

# Exploring the Role of MMPs, IL-1, and TNF- $\alpha$ in MRI Parameters of Lateral Discoid Meniscus Injury: A Quantitative Correlation Study

Laiba Khan<sup>1</sup>, Sidra Mahmood<sup>2</sup>, Pirah Abbasi<sup>3</sup>, Sumera Imran<sup>4</sup>, Zainab Qayyum<sup>5</sup>, Sara Gill<sup>6</sup>, Sampana Fatima<sup>7\*</sup>, Nasma Wabasa<sup>8</sup>

<sup>1</sup> Combined Military Hospital, Abbottabad

<sup>2</sup> Quaid-e-Azam Medical College

<sup>3</sup> Liaquat University of Medical and Health Sciences (LUMHS) Jamshoro

<sup>4</sup> Shifa College of Medicine, Islamabad

<sup>5</sup> Punjab Institute of Neurosciences, Lahore

<sup>6</sup> Allied Hospital Faisalabad

<sup>7</sup> Shahida Islam Medical and Dental College

<sup>8</sup> Bahawal Victoria Hospital, Bahawalpur

## Abstract

**Objective:** The study's purpose was to evaluate the efficacy of MRI in the diagnosis of adult lateral discoid meniscus injury and quantify changes in associated parameters. **Methods:** 80 adults, irrespective of gender, presenting to the radiology department for an already suggested MRI, with and without lateral discoid meniscus injury of the knee joint, were selected. After written informed consent, demographic data were noted, and an MRI was performed. **Results:** The mean age of Group A was  $39 \pm 7$  years and Group B was  $37 \pm 9$  years, with equal gender distribution. Group A had significantly higher free edge height ( $5.39 \pm 0.71$  vs  $1.69 \pm 0.30$ ,  $p < 0.001$ ) and body width ( $31.1 \pm 3.16$  vs  $2.39 \pm 0.31$ ,  $p < 0.001$ ), while capsular edge height was lower ( $4.09 \pm 0.33$  vs  $5.11 \pm 0.59$ ,  $p < 0.001$ ). Group A also showed a significantly lower wedge sign (10% vs 72.5%,  $p < 0.001$ ) and a higher fat angle sign (65% vs 0%,  $p < 0.001$ ). Biomarker levels for MMP-1, MMP-3, MMP-13, IL-1, and TNF- $\alpha$  were higher in Group A, with MMP-13 showing strong correlations with free edge height ( $r = 0.45$ ,  $p < 0.01$ ) and body width ( $r = 0.42$ ,  $p < 0.01$ ), MMP-3 with free edge height ( $r = 0.41$ ,  $p < 0.01$ ), and IL-1 with fat angle sign ( $r = 0.50$ ,  $p < 0.001$ ). **Conclusion:** MRI imaging proves to be efficacious in diagnosing lateral discoid meniscus injuries in adults, exhibiting notable differences in related parameters compared to individuals without injury. This underscores its value in injury diagnosis and highlights its potential clinical application.

**Keywords:** MRI Imaging; Adults; Lateral Discoid Meniscus Injury; Examination Parameters

## Introduction

The lateral discoid meniscus injury is predominantly caused by congenital developmental anomalies but adults are also susceptible to it [1]. As patients age and their knee joint activity increases, varying degrees of meniscal damage often occur [2]. Effective surgical treatment can significantly alleviate discomfort and improve functional outcomes, making early, accurate diagnosis crucial [3, 4]. Recent years have seen a surge in studies examining the role of MRI in diagnosing lateral discoid meniscus injuries, with many concluding that MRI is highly effective for early and precise injury detection [5, 6]. However, inconsistencies in research findings persist, and there is a notable gap in studies focusing on the changes in relevant parameters among these patients. This study aims to investigate the application of MRI imaging in adults with lateral discoid meniscus injuries and to analyze the associated parameter changes, providing valuable insights for the selection of diagnostic methods and the formulation of treatment strategies for these injuries. The results of our study are detailed below.

## Material and Methods

This cross-sectional study was conducted according to STROBE guidelines and Declaration of Helsinki was followed for informed consent. The aim of the present study was to find the clinical

implication of MRI in diagnosis of lateral discoid meniscus injury of knee in adults visiting radiology department of Bahawal Victoria Hospital, Bahawalpur. After institutional and departmental ethical approval from Radiology department, Bahawal Victoria Hospital, Bahawalpur, 80 adults, irrespective of gender, presenting to radiology department for already suggested MRI, with and without lateral discoid meniscus injury of knee joint were selected. Subjects were divided into 2 groups, group A with 40 adults, having grade IV lateral discoid meniscus injury and group B with 40 adults, without lateral discoid meniscus injury.

**Selection criteria:** Adults aged 21-49 years and presenting to radiology department for MRI knee. For group A, people with grade IV lateral discoid meniscus injury were selected while for group B, subjects had no knee meniscus injury on MRI scan. The patients presenting for MRI scan and meniscus injury of grades I and II were excluded along with patients having any other manifestation of knee injury or disease.

After a written informed consent, demographic data was noted. Blood samples were collected from all participants to assess the levels of specific biomarkers associated with meniscus injury. The following biomarkers were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits. 1. Matrix

Metalloproteinases (MMP-1, MMP-3, MMP-13): These enzymes are involved in the breakdown of the extracellular matrix and are indicative of tissue degradation in meniscal injury. 2. Cytokines (IL-1, TNF- $\alpha$ ): These inflammatory cytokines were measured to assess the inflammatory response following meniscal injury. The levels of these biomarkers were analyzed to investigate any correlation with MRI findings and the severity of meniscus injury. MRI was performed and consent for usage of MRI findings for research purpose was also taken from each research participant. The matrix was 256×256, the slice distance and thickness were 0.5mm and 4mm respectively, the field of view was 180mm, and the sagittal T1Spin Echo sequence and Proton Density Fast Spin Sequence, fat-suppressed T2 Fast Spin sequence scan; coronal Proton Density Fast Spin Echo Sequence, fat-suppressed T2 Fast Spin Sequence sequence scan. The morphological parameters (wedge sign, plate sign and fat angle sign) and relative morphological parameters (free edge height/body height and joint capsular edge

height/body height)] were measured by consultant radiologists and conclusions were made. A few of the images of normal and injured lateral discoid meniscus, with patients' permission, are shown below.

### Data Analysis

Data was analyzed with the latest version of SPSS. Descriptive variables were expressed as mean  $\pm$  SD or frequency percentages. For measuring the statistical difference, the chi-square test of association was applied. The relationship between the pathological marker levels (MMPs and cytokines) and MRI findings was assessed using correlation analysis. A p-value of  $<0.05$  was considered significant.

### Results

The mean age of study participants of group A was  $39 \pm 7$  years and group B,  $37 \pm 9$  years. Majority of subjects were males, but equal distribution of gender was followed in both groups. (Table 1)

**Table 1:** Demographic Characteristics of Study Population (n=40,40)

| Variable                 | Group A (Mean $\pm$ SD /n (%)) | Group B (Mean $\pm$ SD /n (%)) |
|--------------------------|--------------------------------|--------------------------------|
| Age (years)              | 39 $\pm$ 7                     | 37 $\pm$ 9                     |
| Weight (Kg)              | 62 $\pm$ 4.5                   | 59 $\pm$ 6                     |
| Height (m)               | 1.59 $\pm$ 0.35                | 1.63 $\pm$ 0.43                |
| BMI (kg/m <sup>2</sup> ) | 23.25 $\pm$ 7                  | 22.5 $\pm$ 4                   |
| Gender                   |                                |                                |
| Males                    | 22(55%)                        | 22(55%)                        |
| Females                  | 18(45%)                        | 18(45%)                        |
| Knee involved.           |                                |                                |
| Right                    | 24(60%)                        | 24(60%)                        |
| Left                     | 16(40%)                        | 16(40%)                        |

There was no significant difference in the rate of the plate sign between both groups ( $p > 0.05$ ). Group A exhibited a significantly

lower rate of the wedge sign and a significantly higher rate of the fat angle sign compared to Group D ( $p < 0.05$ ). Table 2

**Table 2:** Comparison of Morphological Features of Normal and Lateral Discoid Meniscus Injury Groups.

| Variable       | Group A (n=40) | Group B (n=40) | $\chi^2/p$      |
|----------------|----------------|----------------|-----------------|
| Wedge Sign     | 4 (10.00)      | 29 (72.50)     | 32 / $<0.001^*$ |
| Plate Sign     | 10 (25.00)     | 11 (27.50)     | 0.06 /0.798     |
| Fat Angle Sign | 26 (65.00)     | 0 (0.00)       | 39 / $<0.001^*$ |

\*p Value was Significant at Level of 0.001.

There was no significant difference in body height between group A and B ( $p > 0.05$ ), but the free edge height and body width in Group A were significantly higher than Group B ( $p < 0.05$ ). Capsular edge height was significantly lower in group A compared to group B, with a value of  $<0.05$ . (Table 2)

When morphological features were expressed as relative morphological features, free edge height/body height ratio in group A was significantly higher than group B, and the joint capsule edge height/body height ratio was significantly lower in group A compared to group B. ( $p < 0.05$ ). Table 3.

**Table 3:** Group Comparison of Morphological and Relative Morphological Features. (N=40, 40)

| Variable                          | Group A (mean $\pm$ SD) | Group B (Mean $\pm$ SD) | p Value    |
|-----------------------------------|-------------------------|-------------------------|------------|
| Free Edge Height                  | 5.39 $\pm$ 0.71         | 1.69 $\pm$ 0.30         | $<0.001^*$ |
| Body Height                       | 2.46 $\pm$ 0.36         | 25.2 $\pm$ 2.63         | 0.355      |
| Body Width                        | 31.1 $\pm$ 3.16         | 2.39 $\pm$ 0.31         | $<0.001^*$ |
| Capsular Edge Height              | 4.09 $\pm$ 0.33         | 5.11 $\pm$ 0.59         | $<0.001^*$ |
| Free Edge Height / Body Height    | 2.19 $\pm$ 0.29         | 0.71 $\pm$ 0.16         | $<0.001^*$ |
| Capsule Edge Height / Body Height | 1.66 $\pm$ 0.25         | 2.13 $\pm$ 0.30         | $<0.001^*$ |

\*p Value was Significant at Level of 0.001.

**Table 4:** Comparison of Pathological Markers for Healing in Study Population

| Biomarker                                   | Group A (Mean $\pm$ SD) | Group B (Mean $\pm$ SD) | p-value  |
|---------------------------------------------|-------------------------|-------------------------|----------|
| MMP-1 (Collagenase-1)                       | 43.2 $\pm$ 8.3 ng/mL    | 22.4 $\pm$ 4.7 ng/mL    | $<0.01$  |
| MMP-3 (Stromelysin-1)                       | 15.4 $\pm$ 5.1 ng/mL    | 9.1 $\pm$ 3.2 ng/mL     | $<0.05$  |
| MMP-13 (Collagenase-3)                      | 12.5 $\pm$ 3.3 ng/mL    | 6.8 $\pm$ 2.1 ng/mL     | $<0.01$  |
| IL-1 (Interleukin-1)                        | 68.3 $\pm$ 12.2 pg/mL   | 35.4 $\pm$ 9.8 pg/mL    | $<0.001$ |
| TNF- $\alpha$ (Tumor Necrosis Factor-alpha) | 84.7 $\pm$ 20.5 pg/mL   | 50.3 $\pm$ 15.1 pg/mL   | $<0.001$ |

The p-Value of  $<0.05$  was Taken as Statistically Significant.

The strongest and statistically significant correlations are observed between MMP-13 and free edge height ( $r = 0.45$ ,  $p < 0.01$ ) as well as body width ( $r = 0.42$ ,  $p < 0.01$ ), indicating that higher MMP-13 levels are strongly associated with increases in these MRI parameters. MMP-3 also shows significant positive correlations with free edge height ( $r = 0.41$ ,  $p < 0.01$ ) and body width ( $r = 0.39$ ,  $p < 0.01$ ). IL-1 exhibits a

strong positive correlation with fat angle sign ( $r = 0.50$ ,  $p < 0.001$ ), highlighting its prominent role in this parameter.

Additionally, TNF- $\alpha$  shows significant correlations with free edge height ( $r = 0.38$ ,  $p = 0.02$ ), body width ( $r = 0.35$ ,  $p = 0.04$ ), and wedge sign ( $r = 0.46$ ,  $p < 0.01$ ), suggesting a strong link between this inflammatory marker and these specific MRI findings.

**Table 5:** Pearson Correlation for Pathological markers of Healing and MRI Parameters

| Mri Parameter                   | MMP-1        | MMP-3        | MMP-13       | IL-1        | TNF- $\alpha$ |
|---------------------------------|--------------|--------------|--------------|-------------|---------------|
| Free Edge Height                | 0.38 / <0.01 | 0.41 / <0.01 | 0.45 / <0.01 | 0.33 / 0.05 | 0.38 / 0.02   |
| Body Height                     | 0.15 / 0.25  | 0.18 / 0.22  | 0.21 / 0.19  | 0.19 / 0.22 | 0.16 / 0.28   |
| Body Width                      | 0.36 / 0.04  | 0.39 / 0.02  | 0.42 / <0.01 | 0.31 / 0.08 | 0.35 / 0.04   |
| Capsular Edge Height            | 0.18 / 0.21  | 0.20 / 0.18  | 0.19 / 0.20  | 0.23 / 0.18 | 0.18 / 0.21   |
| Free Edge Height/Body Height    | 0.33 / 0.06  | 0.35 / 0.05  | 0.38 / 0.04  | 0.29 / 0.10 | 0.32 / 0.07   |
| Capsule Edge Height/Body Height | 0.28 / 0.08  | 0.30 / 0.06  | 0.33 / 0.07  | 0.25 / 0.12 | 0.27 / 0.09   |

Values are Presented in Terms of  $r/p$ , where  $r$ =Pearson Correlation Coefficient and  $p$  is the statistical Significance.  $R$  Close to 0 Indicates a Poor Relationship, and Close to 1 Shows a Strong Relationship.  $p$ -Value of  $<0.05$  was Considered Statistically Significant.

## Discussion

Lateral discoid meniscus is relatively common in clinical practice, with many adult patients susceptible to injury due to increased knee joint activity and increasing age. This highlights the significant need for prompt diagnosis and management of lateral discoid meniscus injury [6, 7]. The elevated levels of MMPs (MMP-1, MMP-3, MMP-13) and inflammatory cytokines (IL-1, TNF- $\alpha$ ) in patients with lateral discoid meniscus injury suggest a significant role for both tissue degradation and inflammation in the injury process. The correlation between these biomarkers and MRI findings provides further support for the utility of combining imaging with biochemical markers in diagnosing and understanding the pathology of meniscal injuries. Medical imaging, particularly MRI, plays a crucial role in the diagnosis of soft tissue injuries [8]. However, comprehensive studies specifically addressing lateral discoid meniscus injuries in adults remain scarce. Issues such as differences in morphological diagnoses and insufficient studies on the correlation between MRI findings and the severity of damage are notable gaps [9, 10]. The results of this study indicate no significant difference in the plate sign rate and body height between adult patients with lateral discoid meniscus injuries and those without such injuries ( $P > 0.05$ ). The wedge sign was significantly lower; the fat angle sign rate was significantly higher in subjects with lateral discoid meniscus injury than subjects with no discoid injury. ( $p < 0.005$ ) Subjects with discoid meniscus injury showed significantly increased values for free edge height, body width, and free edge height/body height, whereas the joint capsule edge height and joint capsule edge height/body height were significantly decreased ( $P < 0.05$ ). Therefore, MRI is highly effective in detecting lateral discoid meniscus injuries in adults and is valuable for identifying morphological changes caused by these injuries, although it does not significantly differentiate the degree of injury. Our results correspond to the previous researches that morphological differences exist between injured and uninjured lateral discoid menisci in adults, the difference from this study was inclusion of pediatric group while our study included adult population [11]. Our findings of wedge sign

rate and a higher fat angle are consistent with findings of Tyler, that the wedge sign is less frequently observed in patients with meniscal injuries, while the fat angle sign tends to be more prominent, compared to subjects with normal knee discoid meniscus [12]. Another study confirmed that MRI provides a detailed view of meniscal morphology and is superior in identifying subtle changes associated with meniscal injuries, which supports our observation of MRI's capability to display subtle parameter changes [13]. This reinforces the diagnostic relevance of these morphological signs in MRI evaluations of meniscal damage. However, there are some inconsistencies in the literature regarding the diagnostic value of MRI. While our study found no significant difference in the plate sign rate and body height among the groups, a study reported that certain morphological signs, including the plate sign, varied significantly between injured and non-injured menisci in their study population [1]. These discrepancies could be attributed to differences in study design, patient demographics, and the criteria used for morphological assessment. By incorporating MMPs and cytokines, the study adds a molecular layer of understanding that could be valuable for developing diagnostic and therapeutic strategies. Future studies could explore the longitudinal changes in these markers to assess their potential as indicators of injury progression or healing.

## Conclusion

The effectiveness of MRI can be attributed to its advantages of multi-directional imaging and high soft tissue resolution, which provide detailed views of the structure, shape, and internal state of the lateral discoid meniscus. This imaging technique also better displays subtle parameter changes post-injury, aiding in diagnosis and offering a reference for treatment. Traditional MRI criteria for meniscal signal abnormalities are less valuable for diagnosing the relatively unique lateral discoid meniscus injuries. Accurate diagnosis often requires a clear third-level signal for significant detection. MRI imaging is highly effective for diagnosing lateral discoid meniscus injuries in adults, as it reveals significant differences in related parameters compared to those without injuries, proving its diagnostic value.

## References

- [1] M. Saavedra, M. Sepúlveda, M. J. Tuca, and E. Birrer, "Discoid meniscus: current concepts," *EFORT open reviews*, vol. 5, no. 7, pp. 371-379, 2020.
- [2] L.-Y. Ai, M.-Z. Du, Y.-R. Chen, P.-Y. Xia, J.-Y. Zhang, and D. Jiang, "Integrated analysis of lncRNA and mRNA expression profiles indicates age-related changes in meniscus," *Frontiers in Cell and Developmental Biology*, vol. 10, p. 844555, 2022.

- [3] G. Steinbacher, E. Alentorn-Geli, M. Alvarado-Calderón, D. Barastegui, P. Álvarez-Díaz, and R. Cugat, "Meniscal fixation is a successful treatment for hypermobile lateral meniscus in soccer players," *Knee Surgery, Sports Traumatology, Arthroscopy*, vol. 27, no. 2, pp. 354-360, 2019.
- [4] C. Carter and S. Yu, "Understanding and Treating the Discoid Meniscus," in *The Management of Meniscal Pathology: From Meniscectomy to Repair and Transplantation*. Springer, 2020, pp. 113-127.
- [5] J.-H. Kim, J. H. Ahn, J.-H. Kim, and J. H. Wang, "Discoid lateral meniscus: importance, diagnosis, and treatment," *Journal of experimental orthopaedics*, vol. 7, no. 1, p. 81, 2020.
- [6] E. Y. Jung, S. Jeong, S.-K. Kim, S.-S. Lee, D. J. Ryu, and J. H. Wang, "A useful MRI classification for symptomatic discoid lateral meniscus," *Knee surgery & related research*, vol. 33, no. 1, p. 31, 2021.
- [7] Z.-R. Zheng *et al.*, "Discoid medial meniscus of both knees: A case report," *World Journal of Clinical Cases*, vol. 10, no. 25, p. 9020, 2022.
- [8] M. Sajid, M. UPPAL, Z. BAJWA, and R. TAHSEEN, "Diagnostic accuracy of magnetic resonance imaging (MRI) for meniscal knee injuries taking arthroscopy as the gold standard," *Biol Clin Sci Res J*, vol. 325, 2023.
- [9] S. H. Kim, C. I. Bae, K.-I. Kim, J. W. Lee, and S. H. Lee, "Factors associated with bilateral discoid lateral meniscus tear in patients with symptomatic discoid lateral meniscus tear using MRI and X-ray," *Orthopaedics & Traumatology: Surgery & Research*, vol. 105, no. 7, pp. 1389-1394, 2019.
- [10] J. S. Everhart and R. G. Tysklind, "Editorial commentary: the pediatric knee: ultrasound could replace magnetic resonance imaging for evaluating a discoid lateral meniscus," vol. 37, ed: Elsevier, 2021, pp. 891-892.
- [11] J. Beck, A. Wood, A. Bennet, and N. Jackson, "Magnetic resonance image (MRI) measurements of lateral discoid meniscus (LDM) in pediatric patients match adult lateral discoid meniscus definitions," *Orthopaedic Journal of Sports Medicine*, vol. 10, no. 5\_suppl2, p. 2325967121S00490, 2022.
- [12] P. Tyler, V. Jain, T. Ashraf, and A. Saifuddin, "Update on imaging of the discoid meniscus," *Skeletal Radiology*, vol. 51, no. 5, pp. 935-956, 2022.
- [13] B. Wang, L. Wang, Y. Wang, and F. Qin, "Clinical diagnostic value of magnetic resonance imaging in knee joint sports injury," *Journal of Medical Imaging and Health Informatics*, vol. 11, no. 2, pp. 453-461, 2021.



This is an open-access article distributed under the terms of the Creative Commons Attribution License.