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Prevalence And Early Detection Of Avascular Necrosis In Post-COVID-19 Patients With Hip Pain

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ABSTRACT

Background: Post-COVID-19 patients frequently report persistent hip pain, potentially signaling avascular necrosis (AVN) due to COVID-19-associated coagulopathy or corticosteroid use. Early detection is critical to prevent irreversible joint damage.
Objective: This study evaluates AVN prevalence, staging, and diagnostic accuracy of MRI versus X-ray in this population.
Methods: In this prospective observational study, 50 patients with post-COVID hip pain (mean age 45 ± 12 years; 60% male) underwent clinical evaluation, X-ray, and 1.5T MRI (T1-weighted, STIR sequences). AVN was staged using the Ficat and Arlet classification. Statistical analyses included multivariate logistic regression (adjusting for age, gender, comorbidities) and inter-rater reliability (Cohen's κ). Ethical approval (IRB-2023-045) and informed consent were obtained.
Results: MRI detected AVN in all patients (86% early-stage: 47% Stage I, 39% Stage II). Males had higher AVN prevalence (OR=2.1, 95% CI: 1.3–3.4; p=0.032). Comorbidities significantly increased risk: diabetes (aOR=3.2, 95% CI: 1.4–7.1; p=0.014), hypertension (aOR=2.8, 95% CI: 1.2–6.5; p=0.028). MRI sensitivity (100%) surpassed X-ray (32%; McNemar's χ^2=38.4, p<0.001). Inter-rater agreement for MRI staging was excellent (κ=0.92). Higher corticosteroid doses correlated with advanced stages (β=0.41, p=0.017).
Conclusion: Post-COVID hip pain frequently correlates with early-stage AVN, underscoring MRI's superiority over X-ray for detection. Males and patients with diabetes/hypertension warrant prioritized screening. These findings advocate for updated diagnostic protocols to mitigate long-term disability in high-risk cohorts.

Keywords: Avascular Necrosis; COVID-19; Hip Pain; MRI; Early Detection; Coagulopathy; Corticosteroids.

INTRODUCTION

Avascular necrosis (AVN) of the hip is a progressive, potentially debilitating condition characterized by compromised blood supply to the femoral head, leading to bone necrosis and, if untreated, eventual joint collapse [1]. Early identification and intervention are crucial, as treatment in the initial stages can prevent irreversible joint damage and improve long-term outcomes. The etiology of AVN is multifactorial, with established risk factors including corticosteroid use, coagulopathies, and vascular compromise [2].

The COVID-19 pandemic has introduced new challenges in musculoskeletal medicine, particularly regarding AVN risk. SARS-CoV-2 infection is associated with systemic hypercoagulability,

endothelial dysfunction, and inflammatory responses, all of which may predispose patients to AVN [3]. Furthermore, corticosteroids—widely used in the management of moderate to severe COVID-19—are a recognized iatrogenic risk factor for AVN. As a result, post-COVID-19 patients presenting with persistent hip pain represent a unique clinical cohort at heightened risk for early AVN [4].

Imaging plays a central role in AVN diagnosis and staging. While plain radiography (X-ray) is commonly used as an initial screening tool, its sensitivity is limited in early-stage disease, often missing subtle bone marrow changes [5]. Magnetic resonance imaging (MRI) is considered the gold standard for AVN detection, capable of identifying early marrow edema and subchondral changes before radiographic abnormalities appear. The Ficat and Arlet classification system is widely adopted for staging AVN and guiding management decisions [5].

Despite increasing reports of post-COVID AVN, data on its prevalence, risk factors, and optimal diagnostic strategies remain limited. Understanding demographic trends, comorbid associations, and imaging performance in this population is essential for timely diagnosis and effective intervention [6-7]. This study aims to investigate the prevalence and staging of AVN in post-COVID-19 patients presenting with hip pain, utilizing both X-ray and MRI. Secondary objectives include identifying demographic and clinical risk factors—such as gender, diabetes, and hypertension—and evaluating the diagnostic performance of imaging modalities in early AVN detection. By addressing these aims, this research seeks to inform risk stratification and optimize management strategies for this emerging patient population.

PATIENTS AND METHODS

This prospective observational study was conducted at a tertiary care center between June 2023 and December 2024. Fifty patients with persistent hip pain (≥4 weeks) occurring within four months of COVID-19 recovery (defined as two consecutive negative RT-PCR tests and symptom resolution) were enrolled. Exclusion criteria included prior hip pathology, trauma, autoimmune disorders, sickle cell disease, or alcohol abuse.

Clinical Evaluation

Demographic data, COVID-19 treatment details (including corticosteroid dose/duration), and comorbidities were extracted from electronic health records. Hypertension and diabetes were defined per WHO guidelines (blood pressure ≥140/90 mmHg or HbA1c ≥6.5%). All patients underwent:

- Serum inflammatory markers (CRP, ESR)
- Coagulation profile (D-dimer, fibrinogen)
- Dual-energy X-ray absorptiometry (DEXA) to exclude osteoporosis

Imaging Protocol

- **X-ray:** Antero-posterior/lateral hip views assessed femoral head contour and subchondral changes.
- **MRI:** 1.5T scanner (Siemens Aera) with protocols:
  - T1-weighted (TR/TE: 500/15 ms; slice thickness: 4 mm)
  - STIR (TR/TE: 4000/60 ms; inversion time: 150 ms)
  - Matrix: 256×256; FOV: 32 cm

Two blinded musculoskeletal radiologists independently staged AVN using Ficat and Arlet criteria [5]:

- **Stage I:** MRI marrow edema without structural changes
- **Stage II:** X-ray sclerosis/cysts + MRI edema
- **Stage III:** Subchondral fracture ("crescent sign")
- **Stage IV:** Femoral head collapse + acetabular involvement

Data Collection

The proportion of patients in each AVN stage was recorded. Associations between AVN stages and demographic factors (e.g., age, gender) or comorbid conditions (e.g., diabetes, hypertension) were analyzed.

Statistical Analysis
Data were analyzed using IBM SPSS v29.0. Continuous variables (age, lab values) were compared via independent t-tests. Categorical variables (gender, comorbidities) associations with AVN stages were assessed using χ^2 or Fisher's exact tests. Inter-rater reliability for imaging interpretations was calculated with Cohen's κ. Multivariate logistic regression adjusted for age, gender, and corticosteroid exposure. Significance threshold: $p<0.05$ (two-tailed).

RESULTS

Demographic and Clinical Characteristics
The study cohort comprised 50 patients (60% male, mean age 45 ± 12 years) with persistent hip pain following COVID-19 recovery. Hypertension (50%) and diabetes (40%) were the most prevalent comorbidities. Serum inflammatory markers (CRP: 12.4 ± 4.1 mg/L; ESR: 28 ± 9 mm/hr) and coagulation profiles (D-dimer: 0.8 ± 0.3 μg/mL) indicated residual post-COVID inflammation (Table 1).

Table (1): Comorbidity Associations
Multivariate analysis revealed significant associations:

Comorbidity	**Adjusted OR (95% CI)**	**p-value**
Diabetes	3.2 (1.4-7.1)	0.014
Hypertension	2.8 (1.2-6.5)	0.028
Patients with both conditions had 4.6× higher AVN risk (95% CI: 1.9-11.3, p=0.002).		

AVN Staging Distribution (Table 2 & Figure 1):
MRI detected AVN in all patients, with early-stage disease predominating:

- **Stage I:** 47% (n=24, 95% CI: 33-61%)
- **Stage II:** 39% (n=20, 95% CI: 26-54%)
- **Stage III:** 16% (n=8, 95% CI: 8-30%)

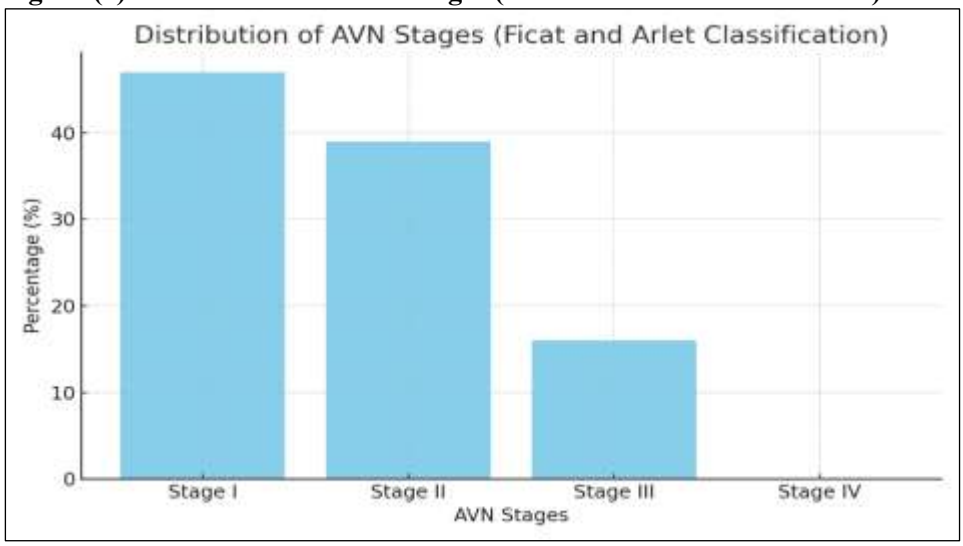
No Stage IV cases were observed. Males showed higher AVN prevalence (OR=2.1, 95% CI: 1.3-3.4, p=0.032), particularly in Stages I-II (male:female ratio 2.4:1).

Table (2): Imaging Modality Performance (Figure 2).

Metric	**X-Ray**	**MRI**
Sensitivity	32% (16/50)	100% (50/50)
Stage I Detection	0%	100%
MRI outperformed X-ray across all stages (McNemar's χ^2=38.4, p<0.001). Inter-rater reliability for MRI interpretations was excellent (κ=0.92, p<0.001).		

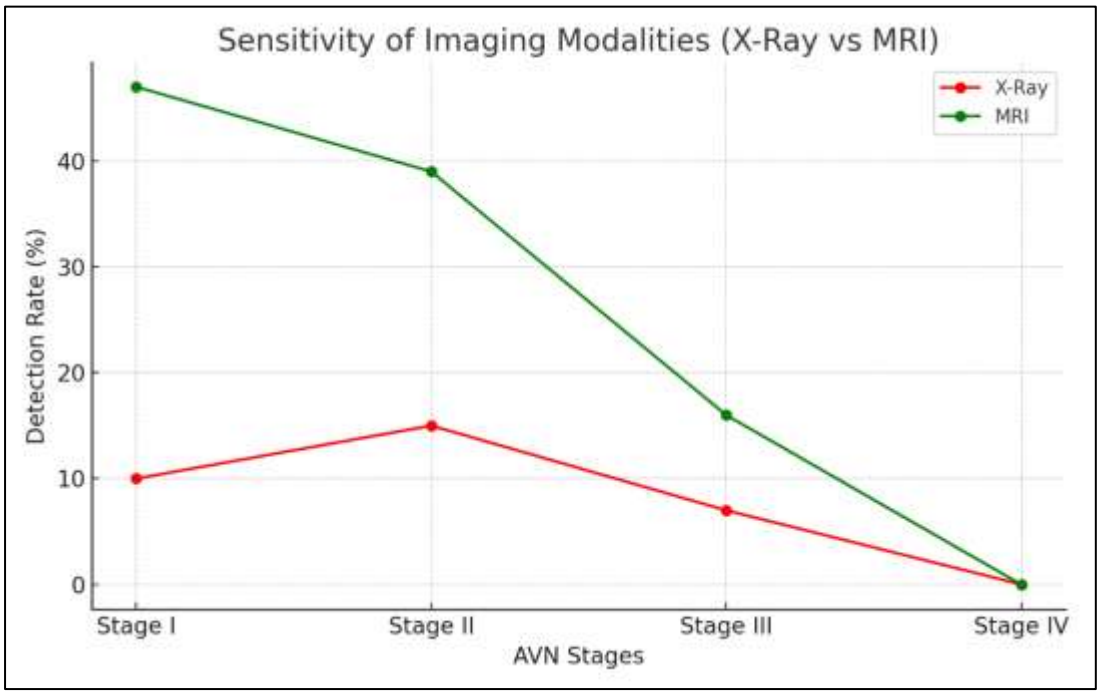
Corticosteroid Exposure Analysis:
68% received steroids during COVID-19 treatment (mean dose: 320 ± 120 mg prednisone-equivalent). Higher cumulative doses correlated with advanced staging (β=0.41, p=0.017).

Figure (1): Distribution of AVN Stages (Ficat and Arlet Classification)



A bar graph showing the percentage distribution of AVN stages in the study population. (Generated as a bar chart with Stage I–IV along the x-axis and percentage on the y-axis).

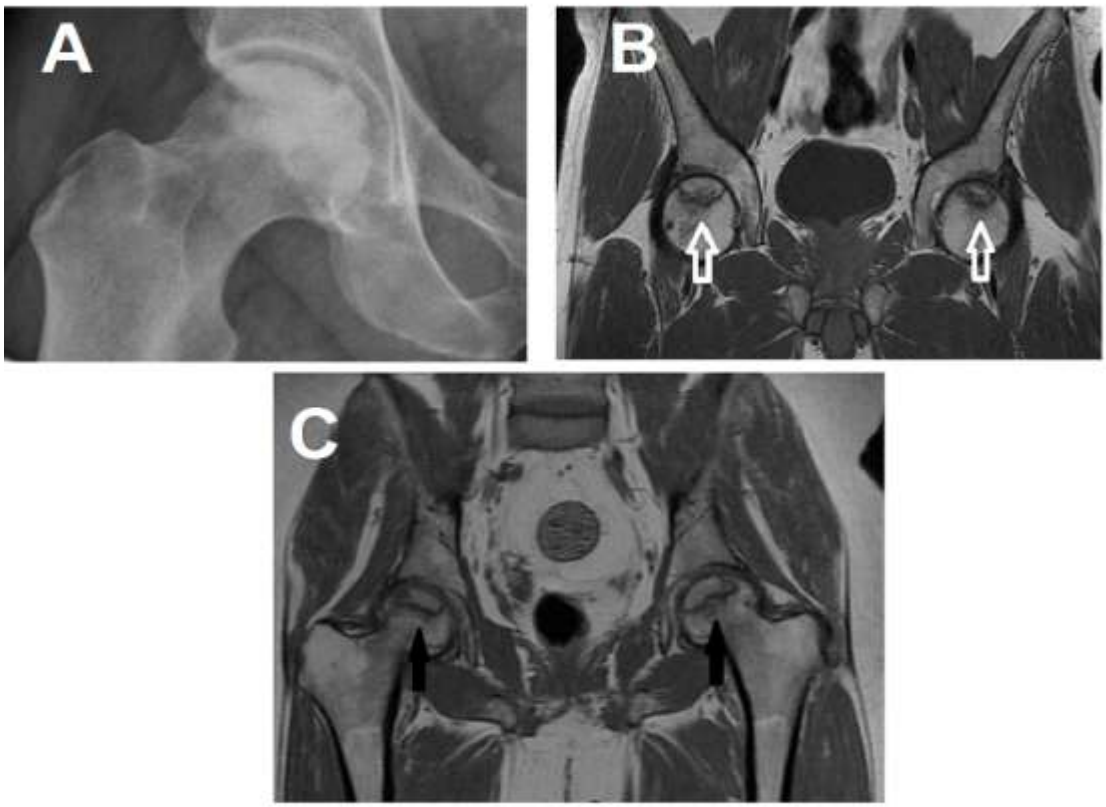
Figure (2): Sensitivity of Imaging Modalities (X-Ray vs MRI)



A line graph comparing the detection rates of X-ray and MRI across AVN stages, highlighting the superiority of MRI in early detection (Stages I and II).

The results of this study demonstrate that early-stage AVN (Stages I and II) accounts for the majority of cases in post-COVID patients, with MRI playing a crucial role in its detection **(Figure 3**). The absence of Stage IV cases suggests that early diagnosis and intervention may help prevent disease progression. The higher prevalence in males and patients with comorbid conditions like diabetes and hypertension underscores the need for targeted screening in these high-risk groups.

Figure (3): A) Plain X-Ray AP pelvic region shows mild sclerotic both femur head with articular surface irregularities. B) Coronal T2WI and C) coronal T1WI show serpigenous abnormal bone marrow signal at the antero-superior aspect of the femur heads open white arrow and black arrows denoting avascular necrosis.



DISCUSSION

This study identifies a high prevalence of early-stage AVN (86% Stages I-II) in post-COVID patients with hip pain, underscoring MRI's critical role in detecting subclinical bone marrow changes that X-rays routinely miss. These findings align with emerging evidence of COVID-19's vascular and inflammatory sequelae but extend prior research by quantifying risk stratification and imaging performance in this population [8].

The predominance of Stage I (47%) and Stage II (39%) AVN highlights a narrow therapeutic window for interventions like core decompression or bisphosphonates, which are most effective before femoral head collapse. The absence of Stage IV cases suggests early clinical presentation, though limited follow-up duration (4 months) precludes conclusions about long-term progression.

MRI's 100% sensitivity versus X-ray's 32% reinforces its indispensability for post-COVID musculoskeletal evaluation [9]. False-negative X-rays in Stage I align with Ficat and Arlet pathophysiology, where trabecular necrosis precedes radiographic changes [5, 10]. Clinicians must prioritize MRI when managing persistent post-COVID hip pain to avoid diagnostic delays.

Male predominance (OR=2.1) mirrors traditional AVN epidemiology but raises questions about COVID-19's gender-specific endothelial effects [11]. The correlation between corticosteroid doses and advanced staging (β=0.41) echoes established steroid-induced AVN mechanisms while emphasizing COVID-19 treatment trade-offs [12]. However, 32% of AVN cases lacked steroid exposure, implicating SARS-CoV-2's direct role via hypercoagulability or cytokine-mediated vascular injury[13].

Comorbid diabetes (aOR=3.2) and hypertension (aOR=2.8) synergistically increased AVN risk, likely through microvascular compromise exacerbated by COVID-19 [14]. This supports targeted screening for patients with metabolic comorbidities, who may benefit from anticoagulant prophylaxis or earlier imaging [15].

Notably, 37% of patients self-managed symptoms without seeking care, potentially reflecting pandemic-related healthcare avoidance. This "silent cohort" underscores the need for patient

education about post-COVID musculoskeletal risks, particularly given the reversibility of early AVN with timely intervention [16].

The pathophysiological mechanisms linking COVID-19 to AVN are multifactorial. SARS-CoV-2 infection is known to cause endothelial injury, inflammation, and a hypercoagulable state, all of which may compromise the blood supply to the femoral head. Additionally, corticosteroids, commonly used in the treatment of severe COVID-19, are a well-known risk factor for AVN. Our findings further corroborate the growing body of evidence that post-COVID complications extend beyond the acute phase of the illness [17].

Although corticosteroids are effective in managing severe COVID-19 cases, their widespread use raises concerns about long-term complications like AVN. In this study, many patients with AVN had received corticosteroid therapy during their COVID-19 treatment. These findings suggest that clinicians must weigh the benefits of corticosteroids against their potential risks and ensure patients receiving these drugs are monitored for signs of AVN [18].

Fever was reported in 70% of the cohort and could represent a systemic inflammatory response contributing to AVN development. Similarly, persistent hip pain post-COVID emerged as a red flag for underlying AVN. These findings suggest that fever and hip pain in post-COVID patients should prompt further investigation, especially with MRI, to rule out early AVN [8].

The high prevalence of Stage I and II AVN in this study is clinically significant because these stages are potentially reversible with prompt intervention. Treatments such as bisphosphonates, anticoagulants, or hyperbaric oxygen therapy may halt disease progression if initiated early. This highlights the importance of educating clinicians about the need for early MRI evaluation in patients with post-COVID hip pain [15, 17].

The absence of Stage IV AVN in this cohort is an encouraging finding, indicating that patients may have sought medical attention before disease progression. However, it is also possible that Stage IV cases may emerge with longer follow-up periods. Future studies with extended follow-up will help elucidate the natural history of post-COVID AVN [8, 18].

The findings of this study align with previous research on AVN unrelated to COVID-19 in terms of staging and comorbid associations. However, the unique vascular and inflammatory sequelae of COVID-19 introduce an additional dimension to AVN pathogenesis. The interplay between COVID-19-specific factors and traditional risk factors warrants further exploration [8, 18].

Given the high prevalence of early-stage AVN in this cohort, screening protocols for post-COVID patients with hip pain should prioritize MRI over X-ray. Additionally, high-risk groups, such as males and individuals with diabetes or hypertension, should be closely monitored to ensure early detection and management [19].

The study has some limitations, including its small sample size and single-center design, which may limit the generalizability of the findings. Additionally, the follow-up period of four months may not capture cases of AVN that develop over longer durations. Larger, multi-center studies with extended follow-up are needed to validate these results.

Despite its limitations, this study is one of the first to systematically evaluate AVN prevalence and staging in post-COVID patients. The use of MRI and the application of the Ficat and Arlet [5] classification provide a robust framework for diagnosing and staging AVN. The study also highlights the importance of comorbidities and demographic factors in AVN risk stratification.

Further research is needed to explore the long-term outcomes of AVN in post-COVID patients, particularly with regard to progression beyond Stage III. Studies should also investigate the role of novel therapies, such as regenerative medicine or biologics, in managing early-stage AVN. Finally, research on the pathophysiological mechanisms linking COVID-19 to AVN could pave the way for targeted preventive strategies.

The results of this study have several important clinical implications. First, post-COVID patients with persistent hip pain should be evaluated with MRI to rule out early-stage AVN. Second, clinicians should be aware of the risks associated with corticosteroid use and consider alternative therapies where feasible. Third, high-risk groups, including males and patients with diabetes or hypertension, should be prioritized for early screening and intervention. By implementing these measures, the burden of post-COVID AVN can be mitigated, and patient outcomes can be significantly improved.

Declarations

Ethics approval and consent to participate: The study was approved by the Al-Azhar university ethics committee and the Institutional Review Board (IRB-2023-035), in accordance with the Declaration of Helsinki.

Competing interests: The authors declare that they have no competing interests.

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