

Evaluation of Avascular Necrosis and Related Factors in COVID-19 Patients Receiving Corticosteroids

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Abstract

Introduction: This study aimed to determine the prevalence of avascular necrosis of the femoral head in COVID-19 patients receiving corticosteroids at Baqiyatallah Hospital.

Methods: In this cross-sectional study, COVID-19 patients who have received corticosteroids and at least six months have passed since receiving corticosteroids were contacted, and they were contacted about any pain in the area. Hip pain, lameness, and movement restrictions were assessed. If the patient had a suspicious history, we invited them to undergo an MRI.

Results: The findings of this study showed that the prevalence of avascular necrosis is 9.2%, and none of the variables of age, sex, body mass index, dose of prednisolone, or remdesivir have a suitable predictive role in the occurrence of this complication ($P < 0.05$).

Conclusion: The study's findings showed that steroid treatment in COVID-19 is valuable. However, the adverse effects of this treatment are very severe. High-dose steroid therapy causes avascular necrosis, but case reports clearly show that steroid therapy cannot fully account for the rapid onset of avascular necrosis after recovery from COVID-19 infection, although it is a contributing factor.

Keywords: Avascular necrosis, COVID-19, corticosteroid.

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Introduction

Each year, the United States diagnoses between 10,000 and 20,000 new cases of avascular necrosis of the scrotum, a disease that disrupts blood transfusion to the progesterone ¹. In some studies, this number is estimated to be between 20,000 and 30,000, and a total of 10 percent of hip hypertension arthroplasties occur annually in the U.S. due to myocardial dysfunction ². The average age of the people involved is between 30 and 38 years, and it mainly occurs with a ratio of 3:1 to 5:1 in men more than in women; however, racial differences have no proven effect on the increase in rates except in the African race, which is more common due to anemia ^{3,4}.

A variety of traumatic and non-traumatic cases, such as head fractures, can cause the disease. In hip joint behaviors, several non-traumatic cases, such as

cavagolopathies, chronic cortisone use, and alcohol, can also cause the disease ⁴.

Chronic use of cortisone as well as alcohol is one of the most common causes of coronavirus, in such a way that after a thrombus, the use of chronic cortisol is the most frequent cause of the disease, and 80 percent of non-thrombus cases also occur due to chronic consumption of cortisol. ^{5,6} However, there are various causes, including a lack of primary cell storage, fatty embolism, hyperlipidemia, and endothelial disorders ⁷.

However, there is a disruption in the progesterin hemorrhage and necrosis formation in the head of the fibromial bone that can cause pain and, consequently, progress towards arthritis and decreased range of movement. The disease develops in four stages: the

fragmentation stage comes before the hemorrhoidal disorder and is when necrosis breaks down bone and makes it clap; the re-skeletalization stage creates tissue bone, which makes the bone stronger and more stable; and the final stage, called the recovery or remodeling stage, decides the lump's main shape based on how bad the initial injury was and how it got worse during the fragmentation phase ⁸.

The coronavirus belongs to the family of coronaviruses, which have different types of viruses. ⁹. The Chinese city of Wuhan first detected a new, unknown virus outbreak on December 30, 2019, which quickly spread worldwide ¹⁰. It caused a pandemic that, today, three years later, still spreads around the world, and despite vaccinations, the mortality rate remains relatively high ¹¹. The disease causes viral pneumonia in an individual that can spread rapidly, cause ARDS, and disrupt multi-organ dysfunction ¹².

Currently, cortisone use has not shown any benefit for non-diabetics; however, studies, including those conducted in the UK on 6,425 patients, have shown that the ten-day pulse significantly reduces the 28-day mortality rate compared to those who did not receive cortisone. As a result, guidelines now recommend cortisol use for cancer patients ^{13, 14}. The country's high coronavirus prevalence and multiple waves of the disease have led to a significant number of individuals receiving cortisone treatment, both for injuries and non-injuries, due to a shortage of available beds. Unfortunately, many of these people do not become fallopian, and cattle visit due to the unconsciousness of the effects of cortisol in the late stages of the disease. Permanent complications have developed. The study examined the frequency of avascular sclerosis in coronavirus patients who received cortisone and related factors. ¹⁵⁻¹⁷

Methods

The study population included patients who visited the rest of the hospital, had coronavirus, had received cortisone, had at least six months since receiving cortisol, and were in the trial with suspicions of cerebral dysfunction. 196 patients were included.

The inclusion criteria were that the patient was over 18 years old and had complete patient medical records. Exclusion criteria included a record of previous surgeries; the patient has had previous surgeries on the underlying organs. Previous post: Hypnosis Infection. Pain spread to the underlying organs. history of the underlying fracture, a history of diseases or birth defects of bones and joints, a history of neurovascular or bone metabolic diseases, and the use of immunocamps medicines; using medications to either lose or gain weight; a history of fractures.

We contacted COVID-19 patients who had received corticosteroids, as well as at least six months after their coronavirus diagnosis. We asked if they had any suspicions about pain in the longitudinal area, tenderness, or restriction of movement. We explained that the patient was invited to perform an MRI and that they had been examined in the event of suspected avascular neurosis of the head of the vagina based on the injections and the examination for the patient's MRI. Notably, the patient requested an additional charge for the MRI injection, which he performed to his satisfaction. The patient's MRI revealed a diagnosis of neurovascular nerve disease.

Data analysis

The data analysis was done with the use of SPSS-22. The frequency, percent, mean and standard deviation (SD) were used to show the distribution of the data. Tests such as the t-test and Chi-2 were used, and the final analysis was based on logistical regression. A P-value less than 0.05 level was considered statistically significant.

Results

The average age of the patients was 14.85 ± 53.75 years. 114 (58.2 percent) women and 82 (41.8 percent) men were studied.

The patients' average weight was 9.5 ± 76.10 . The average height was 7.1 ± 167.1 . The average body mass index was 3.25 ± 27.2 .

178 (90.8%) had no ocular necrosis, and 18 (9.2%) had ocular neurosis.

The results showed that the average age ($P = 0.307$) and body mass index ($P = 0.581$) had no statistically significant differences between patients with and without avascular necrosis ([Table 1](#)).

Table 1. Examination of avascular necrosis patients by age and body mass index.

Items	avascular necrosis	N	SD	mean	P-value
Age	No	178	14.51	54.1	0.307
	Yes	18	17.94	50.33	
BMI	No	178	3.3	27.31	0.581
	Yes	18	2.71	26.86	

The results showed that there was no statistically significant difference between patients with and without avascular necrosis in their gender ($P = 0.216$) ([Table 2](#)).

Table 2. The distribution of avascular necrosis is related to gender.

Items	necrosis		P-value
	Yes	No	
Female	N	8	0.216
	%	7.00%	
Male	N	10	
	%	12.20%	

The results showed that there was no statistically significant difference between patients with and without avascular necrosis receiving Remdesivir ($P = 0.968$) ([Table 3](#)).

Table 3. Distribution of avascular necrosis in patients according to remdesivir intake

Items	necrosis		P-value
	Yes	No	
No	N	8	0.968
	%	9.10%	
Yes	N	10	
	%	9.30%	

Patients with avascular necrosis had received a high dose of prednisolone, but no statistically significant difference was found between the level of prednisolone received ($P = 0.364$) ([Table 4](#)).

Table 4. Comparing prednisolone intake levels in patients with and without avascular necrosis

Items	necrosis		P-value
	Yes	No	
Low	N	0	0.364
	%	0.00%	
Moderate	N	18	
	%	100.00%	
High	N	158	
	%	89.80%	

Regression analysis revealed that age, patient sex, body mass index, receiving remdesivir, and prednisolone were not good variables for predicting vascular necrosis ([Table 5](#)).

Table 5. Examining regression variables to predict avascular necrosis

Items	Beta	S.E.	95% C.I.for EXP(B)		Exp(B)	P-value	df	Wald
			Upper	Lower				
Age	-0.015	0.017	1.018	0.953	0.985	0.363	1	0.828
Sex	0.526	0.509	4.585	0.624	1.692	0.302	1	1.067
MRI	-0.025	0.08	1.142	0.833	0.976	0.758	1	0.095
Remdesivir	0.013	0.505	2.725	0.376	1.013	0.98	1	0.001
Constant	-1.165	2.352			0.312	0.62	1	0.246

Discussion

High doses of steroids are necessary to save lives due to the severity and danger of the COVID-19 infection, as well as the cytokine storm it generates. As with all drug treatments, there are side effects. Steroid avascular necrosis of the femoral head (ONFH) ¹⁸ is one such reported side effect. In our study, the prevalence of this complication was 9%. However, none of the variables age, gender, coronet dose, or remdesivir were good predictors for the occurrence of this complication.

The mechanism by which steroids cause avascular necrosis of the femoral head is based on drug therapy's group actions. Note that avascular necrosis primarily impacts the femoral head, particularly its antero-frontal side, which serves as the axis of weight transfer. Corticosteroids stimulate fat mobilization, which in turn increases the likelihood of fat emboli developing from the liver to occlude small blood vessels in the femur, depleting the microvascular environment. In addition to this, steroid treatment disrupts calcium metabolism and homeostasis, which increases the volume of intraosseous fat cells, gaucher cells, and inflammatory cells while increasing the activity of osteoclasts, thus increasing calcium absorption and deposition, ultimately leading to the lack of dark and cortical bones. This deficiency, therefore, leads to increased intraosseous pressure, which causes impaired intraosseous circulation and avascular necrosis ^{19,20}.

Agarwala et al. conducted a study on three cases of patients who recovered from COVID-19 after treatment with corticosteroid therapy and then developed avascular bone necrosis (AVN). The study revealed that the patients received an average dose of 758 mg of prednisolone. Bilateral pain in the buttocks and femoral areas simultaneously affected the patients. This study holds great significance as it diagnosed AVN after patients took doses below the 2,000 mg ceiling that current guidelines set for AVN prevention. Furthermore, our study revealed that an average of 58 days passed after the initial diagnosis and treatment of COVID-19 in patients with

AVN features. This is in contrast to the results of our study, which stated that the dose of prednisolone after treatment with avascular necrosis patients was not different from that of healthy patients ²¹.

Steroids have long been known to cause the development of avascular bone necrosis, but reports of rapid AVN development in post-treatment COVID-19 patients suggest that specific treatment guidelines to prevent AVN may also play a role in the development of AVN, and steroid use is not the only major cause of AVN after steroid treatment ¹⁸.

Other studies include the ones listed below: This study's result indicated that doctors treating SCD patients should focus on ANFH to prevent or avoid this catastrophic complication, particularly in younger patients who frequently present with hemolytic crises ²². Saito M. et al. conducted a study to investigate the risks associated with the development of AVN in the early stages after renal transplantation. The study's result indicated a relationship between the development of AVN and the steroid dose in the early postoperative period, and they also determined a dose-response relationship ²³. Our study, naturally, did not find a dose-response relationship. Fathi et al.'s study, which looked at the prevalence of femoral head necrosis in 6420 MS patients who received interferon beta, included 4900 patients in their descriptive cross-sectional analysis. Of these, 8 patients had femoral head necrosis equivalent to 0.16%; their average age was 30.25 ± 10.09 ; most of them, 75%, were women; 5 patients had unilateral involvement; and three patients had bilateral involvement. Based on this study, this hypothesis is proposed. It is possible for MS patients to develop femoral head necrosis after using beta-interferon ²⁴. In the study Guo et al. conducted a study on the prevalence of osteonecrosis of the femoral head in patients with SARS who received corticosteroids, examining 539 patients with an average age of 33.7, including 129 men and used MRI and CT scans for screening. Of these, 51 (39.5%) had ONFH, while only 79 of 410 patients (19.3%) were female. The incidence of

ONFH was significantly higher in patients between 20 and 49 years than in the group between 50 and 59 years (25.9% (127 of 491) vs. 6.3% (3 of 48); $p = 0.018$)²⁵. Given all the reviewed results, it is crucial to administer the minimum effective dose of steroid.

Conclusion

The use of steroid therapy in COVID-19 is valuable. But the harmful effects of this type of treatment are clear, and we should always consider the side effects caused by corticosteroids, such as avascular necrosis of the femoral head, the main non-traumatic cause of which was the chronic use of corticosteroids. Also, to stop avascular necrosis of the femoral head from getting worse, we should check up on patients who have been taking corticosteroids for a long time at the right time. This will help to prevent the disease from getting worse by detecting avascular necrosis of the femoral head early on, even when it is still in its early stages. Our study found that the avascular necrosis frequency was less than ten percent, and this frequency had no statistically significant relationship with other findings investigated in the study.

Highlights

What Is Already Known?

The high prevalence of coronavirus and multiple waves of the disease have resulted in a significant number of individuals receiving cortisone treatment, both for injuries and non-injuries, due to a shortage of available beds.

What Does This Study Add?

The adverse effects of steroid treatment are very severe. High-dose steroid therapy can lead to avascular necrosis. However, case reports indicate that it cannot fully explain the rapid onset of avascular necrosis after recovery from COVID-19 infection, although it is a contributing factor.

Authors' Contributions

Concepts, design, data gathering, data analysis, writing and editing: Sadra Haji, Mohammad Kazem Emami Meybodi, Mahdi Abbaszadeh, Mehdi Raei, Soheila Javadi Narab, Mohammad Mahdi Shater.

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Conflicts of Interest Disclosures

We declare that there is no conflict of interest.

Consent For Publication

We consent to the publication of this paper.

Ethics approval

The ethical committee of Baqiyatallah University of Medical Sciences confirmed the protocol of this study with IR.BMSU.BAQ.REC.1401.013 code.

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