



**Association of Covid19 Infection in Patients with AVN Admitted for
THR: A Case Series**

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Introduction:

The COVID-19 pandemic has not only presented unprecedented challenges to healthcare systems worldwide but has also unveiled a range of interconnected health issues. Among these is a notable connection between COVID-19 infection and the onset of avascular necrosis (AVN) in the hip joint.¹ AVN, characterized by insufficient blood supply to bone tissue, particularly affects the hip, leading to its progressive deterioration and potentially severe consequences.² While the direct mechanisms linking COVID-19 to AVN are still being investigated, emerging evidence suggests a complex interplay involving viral pathophysiology, hypercoagulable states, and compromised vascular function. This association highlights the need for further research and understanding.^{3,4} It underscores the intricate nature of COVID-19's impact on human health, emphasizing the importance of developing comprehensive approaches to research and manage this evolving challenge in clinical practice.

Aims and Objectives:

1. To determine the prevalence of prior history of COVID-19 in patients with AVN of hip.
2. To assess the potential risk factors underlying the development of AVN as a COVID-19 sequelae.
3. To determine the mean duration of development of AVN after COVID19 infection.

Materials and Methods:

Study design and setting:

This is a single centre retrospective study, done from October 2022 to December 2023, that included all patients with grade 3 or grade 4 AVN of hip who were admitted for total hip replacement (THR) in the Orthopedic department of SGITO hospital, Karnataka.

Study population and sample size:

All patients with grade 3 or grade 4 AVN of hip, diagnosed with the help of radiographic imaging, who were admitted for THR were included. The exclusion criteria included patients with chronic or autoimmune diseases like RA, H/o AVN prior to COVID-19 infection, patients under chemotherapy for bone cancer. A total of 62 patients met the inclusion criteria and were analysed.

Data collection and data analysis:

The demographic data like age, gender were collected for all the patients enrolled in the study. History of COVID-19 infection in the past was analysed and documented. None of the patients had previous hip pain confounding to the development of AVN. Risk factors like history of smoking and alcohol intake were also documented along with any pre-existing co-morbidities like diabetes mellitus and hypertension. The Fisher exact test was used to analyse the data and express in numbers and percentages. $p < 0.05$ was considered statistically significant.

Results:

Among the cohort of 62 patients diagnosed with stage 3 or stage 4 Avascular Necrosis (AVN) of the hip, only 12 individuals (19.35%) disclosed a history of prior COVID-19 infection. The demographic characteristics and clinical features of these patients are detailed in Table 1. Notably, the majority of patients with a history of COVID-19 were males, comprising 91.67% of the subgroup, while only one female patient was identified. Regarding age distribution, half of the patients (50%) fell within the 50-60 years age group, with smaller proportions in the 30-40 years (25%) and one patient each in the 40-50 years and over 60 years (8.33%) age groups.

Interestingly, AVN of the hip was more frequently observed on the right side (50%) compared to the left (41.67%) and bilateral presentation (8.33%) among patients with a history of COVID-19. Figures 1 and 2 describe Plain X-rays of pelvis with both hip joints of a 51 year old male and a 43 year old male, having stage 4 AVN of hip, involving the right and left sides respectively. Figures 3 and 4 represent the post-operative X-rays of the above mentioned patients after uncemented THR on the respective sides.

Furthermore, a subset of these patients reported a history of alcohol intake and smoking (33.33% each), while 41.67% disclosed the use of steroids as part of their COVID-19 treatment regimen. However, statistical analysis did not reveal a significant association between steroid usage and the development of AVN hip ($p > 0.5$).

Regarding comorbidities, 16.67% of patients had diabetes mellitus and only 8.33% had hypertension. The average duration between COVID-19 infection and onset of AVN hip was approximately 6.33 months, with one patient developing the disease immediately after contracting COVID-19.

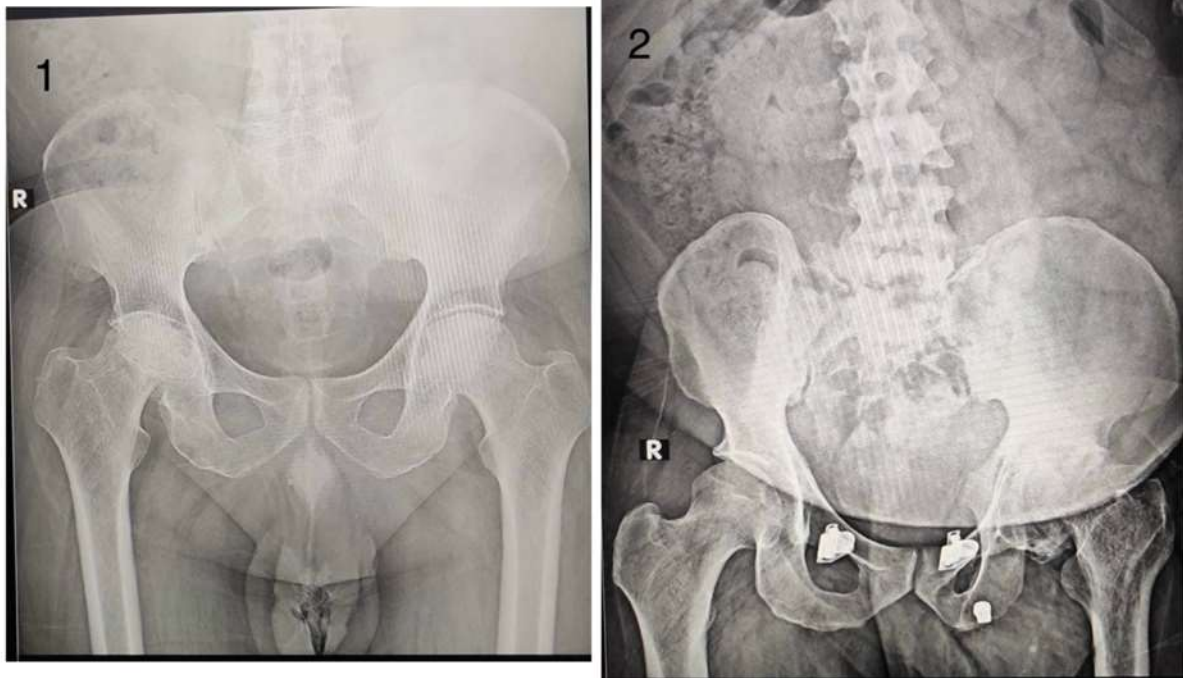


Figure 1: Plain X-ray of pelvis with both hip joints of a 51 year old male having stage 4 AVN of hip, involving the right side.

Figure 2: Plain X-ray of pelvis with both hip joints of a 43 year old male having stage 4 AVN of hip, involving the left side.

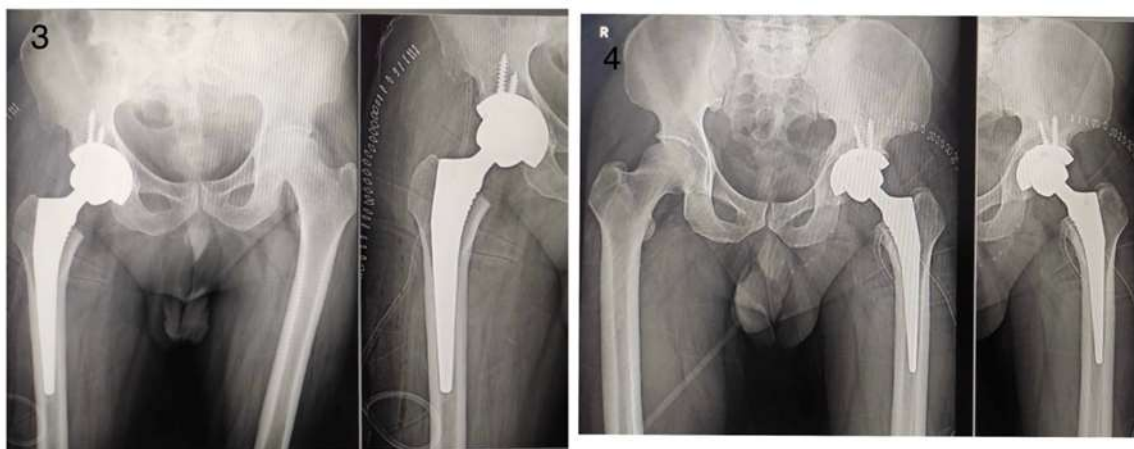


Figure 3: Post-operative X-ray of right hip AVN after uncemented THR on right side.

Figure 4: Post-operative X-ray of left hip AVN after uncemented THR on left side.

Table 1: Descriptive statistics for patients with prior history for COVID-19:

Patient No.	Age	Sex	Side of presentation of AVN hip	Steroid use for COVID-19 infection (Yes/No)	Smoking (Yes/No)	Alcohol (Yes/No)	Co-morbidities	Onset of AVN hip after COVID-19 infection (in months)
1	55	Male	Right	Yes	No	Yes	Nil	4
2	72	Male	Bilateral	Yes	No	No	Nil	5
3	30	Male	Right	Yes	Yes	Yes	Nil	8
4	42	Male	Right	No	Yes	Yes	DM	7
5	56	Male	Left	Yes	No	No	DM	3.5
6	38	Male	Left	Yes	No	No	Nil	6
7	58	Male	Right	No	No	No	Nil	8
8	32	Male	Left	No	Yes	Yes	Nil	7
9	55	Male	Left	No	Yes	No	Nil	6.5
10	65	F	Right	No	No	No	Nil	8
11	55	Male	Left	No	No	No	Nil	6
12	55	Male	Right	No	No	No	HTN	0

Discussion:

Avascular necrosis (AVN) is a complex condition influenced by various factors such as genetic predisposition, corticosteroid usage, hypercoagulable states, vasculitis, and alcohol consumption.³ Lang et al. highlighted the incomplete understanding of AVN's pathophysiology and progression, partly due to its early asymptomatic stages. The disease process likely involves inadequate angiogenesis post-infarction, leading to demineralization, trabecular thinning, and eventual cortical bone collapse.⁵ Recent clinical research has focused on elucidating COVID-19 complications, including musculoskeletal system pathology.⁶⁻⁸ In our study, out of the 62 patients diagnosed with stage 3 or stage 4 AVN, 12 individuals (19.35%) had a documented history of prior COVID-19 infection, indicating a potential association between the two conditions.

Our study showed a predominance of male patients, constituting 91.67% of the cases, while only one patient was female. This gender distribution aligns with previous observations suggesting that males may be more susceptible to severe outcomes following COVID-19 infection. Our results are in accordance with the study conducted by Santhosh U et. al., where males were affected more than females, with a ratio of 70% versus

30%.⁹

Additionally, the majority of patients with a history of COVID-19 infection, in the current study, were in the age group of 50-60 years, highlighting a potential age-related susceptibility to the development of AVN post-COVID-19. In one investigation, patients with avascular necrosis (AVN) of the femoral head following COVID-19 infection had a mean age of 59.1 years, ranging from 38 to 72 years, which aligns with the demographic characteristics observed in our study.¹⁰ Another study reported a mean age of 37 years among patients diagnosed with AVN of the hip post-COVID-19 infection, with an age range of 23 to 60 years.¹¹ Moreover, a case report documented a 60-year-old individual who developed bilateral AVN of the femoral head subsequent to severe COVID-19 infection.¹² These collective findings suggest that AVN can manifest across a broad age spectrum following COVID-19 infection. However, further investigation is warranted to comprehensively elucidate the relationship between age and the occurrence of AVN in individuals affected by COVID-19.

Regarding the side of hip involvement, AVN was more commonly observed on the right side (50%) compared to the left (41.67%) and bilateral presentation (8.33%) in our study. This asymmetry in hip involvement may suggest differential effects of COVID-19 infection on vascular perfusion in the body. Furthermore, a substantial proportion of patients with prior COVID-19 infection reported a history of alcohol intake and smoking (33.33% each), which are known risk factors for AVN. Alcohol consumption and tobacco smoking have been found to be major risk factors for avascular necrosis (AVN) of the femoral head in the adult Indian population.¹³ A study conducted on AVN patients showed that 55% had a history of alcohol consumption and 60% were smokers, indicating a positive correlation between cellular toxicity and AVN.¹⁴

The use of steroids is recognized as a risk factor for the onset of AVN.¹ This risk may be heightened due to the induction of a hypercoagulable state during COVID-19.³ In our investigation, 41.67% of patients reported receiving steroids as part of their COVID-19 treatment regimen. While this observation might raise concerns regarding the potential contribution of steroid therapy to AVN development, our statistical analysis did not reveal a significant correlation between steroid use and the occurrence of AVN hip ($p>0.5$). Becker et al. suggested that interactions among pro-inflammatory cytokines could lead to increased platelet aggregation and damage to endothelial cells.¹⁵ Tang et al. noted similar instances of AVN during the SARS epidemic in the early 2000s, prompting cautionary advice against excessive corticosteroid administration, particularly in critically ill or septic COVID-19 patients.¹⁶ Literature searches yielded case reports linking

unilateral femoral head necrosis to both COVID-19 infection and steroid administration, suggesting a potential connection between COVID-19, corticosteroid therapy, and AVN. However, age might serve as a confounding factor, given that advancing age is associated with an increased risk of AVN.¹⁷

Comorbidities such as diabetes mellitus and hypertension were also observed in a subset of patients with prior COVID-19 infection, although the prevalence was relatively low.

The onset of AVN in COVID-19 is poorly documented; however, select articles suggest its prevalence. Notably, in our study, the average time of onset of AVN hip after COVID-19 infection was approximately 6.33 months, with one patient developing the disease immediately after contracting COVID-19. Dhanasekararaja et al. documented 22 instances of AVN in patients recovering from COVID-19, with symptoms manifesting within a range of three weeks to three months.¹ Similarly, Agarwala et al. presented a case series involving three patients who exhibited symptoms 45-57 days after confirming COVID-19 infection.¹⁸ Interestingly, our study contrasts with these findings, as the average duration for the development of AVN was notably longer than reported in these studies. This variance may suggest the need for clinicians to maintain a heightened suspicion of AVN in post-COVID patients reporting hip discomfort.

Overall, our study underscores the need for further research to elucidate the complex interplay between COVID-19 infection, potential risk factors, and the development of AVN of the hip.

Limitations:

Our study has few limitations. Firstly, the sample size was small, and we lacked data on the dosage of steroids administered for the treatment of COVID-19 infection. Additionally, our study only included patients with stage 3 or stage 4 Avascular Necrosis (AVN) of the hip. This limitation arises because our center primarily handles advanced cases, potentially resulting in the underrepresentation of patients with stages 1 and 2 AVN hip.

Conclusion:

The findings of studies examining the association between COVID-19 and AVN underscore the importance of vigilance in monitoring recovered patients, particularly those with risk factors such as steroid use or a history of severe illness. Moreover, clinicians should remain attentive to the potential onset of hip pain or dysfunction in post-COVID-19 individuals, promptly assessing and managing any suspected cases of AVN

to mitigate long-term morbidity and disability. Furthermore, longitudinal studies with extended follow-up periods will be crucial in assessing the long-term implications of COVID-19 infection on orthopedic health, thereby informing clinical practice and improving patient outcomes in this evolving landscape of post-pandemic healthcare.

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