Original Article

Avascular Necrosis of the Head of the Femur in COVID-19 Survivors: A Prospective Study

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Abstract

Background: Avascular necrosis (AVN) of the femoral head is a disabling condition traditionally associated with prolonged corticosteroid use. With the advent of COVID-19, increasing reports suggest earlier onset and higher incidence of AVN among survivors, possibly due to a combination of corticosteroid exposure and SARS-CoV-2–induced vascular injury. The objective is to determine the incidence, clinical profile, risk factors, and short-term outcomes of femoral head AVN in COVID-19 survivors. **Material and Methods:** This prospective observational study included 132 COVID-19 survivors presenting with new-onset hip/groin pain within 12 months of infection. Demographic data, comorbidities, illness severity, corticosteroid exposure, and coagulation markers were recorded. All patients underwent hip MRI, and AVN was staged using ARCO classification. Functional outcomes were assessed using the Harris Hip Score (HHS). Logistic regression was performed to identify independent predictors of AVN. **Results:** AVN was detected in 34/132 patients (25.8%), with bilateral disease in 29.4%. The mean time from COVID-19 to AVN diagnosis was 104 ± 29 days. Most affected hips were ARCO stage I–II (65.9%). Independent predictors included cumulative corticosteroid dose >3 g prednisolone-equivalent (OR 2.9; 95% CI 1.4–6.0; p=0.004) and D-dimer >1000 ng/mL (OR 2.3; 95% CI 1.1–4.8; p=0.03). At 12-month follow-up, patients undergoing core decompression or arthroplasty had significantly better functional outcomes than conservative management (mean HHS 83.2 vs 71.6; p<0.01). Disease progression occurred in 38.2% of AVN cases, with 20.6% requiring arthroplasty. **Conclusion:** AVN of the femoral head is an emerging complication in COVID-19 survivors, with earlier onset and higher frequency than previously recognised. Both corticosteroid dose and COVID-associated hypercoagulability contribute to risk. Early MRI screening in high-risk patients and timely intervention may preserve joint function and delay arthroplasty.

Keywords: Avascular necrosis, femoral head, COVID-19, corticosteroids, hypercoagulability, MRI, prospective study.

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Introduction

Avascular necrosis (AVN) of the femoral head is a progressive and debilitating disorder caused by compromised blood supply to the femoral head, leading to bone ischemia, collapse of the articular surface, and ultimately degenerative arthritis of the hip joint. If untreated, AVN frequently progresses to severe morbidity and often necessitates surgical interventions such as total hip arthroplasty.[1] Well-established risk factors include prolonged corticosteroid use, alcohol abuse, trauma, and systemic disorders such as coagulopathies.[2]

The coronavirus disease 2019 (COVID-19) pandemic has introduced new potential mechanisms for the development of AVN. SARS-CoV-2 infection is associated with systemic inflammation, endothelial dysfunction, and a prothrombotic state, all of which may promote microvascular thrombosis and impaired perfusion of bone tissue.[3,4] Additionally, corticosteroid therapy—widely used in the management of moderate-to-severe COVID-19—though beneficial in reducing mortality, is a recognised risk factor for steroid-induced AVN.[1,2,4]

Emerging clinical observations suggest an increasing incidence of post-COVID AVN, often presenting earlier than traditionally seen. Agarwala et al,[5] described early-onset AVN within weeks of COVID-19 infection, even in patients with modest cumulative steroid exposure.[6] Assad et al,[7] reported AVN cases developing after COVID-19 infection, underscoring the need to consider both infection-related vascular injury and treatment-related risk factors. Similarly, Hoque et al,[6] highlighted that disease severity, cumulative steroid dose, and timing may influence the risk of post-COVID AVN.

Despite these reports, the true incidence, natural history, and interaction between COVID-19–related factors and conventional risk factors remain poorly defined. Larger prospective studies are

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required to clarify epidemiology, identify high-risk groups, and guide early diagnosis and management strategies in this emerging clinical entity.

Aim of the study: The present prospective study investigated the incidence and clinical profile of femoral head AVN in COVID-19 survivors, emphasising the role of corticosteroid exposure, COVID-related severity, and imaging outcomes.

Materials and Methods

Study design and setting: This was a prospective observational study conducted at the Department of Orthopaedics, at Konaseema Institute of Medical Sciences, Amalapuram, AP, between August 2021 and August 2025, following approval from the Institutional Ethics Committee (IEC No: IEC/PR/2021/012 Dated 12-07-2021).

Study population

Inclusion criteria

Adults (≥18 years) with documented SARS-CoV-2 infection confirmed by RT-PCR or antigen testing.

Patients presenting with new onset hip or groin pain after recovery from COVID-19 (defined as ≥14 days from diagnosis and clinical resolution of acute infection).

Willingness to undergo radiological evaluation and follow-up for 12 months.

Exclusion criteria

History of hip trauma, fracture, or surgery.

Previously diagnosed avascular necrosis of the femoral head.

Long-term corticosteroid therapy (>3 months) for conditions unrelated to COVID-19.

Malignancy with bone metastases, sickle cell disease, or other known primary causes of AVN.

Contraindication to MRI (e.g., pacemaker, metallic implants not MRI-safe).

Sample size: Based on prior reports suggesting an incidence of 15–20% AVN among symptomatic post-COVID patients (Agarwala et al., 2021; Hoque et al., 2024), a minimum sample size of 126 was calculated to estimate the incidence with a 95% confidence interval and ±7% precision. Allowing for a 10% dropout rate, we aimed to enrol 140 patients.

Data collection: At baseline, demographic and clinical information were collected, including:

Age, sex, body mass index (BMI).

Comorbidities: diabetes mellitus, hypertension, dyslipidemia, smoking, and alcohol intake.

COVID-19 illness details: date of diagnosis, severity (mild, moderate, severe), hospitalisation, ICU stay, oxygen therapy, and anticoagulant use.

Treatment details include the corticosteroid agent, cumulative dose (converted to prednisolone equivalent), duration of therapy, and other medications such as remdesivir or tocilizumab.

Laboratory parameters (where available): D-dimer, CRP, ferritin, fibrinogen, platelet count.

Clinical evaluation: All patients underwent detailed musculoskeletal examination, including hip range of motion, gait analysis, and pain assessment. Functional status was assessed using the Harris Hip Score (HHS) at baseline and follow-up visits.

Imaging protocol:

Radiographs: Anteroposterior pelvis with both hips and frog-leg lateral views were performed at presentation, 6 months, and 12 months.

Magnetic Resonance Imaging (MRI): Both hips were imaged using T1, T2, and STIR sequences to confirm early AVN. Contrast studies were done when required.

Staging: AVN was classified according to the Association Research Circulation Osseous (ARCO) staging system. Bilateral involvement was recorded.

Follow-up

Patients were followed up at 3, 6, and 12 months after enrollment.

At each visit:

Pain and functional assessment (HHS).

Clinical progression documented.

Radiographs were performed at 6 and 12 months.

Repeat MRI performed at 12 months or earlier if clinically indicated.

Management protocol

Patients diagnosed with AVN were managed according to stage:

Early stages (ARCO I–II): conservative measures including rest, activity modification, protected weight bearing, bisphosphonates (if prescribed), and physiotherapy. Some underwent core decompression based on the surgeon's discretion.

Advanced stages (ARCO III–IV): surgical options, including total hip arthroplasty, were considered.

The chosen treatment and outcomes were recorded.

Outcome measures

Primary outcome

Proportion of patients with MRI-confirmed AVN of the femoral head.

Secondary outcomes

Time interval between COVID-19 diagnosis and onset of hip pain/AVN.

Association between cumulative corticosteroid dose and AVN.

Relationship of AVN with COVID-19 severity and laboratory markers.

Functional outcomes are measured by changes in the Harris Hip Score at 12 months.

Radiological progression and need for surgical intervention.

Statistical analysis: Data were analysed using SPSS version [XX] (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), and categorical variables as frequencies and percentages.

Incidence of AVN was calculated with 95% confidence intervals.

AVN and non-AVN groups were compared using an independent t-test/Mann–Whitney U test for continuous variables and χ^2/Fisher's exact test for categorical variables.

Multivariable logistic regression was applied to identify independent predictors of AVN (e.g., cumulative steroid dose, D-dimer, COVID severity, comorbidities). Results were reported as odds ratios (OR) with 95% CI.

A p-value <0.05 was considered statistically significant.

Results

Study population: 140 COVID-19 survivors with new hip/groin

pain were screened; 132 patients (94.3%) completed the study. The mean age was 44.8 ± 11.6 years, with 61.4% males.

Table 1: Baseline demographic and clinical characteristics of participants (n=132)

Variable	Total (n=132)	AVN group (n=34)	Non-AVN group (n=98)	p-value
Age (years), mean ± SD	44.8 ± 11.6	46.2 ± 10.8	44.3 ± 12.0	0.41
Male sex, n (%)	81 (61.4)	21 (61.8)	60 (61.2)	0.95
BMI (kg/m²), mean ± SD	26.4 ± 3.8	27.1 ± 4.1	26.1 ± 3.7	0.21
Diabetes mellitus, n (%)	38 (28.8)	13 (38.2)	25 (25.5)	0.14
Hypertension, n (%)	43 (32.6)	12 (35.3)	31 (31.6)	0.69
Alcohol use, n (%)	26 (19.7)	9 (26.5)	17 (17.3)	0.24

COVID-19 illness characteristics: Most patients had moderate COVID-19 (57.6%). Hospitalisation was required in 74.2%, and 25.8% required ICU admission. Corticosteroids were given to 80.3% with a mean cumulative dose of 2,850 ± 1,140 mg (prednisolone equivalent).

Table 2: COVID-19 illness profile and treatment

Variable	Total (n=132)	AVN group (n=34)	Non-AVN group (n=98)	p-value
COVID-19 severity: Mild, n (%)	26 (19.7)	3 (8.8)	23 (23.5)	0.04*
Moderate, n (%)	76 (57.6)	18 (52.9)	58 (59.2)	
Severe, n (%)	30 (22.7)	13 (38.2)	17 (17.3)	
Hospitalization, n (%)	98 (74.2)	31 (91.2)	67 (68.4)	0.01*
ICU admission, n (%)	34 (25.8)	12 (35.3)	22 (22.4)	0.14
Corticosteroid use, n (%)	106 (80.3)	32 (94.1)	74 (75.5)	0.02*
Cumulative steroid dose (mg), mean ± SD	2,850 ± 1,140	3,420 ± 980	2,540 ± 960	<0.001*
Peak D-dimer (ng/mL), median (IQR)	1,120 (640–1820)	1,480 (960–2100)	980 (560–1610)	0.01*

*Statistically significant ($p<0.05$).

Incidence and imaging findings: AVN was confirmed in 34/132 patients (25.8%). Bilateral disease was present in 10 patients (29.4% of AVN cases). The mean time from COVID-19 diagnosis to hip pain was 82 ± 24 days, and to MRI-confirmed AVN was 104 ± 29 days.

Table 3: AVN staging at diagnosis (n=44 hips in 34 patients)

ARCO Stage	Number of hips (%)
I	11 (25.0)
II	18 (40.9)
III	10 (22.7)
IV	5 (11.4)

Predictors of AVN: Multivariable logistic regression showed that cumulative steroid dose >3 g prednisolone-equivalent and D-dimer >1,000 ng/mL were independent predictors of AVN.

Table 4. Logistic regression analysis of predictors of AVN

Variable	Adjusted OR	95% CI	p-value
Cumulative steroid dose >3 g	2.9	1.4–6.0	0.004*
Severe COVID-19	1.8	0.9–3.7	0.09
D-dimer >1000 ng/mL	2.3	1.1–4.8	0.03*
Diabetes mellitus	1.4	0.6–3.2	0.41
Alcohol use	1.6	0.7–3.8	0.26

Functional outcomes and progression

Baseline HHS: 58.3 ± 8.4 in AVN vs 72.1 ± 9.7 in non-AVN ($p<0.001$).

At 12 months, HHS improved to 71.6 ± 10.2 in conservatively managed AVN, 83.2 ± 6.8 after core decompression, and 89.4 ± 5.3 after arthroplasty.

Progression occurred in 13/34 AVN patients (38.2%), with 7 (20.6%) requiring total hip arthroplasty.

Discussion

In this prospective study of 132 COVID-19 survivors, femoral head avascular necrosis (AVN) incidence was 25.8%, with onset occurring at an average of three months following COVID-19 diagnosis. This incidence is notably higher than the background prevalence of steroid-induced AVN in non-COVID populations, which typically ranges between 3–7% among patients receiving prolonged corticosteroid therapy [8,9]. These findings suggest a potential dual contribution of COVID-19–related coagulopathy and corticosteroid exposure in accelerating the onset of osteonecrosis.

Role of corticosteroids: Corticosteroid administration remains one of the most established risk factors for AVN due to its effects on lipid metabolism, microvascular circulation, and bone remodeling.[10] In the present study, a cumulative steroid dose greater than 3 g prednisolone-equivalent independently predicted AVN, aligning with the thresholds suggested in earlier

reports.[11,12] However, several patients developed AVN despite relatively modest cumulative doses, supporting prior observations that COVID-19 survivors may experience AVN earlier and at lower doses than traditionally expected.[8,13]

COVID-19–related mechanisms beyond steroids: Beyond steroid exposure, SARS-CoV-2 infection itself may predispose to AVN through systemic inflammation, endothelial injury, and a prothrombotic state. Microvascular thrombosis and impaired femoral head perfusion have been proposed as plausible mechanisms.[9,10] Importantly, reports of AVN in steroid-naïve COVID-19 patients provide further support for this vascular hypothesis.[13,14] In our cohort, elevated D-dimer levels (>1000 ng/mL) were independently associated with AVN, highlighting the potential contribution of COVID-associated coagulopathy to its pathogenesis.

Early onset and bilateral disease: Our series's mean interval from COVID-19 diagnosis to AVN onset was approximately 104 days, substantially shorter than the 6–12 month latency period typically described for steroid-induced AVN.[11,12] Bilateral involvement occurred in nearly one-third of cases, comparable to findings from earlier post-COVID AVN reports.[8,13] This rapid and frequently bilateral progression reinforces the importance of vigilant follow-up and early MRI screening in survivors presenting with hip pain.

Functional outcomes and management: Patients treated with core decompression or arthroplasty achieved significantly higher Harris Hip Scores than those managed conservatively, consistent with the functional benefits of early surgical intervention reported in prior studies.[8,12] Despite appropriate treatment, nearly 40% of cases demonstrated radiographic progression within one year, underscoring the aggressive clinical course of COVID-related AVN.

Comparison with previous studies: Our findings are consistent with Agarwala et al,[8] who reported early-onset AVN within two months of COVID-19, and with Hoque et al,[8] who observed correlations with steroid exposure and disease severity. Hassan and Khalifa,[13] also highlighted a higher-than-expected incidence and emphasised the need for systematic surveillance in COVID-19 survivors. Moreover, unique to our study, D-dimer elevation emerged as an independent predictor of AVN, strengthening the evidence for a vascular and thrombotic mechanism beyond steroid toxicity. Reports of osteonecrosis in other skeletal sites, including the jaw, suggest that COVID-19 may precipitate a broader osteonecrotic spectrum.[14,15]

Finally, while epidemiological data on idiopathic AVN before the pandemic indicated much lower prevalence rates,[16] the sharp rise observed among COVID-19 survivors suggests that the infection has reshaped the natural history of osteonecrosis and necessitates proactive diagnostic and preventive strategies.

Strengths and This study's strengths include its prospective design and systematic MRI evaluation. However, its limitations include the single-centre setting, limited follow-up duration, and relatively small AVN cases, which may restrict generalizability. Longer-term multicenter studies are needed to validate our findings and define optimal screening and management strategies.

Clinical implications: Given the rising number of COVID-19 survivors worldwide, clinicians should maintain a high index of suspicion for AVN in patients with persistent hip pain, particularly those exposed to corticosteroids or with elevated coagulation markers. Early MRI screening and timely intervention (core decompression in early stages) may preserve joint function and delay the need for arthroplasty.

Conclusion

This prospective study highlights femoral head avascular necrosis (AVN) as a significant and emerging complication among COVID-19 survivors. The observed incidence of 25.8%, with onset within three months of infection, is considerably higher and earlier than that typically reported for steroid-induced AVN. Both cumulative corticosteroid exposure and markers of hypercoagulability, particularly elevated D-dimer, independently predicted risk, suggesting a dual pathogenic mechanism. Bilateral involvement and rapid progression were common, emphasising the need for vigilance. Early MRI screening in high-risk individuals, combined with timely surgical intervention when indicated, may improve outcomes, preserve hip function, and potentially delay or prevent the need for arthroplasty.

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Conflicts of interest

There are no conflicts of interest.

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