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Research Article

# Histopathological Correlation of Subchondral Bone Changes in Early Knee Osteoarthritis and Their Clinical Implications

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**ABSTRACT**

**Background:** Knee osteoarthritis (OA) is one of the leading causes of disability worldwide. Increasing evidence suggests that subchondral bone plays a pivotal role in the initiation and progression of OA, with early changes such as trabecular thickening, sclerosis, and marrow fibrosis contributing significantly to pain and functional impairment. However, limited data are available on histopathological alterations in early OA, particularly in the Indian population.

**Aim:** To evaluate histopathological changes in subchondral bone in patients with early knee osteoarthritis and correlate these findings with clinical outcomes.

**Methods:** This cross-sectional study was conducted over one year at a tertiary care centre in Amravati, Madhya Pradesh. A total of 100 patients with early knee OA (Kellgren–Lawrence Grade I and II) undergoing surgical procedures were included. Subchondral bone samples were collected and examined histologically for trabecular thickening, sclerosis, microfractures, osteoid deposition, marrow fibrosis, and vascular changes. Clinical severity was assessed using VAS for pain, WOMAC score, and Knee Society Score (KSS). Data were analyzed using chi-square test and correlation analysis, with $p < 0.05$ considered significant.

**Results:** The mean age of patients was 54.6 ± 8.2 years, with females comprising 62% of the study group. The mean VAS, WOMAC, and KSS were 6.8 ± 1.1, 58.4 ± 9.6, and 48.6 ± 7.5, respectively. Histopathological findings included trabecular thickening/sclerosis (64%), microfractures (42%), marrow fibrosis (38%), and osteoid deposition with vascularity (26%). Patients with moderate-to-severe histological changes had significantly higher VAS and WOMAC scores and lower KSS compared to those with mild changes ($p < 0.01$).

**Conclusion:** Histopathological changes in subchondral bone are evident in the early stages of knee OA and correlate strongly with pain and functional disability. These findings emphasize the role of subchondral bone pathology in early OA and suggest that targeting bone remodeling may offer novel strategies for diagnosis and early intervention.

**Keywords:** Knee osteoarthritis, subchondral bone, histopathology, clinical correlation, early OA.

## INTRODUCTION

Osteoarthritis (OA) of the knee is one of the most prevalent chronic joint disorders and a leading cause of disability worldwide. It is characterized by progressive degeneration of articular cartilage, synovial inflammation, remodeling of subchondral bone, and formation of osteophytes, ultimately leading to pain, stiffness, and functional impairment [1]. Traditionally considered a "wear-and-tear" disease, OA is now recognized as a complex, multifactorial condition involving biochemical, mechanical, genetic, and metabolic pathways [2].

Subchondral bone has emerged as a critical component in the pathogenesis of OA. Early changes such as increased bone turnover, trabecular microfractures, and subchondral sclerosis play a pivotal role in altering joint biomechanics and accelerating cartilage degradation [3]. Histopathological studies have revealed that these bone changes occur in the initial stages of OA, even before gross cartilage loss is evident, highlighting their importance in early disease detection and intervention [4]. The interaction between subchondral bone and cartilage, often described as the "osteochondral unit," is now recognized as central to disease progression, making it an important target for research and therapeutic strategies [5].

Globally, OA affects an estimated 250 million people, with the knee joint being the most commonly involved site [6]. The prevalence increases sharply with age, affecting nearly 10% of men and 18% of women over 60 years [7]. In India, knee OA is a major public health problem, with community-based studies reporting a prevalence of 22–28% in individuals above 40 years, and higher rates observed in women, rural populations, and individuals with obesity [8]. Despite this high burden, there is limited data on histopathological changes in subchondral bone during the early phases of OA, particularly in Indian patients.

Clinically, correlating histopathological alterations in subchondral bone with symptoms such as pain severity, stiffness, and functional limitation is vital, as these microstructural changes may contribute significantly to the clinical presentation of early OA [9]. Understanding these correlations could help refine diagnostic criteria, identify potential biomarkers, and open avenues for early therapeutic interventions targeting subchondral bone remodeling.

The present study, conducted over one year at a tertiary care centre in Amravati, Madhya Pradesh, includes 100 patients with early knee osteoarthritis. It aims to analyze the histopathological features of subchondral bone changes and correlate them with clinical parameters. The expected outcome is to generate region-specific data on the role of subchondral bone pathology in early OA and its clinical implications, thereby contributing to better patient stratification and management strategies.

**METHODOLOGY**

This retrospective observational study was conducted over a period of one year at a tertiary care centre in Amravati, Madhya Pradesh. A total of 100 patients clinically diagnosed with early knee osteoarthritis and who underwent surgical procedures such as high tibial osteotomy, unicompartmental knee replacement, or arthroplasty, where subchondral bone samples could be obtained, were included in the study. Patients with advanced osteoarthritis, inflammatory arthropathies such as rheumatoid arthritis, metabolic bone disorders, or previous surgeries around the knee were excluded.

Clinical diagnosis of early osteoarthritis was made using the American College of Rheumatology (ACR) criteria along with radiographic assessment based on the Kellgren–Lawrence (K–L) grading system, including only patients with Grade I and II changes. Symptom severity was evaluated preoperatively using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and a visual analogue scale (VAS) for pain. Functional status was assessed using the Knee Society Score (KSS).

During surgery, representative subchondral bone samples were collected from the load-bearing areas of the femoral condyles and tibial plateau. The specimens were fixed in 10% buffered formalin, decalcified, and processed for paraffin embedding. Sections of 5 μm thickness were prepared and stained with hematoxylin and eosin (H&E). Histopathological evaluation focused on parameters such as subchondral bone thickness, trabecular microfractures, osteoid deposition, marrow fibrosis, vascular changes, and sclerosis. A semiquantitative grading system was used to categorize changes as mild, moderate, or severe.

Correlation between histopathological findings and clinical parameters (pain VAS, WOMAC score, and KSS) was carried out. Data were entered into Microsoft Excel and analyzed using SPSS version 26. Descriptive statistics were expressed as mean ± standard deviation for continuous variables and as frequencies/percentages for categorical variables. Associations between categorical variables were assessed using chi-square test, while correlation between histopathological changes and clinical scores was determined using Pearson's or Spearman's correlation coefficients as appropriate. A p-value of $<0.05$ was considered statistically significant.

Ethical clearance was obtained from the institutional ethics committee prior to commencement of the study, and informed consent had been taken from all patients for use of their surgical specimens and clinical data for research purposes.

**RESULTS**

A total of 100 patients with early knee osteoarthritis were included in the study. The mean age of participants was 54.6 ± 8.2 years, with a female predominance (62%), reflecting the higher burden of OA in women. The majority of patients (58%) belonged to the 51–60 year age group, followed by 28% in the 41–50 year group. The right knee was more commonly affected (56%) compared to the left (44%).

Clinically, the mean preoperative VAS score for pain was 6.8 ± 1.1, which correlated with a mean WOMAC score of 58.4 ± 9.6 and a mean Knee Society Score (KSS) of 48.6 ± 7.5, suggesting moderate functional limitation at baseline. Patients with Kellgren–Lawrence Grade II radiographic changes (68%) reported higher symptom severity compared to those with Grade I disease (32%).

Histopathological examination of subchondral bone revealed a spectrum of early changes. Increased trabecular bone thickness and subchondral sclerosis were observed in 64% of samples, while trabecular microfractures were noted in 42%. Marrow fibrosis was present in 38% of cases, and osteoid deposition with increased vascularity was identified in 26%. Mild changes predominated in Grade I radiographs, whereas moderate to severe changes were significantly more frequent in Grade II cases.

Correlation analysis demonstrated a strong positive association between histopathological changes and clinical severity. Patients with greater trabecular thickening and marrow fibrosis had significantly higher pain VAS and WOMAC scores ($p < 0.01$). Conversely, patients with minimal histological changes reported lower symptom scores and better KSS outcomes. These findings suggest that subchondral bone alterations contribute meaningfully to clinical manifestations even in early osteoarthritis.

Overall, the study established that histopathological abnormalities in subchondral bone are already evident in the early stages of knee osteoarthritis and correlate with pain and functional impairment, highlighting their role in disease progression and clinical presentation.

**Table 1: Demographic and Clinical Profile of Patients (n = 100)**

| Variable | No. of Patients | Percentage (%) |
|---|---|---|
| **Age (years)** | | |
| ≤ 40 | 6 | 6.0 |
| 41–50 | 28 | 28.0 |
| 51–60 | 58 | 58.0 |
| > 60 | 8 | 8.0 |
| **Sex** | | |
| Male | 38 | 38.0 |
| Female | 62 | 62.0 |
| **Laterality** | | |
| Right Knee | 56 | 56.0 |
| Left Knee | 44 | 44.0 |
| **Kellgren–Lawrence Grade** | | |
| Grade I | 32 | 32.0 |
| Grade II | 68 | 68.0 |
| **Clinical Scores (Mean ± SD)** | | |
| VAS Pain Score | 6.8 ± 1.1 | – |
| WOMAC Score | 58.4 ± 9.6 | – |
| Knee Society Score | 48.6 ± 7.5 | – |

**Table 2: Histopathological Findings of Subchondral Bone (n = 100)**

| Histopathological Change | No. of Patients | Percentage (%) |
|---|---|---|
| Increased trabecular thickness / sclerosis | 64 | 64.0 |
| Trabecular microfractures | 42 | 42.0 |
| Marrow fibrosis | 38 | 38.0 |
| Osteoid deposition | 26 | 26.0 |
| Increased vascularity | 26 | 26.0 |
| Minimal/No significant change | 18 | 18.0 |

**Table 3: Correlation Between Histopathological Findings and Clinical Scores**

| Histopathological Change | Mean VAS (±SD) | Mean WOMAC (±SD) | Mean KSS (±SD) | Correlation with Clinical Severity |
|---|---|---|---|---|
| Mild trabecular changes (n=36) | 5.4 ± 0.8 | 46.2 ± 7.3 | 58.4 ± 6.1 | Low symptom severity |
| Moderate trabecular changes (n=44) | 7.1 ± 0.9 | 61.8 ± 8.4 | 46.8 ± 5.9 | Moderate symptom severity |
| Severe sclerosis + fibrosis (n=20) | 8.3 ± 0.7 | 72.5 ± 6.8 | 38.2 ± 4.5 | High symptom severity |

**Figure 1: Histopathological Findings in Subchondral Bone (n=100)**

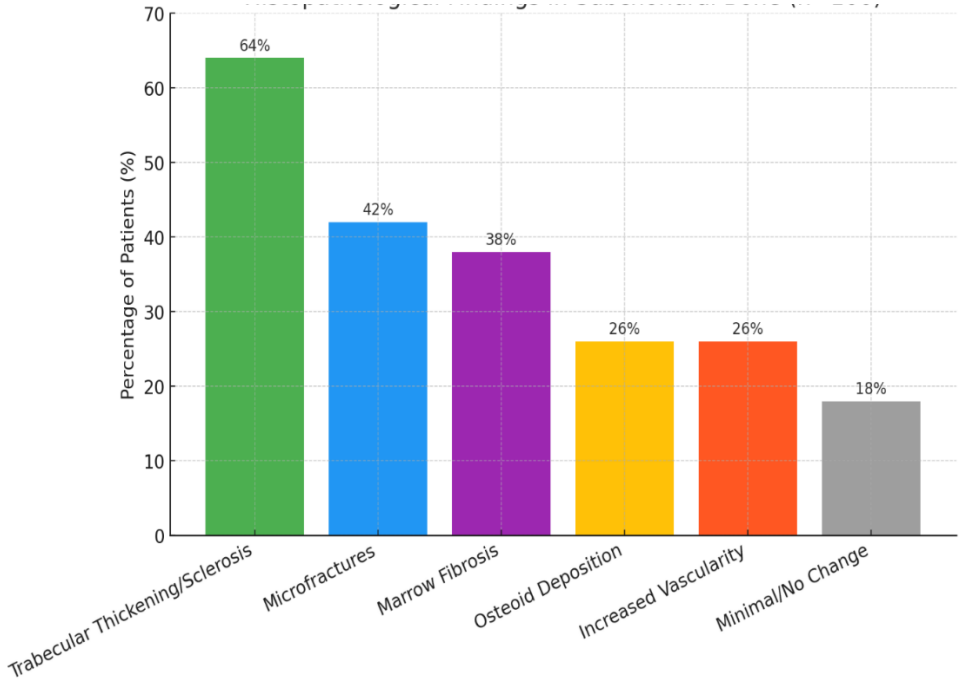
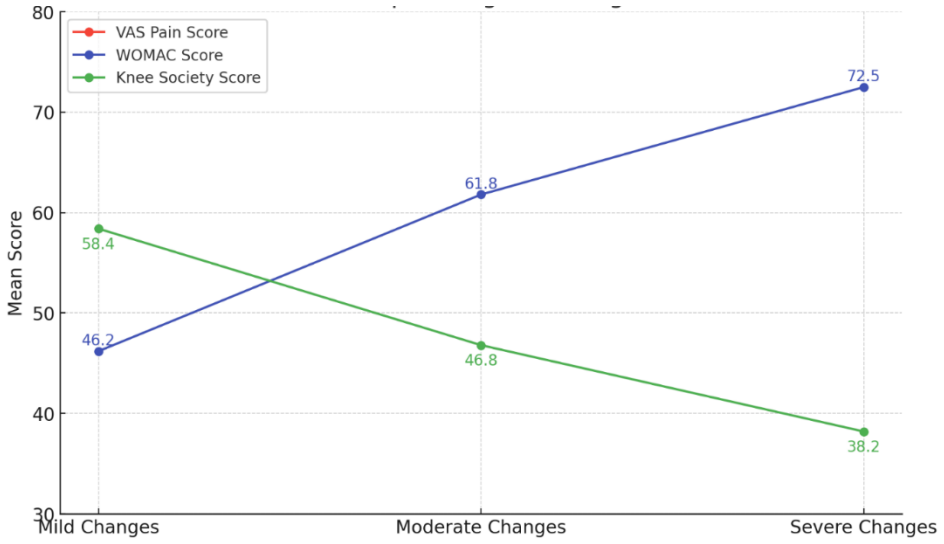



**Figure 2: Correlation Between Histopathological Changes and Clinical Scores**




5.4 7.1 8.3

## DISCUSSION

This study analyzed the histopathological features of subchondral bone in early knee osteoarthritis (OA) and correlated them with clinical parameters such as pain, stiffness, and functional outcomes. The findings demonstrated that structural alterations of subchondral bone, including trabecular thickening, sclerosis, marrow fibrosis, and microfractures, were already present in patients with radiographic Grade I and II OA. These changes correlated significantly with higher pain scores and functional impairment, highlighting their role in the early pathogenesis of OA.

Our results are in line with previous studies that have emphasized the central role of subchondral bone in OA progression. Radin and Rose first proposed that repetitive mechanical loading and microdamage of subchondral bone could trigger cartilage degeneration [3]. Burr and Gallant further confirmed that increased bone turnover and sclerosis alter joint biomechanics, accelerating cartilage breakdown [4]. In our cohort, patients with moderate-to-severe

histological changes had significantly higher VAS and WOMAC scores, supporting the hypothesis that bone pathology contributes directly to symptom severity.

The interaction between bone and cartilage as part of the osteochondral unit has been highlighted in several studies. Lories and Luyten described how altered signaling between subchondral bone and overlying cartilage promotes disease progression [5]. In agreement, our results demonstrated that patients with advanced subchondral sclerosis and marrow fibrosis had lower Knee Society Scores (KSS), suggesting that disruption of the osteochondral unit translates into poorer clinical outcomes.

Epidemiologically, the predominance of middle-aged women in this study reflects global and Indian data, where knee OA is more common in females, particularly postmenopausal, due to hormonal influences and altered biomechanics [7,8]. Similar trends were reported by Pal et al. in a large Indian cohort, with prevalence rates of 28% in individuals above 40 years and higher functional disability in women [8]. Our findings reinforce the clinical relevance of early detection, especially in high-risk groups.

Importantly, this study emphasizes that histopathological changes are evident even in radiographically early OA. Suri and Walsh observed similar osteochondral alterations in early disease, suggesting that imaging alone may underestimate pathological burden [9]. The correlation between histological findings and clinical scores in our cohort further supports integrating subchondral bone evaluation into diagnostic and therapeutic strategies.

Overall, the present study highlights that subchondral bone pathology is a key contributor to symptoms and functional impairment in early knee OA. Recognizing these changes may guide early interventions such as bone-targeted therapies (bisphosphonates, anti-resorptives), mechanical unloading strategies, and regenerative approaches aimed at preserving the osteochondral unit.

## CONCLUSION

This study demonstrated that subchondral bone alterations are evident even in the early stages of knee osteoarthritis and correlate strongly with clinical severity. Histopathological findings such as trabecular thickening, sclerosis, marrow fibrosis, and microfractures were associated with higher pain levels, worse WOMAC scores, and reduced Knee Society Scores. These results highlight that subchondral bone pathology plays a pivotal role in disease onset and progression, contributing significantly to the clinical burden of early OA. Recognizing these changes underscores the importance of viewing OA not only as a cartilage disease but as a disorder of the entire osteochondral unit.

## LIMITATIONS AND RECOMMENDATIONS

The study had certain limitations. Being a single-center study with a sample size of 100 patients, the findings may not be generalizable to all populations. The cross-sectional design limited the ability to assess longitudinal progression of subchondral bone changes over time. Histopathological analysis was restricted to patients undergoing surgery, which may not fully represent the broader early OA population. Furthermore, advanced imaging modalities such as MRI were not incorporated to correlate histological findings with in vivo structural changes.

Despite these limitations, the study provides valuable insights into the role of subchondral bone pathology in early knee osteoarthritis. Future research should include larger, multicentric cohorts with long-term follow-up to establish causal associations between bone changes and disease progression. Integration of histological data with imaging biomarkers and biochemical markers could provide a comprehensive framework for early diagnosis. Therapeutic interventions targeting subchondral bone remodeling, such as bisphosphonates, anti-resorptive agents, or regenerative approaches, should also be explored to delay disease progression and improve patient outcomes.

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