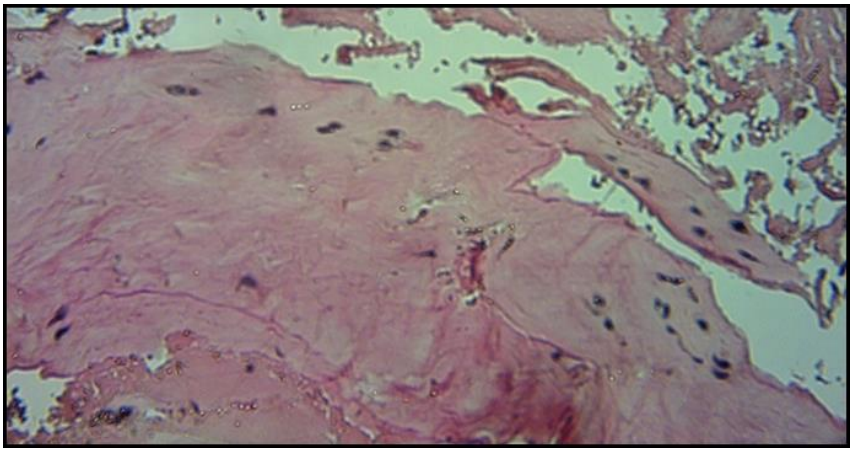
All tissue samples were obtained intraoperatively and tissues were immediately fixed in 10 % buffered formaldehyde for a period of 16-18 hours. Thereafter, fixed tissues were subjected to routine histological processing using an automated tissue processor. Processed tissue was embedded manually in paraffin wax to make paraffin blocks and trimming (5 µm) and cutting (3 µm) was done using manual rotary microtome. Histology slides were made and van-Gieson stain for collagen was performed for each specimen (Fibrous tissue of the uterus was used as controls for the staining). Histomorphology of the stained specimens were observed under light microscope (Olympus BX 50, Japan), under polarized light allowing the evaluation of collagen network. Degree of disc degeneration was reported as mild, moderate and severe degeneration depending on the appearance of the collagen network in AF and cellularity of NP by a consultant histopathologist where the clinical history and MRI findings of the patient were blinded for the observer. Disc degeneration and degree of degeneration was assessed by a self-developed method where cellularity, homogeneity, presence of clefts, cell necrosis and disruption of the arrangement of NP were considered when reporting degree of degeneration of NP, while arrangement of lamellae (infolding (mile, moderate and severe), distortion and fragmentation of lamellae, presence of tearing and clefts were used as factors to determine the extent of degree of degeneration in AF.

3 RESULTS & DISCUSSION

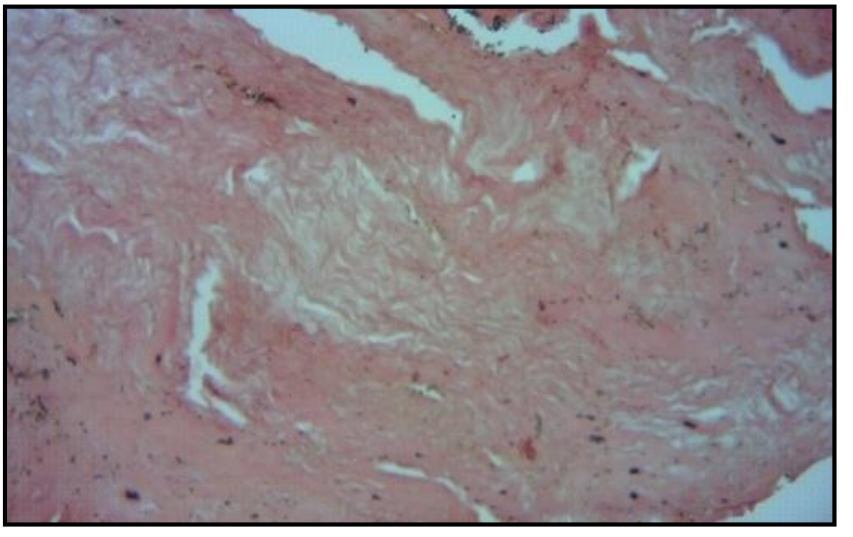
In the histological assessment, the majority of the subjects (94.2%) showed degenerative changes of the collagen network of excised portion of lumbar discs. However, radiographical findings of degenerative changes of the discs were comparatively less (35.6%). According to the histological assessment, a higher percentage of discs was moderately degenerated (61.5 %) while 7.7 % had severely degenerated discs. Further, all the cases who were confirmed for degeneration with MRI (n=37) had confirmed degenerative changes in the histological assessment as well.

Table 01: Degenerative changes in the herniated lumbar intervertebral discs as indicated by magnetic resonance imaging and histological assessment

Variable	No of cases (n)	Percentage (%)
Degenerative changes confirmed with T2-weighted MRI	37	35.6
Degenerative changes confirmed with histology	98	94.2
- Mild degeneration	26	25
- Moderate degeneration	64	61.5
- Severe degeneration	08	7.7



(a)



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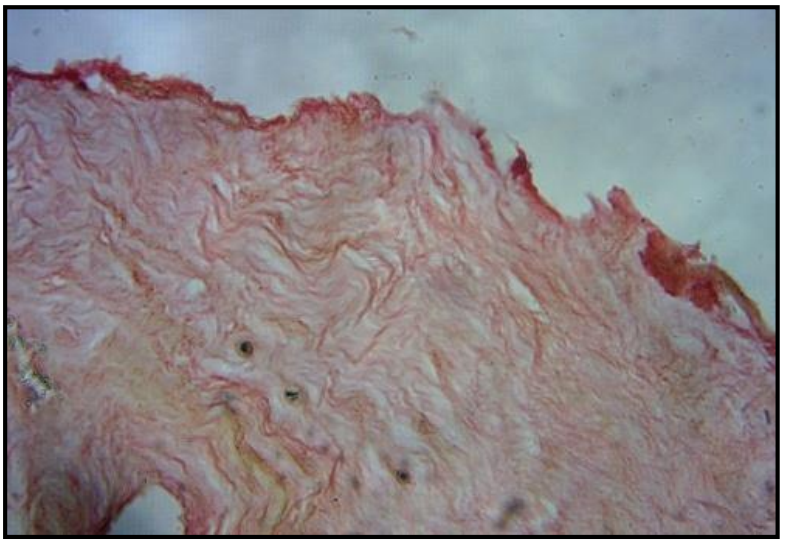

(c)

Figure 01: Histomorphological changes of pathological disc tissues (van-Gieson stain (× 10)) (a) Mild degeneration (b) Moderate degeneration (c) Severe degeneration

Magnetic Resonance Imaging is considered as the most widely used method to assess degeneration and it is also regarded as the gold standard among imaging modalities to assess degeneration (Samartzis *et al.*, 2012; Griffith *et al.*, 2007). MRI technique is based on several factors such as proton density, water content and chemical environment of protons. In the cascade of degeneration, there will be loss of proteoglycans and collagen type II proteins. When the content of proteoglycans is reduced, there will be reduction in capacity to bind water and this will lead to disc dehydration. Loss of water and proteoglycan content of the disc significantly correlate with MRI signal intensity and thus detected as degeneration in MRI (Griffith *et al.*, 2007; Benneker *et al.*, 2005). There are many reported studies that have assessed intervertebral disc degeneration using MRI technique. However, some authors also suggested that early degenerative changes of the intervertebral disc could not be identified using standard T1-and T2-weighted MRI technique (Wang *et al.*, 2007). Hence, the present study focused on comparison of histological degenerative assessment of the excised fragments of intervertebral disc IVD, over degenerative changes observed in the T2-weighted MRI.

Results of the present study confirmed that degenerative changes that appeared on histological assessment were more prominent and detectable (94.2 %) compared to detectable degenerative changes in T2-weighted MRI (34.9 %). In histological investigation, the majority of disc degeneration showed moderate degeneration (61.5 %).

Present study finding of low rate detection of degeneration by T2-weighted MRI could be supported by several other

reported studies. Findings have indicated that initial stage of degeneration characterized by clefts and tears of the IVD can be observed in histology, whereas loss of fluid content of the disc, which is called the secondary stage of disc degeneration, is detected by T1-and T2-weighted MRI later. Authors have further argued that X-ray imaging can detect the degeneration only at very late stage, which is significant when the space of the disc height is reduced (Siepe *et al.*, 2012). Siepe and co-workers (2012) further emphasized that variations in the histological, X-ray and MRI parameters of disc degeneration did not show correlation with the patient's clinical symptoms.

Similar argument on the theme was reported by Johannessen et al (2006), stating that conventional MRI provide better detection of the late stage of degenerative changes which comprises of revealing changes in disc morphology, height, hydration, bulging of the disc and herniation. Authors further emphasized that MRI is not sensitive to detect early degenerative changes of the IVD (Johannessen *et al.*, 2006).

Another study also indicated a similar argument that supported the present study findings. They have stated that early disc degenerative changes may not cause loss of disc height or changes in signal intensity of T2-weighted MRI when compared to histology (Luoma *et al.*, 2001). Thus, the reported studies strengthen the findings of the present study where early disc degeneration was detected in histological studies.

However, in the histological investigation of the present study, only a portion of excised IVD material was examined. In the surgical procedure, we were able to get only a limited portion of the removed disc fragments, as in all surgical cases entire disc is not removed. Further, the present study used two portions of excised disc tissue fragments for the microbiological investigations; therefore, we could only process a small piece of disc tissue for histology investigations. It was evident that there is less information available on histomorphological changes of surgically removed disc during discectomy and total disc replacement, whereas most of the available literature on this aspect is predominantly based on cadaveric samples (Weiler *et al.*, 2011). In the present study, extensive grading of disc degeneration could not be performed as reported in available literature on grading of disc degeneration, as investigators did not receive the entire IVD following lumbar discectomy. Hence, investigators of the present study established a self-developed method to assess only the degree of disc degeneration as mild, moderate and severe rather than reporting different grades of disc degeneration and this should be considered as a major limitation of the study.

It would have been beneficial if we could have compared the morphological changes with normal IVD obtained from cadavers as initially planned. Experts on the field have suggested that cadaver IVD should be obtained from young individuals who have died between the age of 30 - 40 years in order to consider them as normal IVD, prior to major degenerative changes. Therefore, lack of comparison with normal

IVD remains a limitation in the present study.

However, in current surgical practice, histological assessment of excised IVD is not recommended. It was assumed that this could be due to the absence of a reliable and flexible histological grading system to evaluate the morphological changes in contrast to generally accepted MRI classification and lack of clinical interest in the removed IVD due to unfavourable cost effectiveness and loss of therapeutic consequences (Weiler *et al.*, 2011).

CONCLUSIONS

Histological degenerative alterations were observed in majority of patients when compared to detectable degenerative changes in T2-weighted MRI suggesting the importance of histological assessment of degeneration in excised intervertebral disc fragments. As early degenerative changes are not detected by the MRI technique, if neglected, it can progress to severe stages resulting in more uncomforting to the patients. Further, if early degenerative features of the vertebral column could be detected, patients can be advised in this regard and factors leading to progression of degeneration can also be avoided.

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