

AN OVERVIEW ON COVID-19 INDUCED AVASCULAR HIP NECROSIS**Dr. Vankodoth Sireesha*¹, M. Pratibha², M. Sunil Kumar³, CH. Kanna Reddy⁴ and R. Lavanya⁵**¹Assistant Professor, Department of Pharm D, CMR College of Pharmacy.^{2,3,4,5}Pharm-D Intern, Department of Pharm-D, CMR College of Pharmacy.***Corresponding Author: Dr. Vankodoth Sireesha**

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ABSTRACT

COVID-19 adversely impacts a number of human body systems as a part of 'long COVID-19, such as Guillain-Barré syndrome, lung fibrosis, pulmonary thromboembolism, cardiomyopathy, and sensory dysfunction, one of which is Avascular Necrosis. The purpose of this article is to review AVN as a long-term sequel to COVID-19 by describing an overview of pathogenesis, diagnosis, and management. Avascular necrosis (AVN) is a degenerative bone condition characterized by cellular death and bone collapse from compromised subchondral blood circulation. Vascular disruption, hypertension, intravascular occlusion, or extravascular impingement all contribute to the onset of AVN by decreasing bone circulation. AVN can be caused by a variety of conditions, but the most frequent predisposing factor for AVN is corticosteroids used in the management of COVID-19. Although the pathogenesis of steroid-induced AVN is not fully understood, several hypothesized mechanisms have been put forth, including abnormalities in bone marrow stem cells, vascular endothelial dysfunction, fat emboli, fat hypertrophy, and a hypercoagulable state. The breakdown of vascular function and the emergence of bone necrosis are caused by the interaction of a hyperinflammatory and hypercoagulable condition. Along with a comprehensive medical history and physical examination, the diagnosis can be verified by performing one of the following tests: X-ray, CT, MRI, bone scan, biopsy, and bone functionality assessment. The goals of treatment for AVN include reducing pain, slowing the disease's progression, avoiding collapse, and restoring joint function, which are achieved by using medications, surgical procedures, and lifestyle modifications.

KEYWORDS: Avascular necrosis, Covid-19, Corticosteroids, Bone Necrosis.**INTRODUCTION**

The coronavirus illness, caused by the novel coronavirus that is now known as severe acute respiratory syndrome-coronavirus type 2 (SARSCoV-2). The COVID-19 virus frequently causes fever, coughing, exhaustion, and breathe problems. Many patients infected show very mild or no symptoms, a small percentage go on to develop pneumonia, acute respiratory distress syndrome (ARDS), and multiple organ failure.

The SARS-CoV-2 (COVID-19) coronavirus pandemic has sparked an unprecedented response from the world's scientific community to learn more about the illness. But there are still a lot of unsolved questions regarding SARS-CoV-2. Numerous studies have been done on the long-term effects of the virus, which also affect the musculoskeletal system. In patients with COVID-19, systemic inflammation may affect the physiology of bone and joint tissue. COVID-19 induces the production of CXCL10, IL-17, and TNF-alpha among other cytokines. They are responsible for lowering osteoblast proliferation and differentiation. Most COVID-19 hospital patients receive corticosteroids, which have a negative impact on bone tissue. Additionally,

proinflammatory proteins including IL-1b, IL-6, and IL-8 that are encoded by single nucleotide polymorphisms in a number of genes may influence biological activity and contribute to hypercoagulability in COVID-19 patients, raising the risk of bone necrosis. Vasculitis, leukocyte aggregation, and hypercoagulability all work together to reduce blood flow in bone blood vessels, which can lead to bone necrosis.^[1]

Complications in recovered coronavirus patients, including mucormycosis, blood clots, newly diagnosed diabetes, and persistent weariness, increased during the second wave of Covid-19 in India. The most recent is called osteonecrosis or avascular necrosis. It is known as "death of bone tissue owing to lack of blood flow" in everyday language. As AVN is a degenerative bone disease that predates Covid-19. However, experts believe that this may be the next unsettling development in post-Covid problems.

The avascular necrosis manifests itself when the blood supply to the bone is either temporarily or permanently interrupted. The ends of lengthy bones are most frequently affected by this, which results in small cracks

in the bone and causes the bone to collapse. One bone, many bones, or various bones at various times may all be impacted. But the hip is where it usually manifests.

"The cells in the femoral head, the highest portion of the thigh bone, die for a variety of reasons, the majority of which are related to steroid use, alcohol consumption, and sickle cell disease. Avascular necrosis may result from this.

The patient will complain of pain in the hip or groin area, which could make it very difficult for them to walk and cause them to limp. It is quite difficult for them to move around because of the excruciating discomfort in their lower back, groin, and knee area. The prevalence of this illness has been increasing quickly and presents as the introduction of Covid-19, and after mucormycosis, as one of the major problems after COVID-19.^[2,3]

STAGES^[4]

Avascular necrosis has five distinct stages, which are as follows:

- **Stage 1:** Minor osteopenia or no radiographic alterations are present. Identification requires an MRI scan (can show oedema). This illness starts out asymptotically.
- **Stage 2:** The initial stage with radiographic modifications. Osteopenia, subchondral cysts, and sclerosis of the joint head's superior central region are all symptoms of this stage.
- **Stage 3:** During this stage, the articular surface is depressed just enough to jeopardise the round contour without considerably deforming it. As a result, the joint space gets smaller. An unadorned radiograph displays a crescent symbol.
- **Stage 4:** The subchondral bone collapses widely during this stage, and the underlying trabecular pattern is destroyed.
- **Stage 5:** The last stage results in a dysfunctional joint when both articular surfaces are compromised.

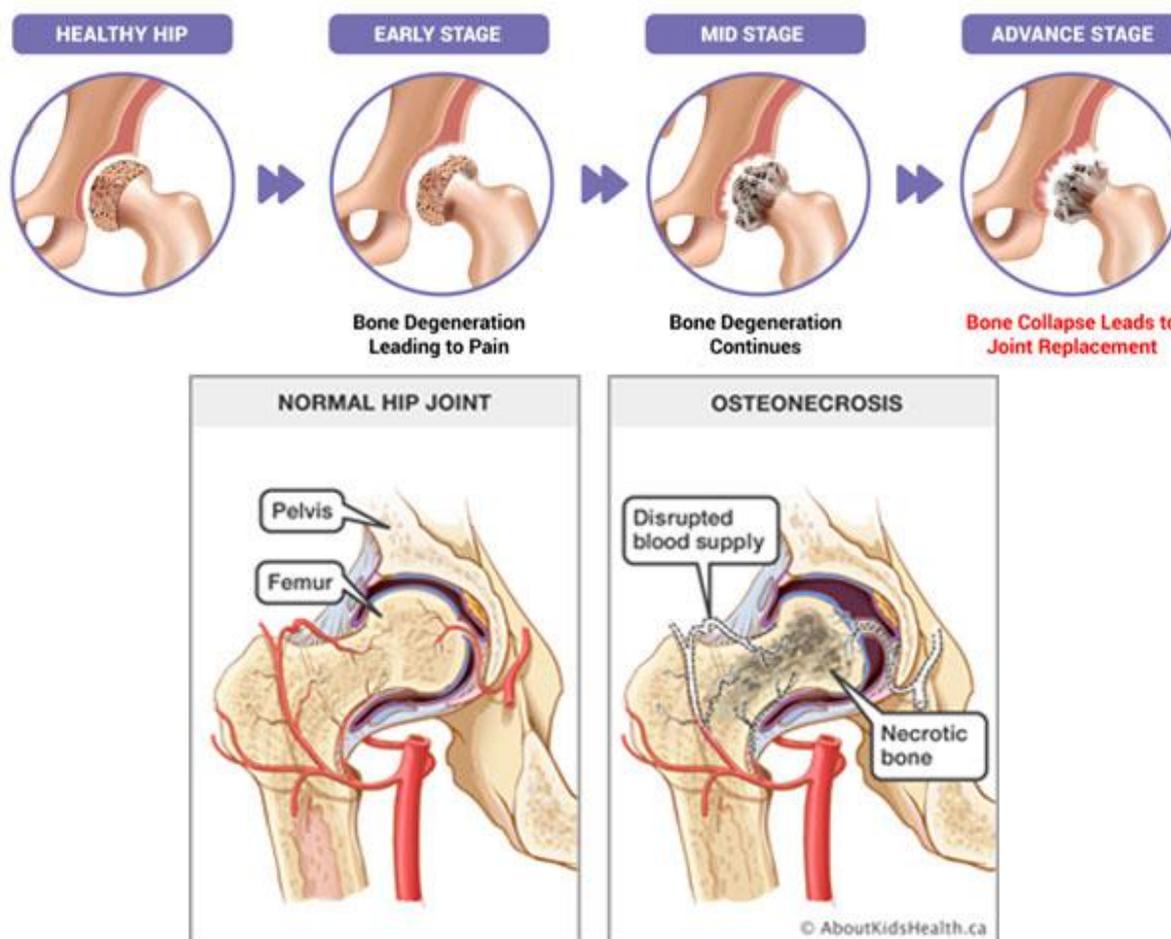


Fig. 1: Normal Hip Joint vs Avascular Necrosis (AVN) or Osteonecrosis.

Long bones are afflicted at their ends in this disorder, which causes little fissures that could eventually cause

the bone to collapse. The hip joint is most frequently impacted by AVN, though it can happen in any bone.^[5]

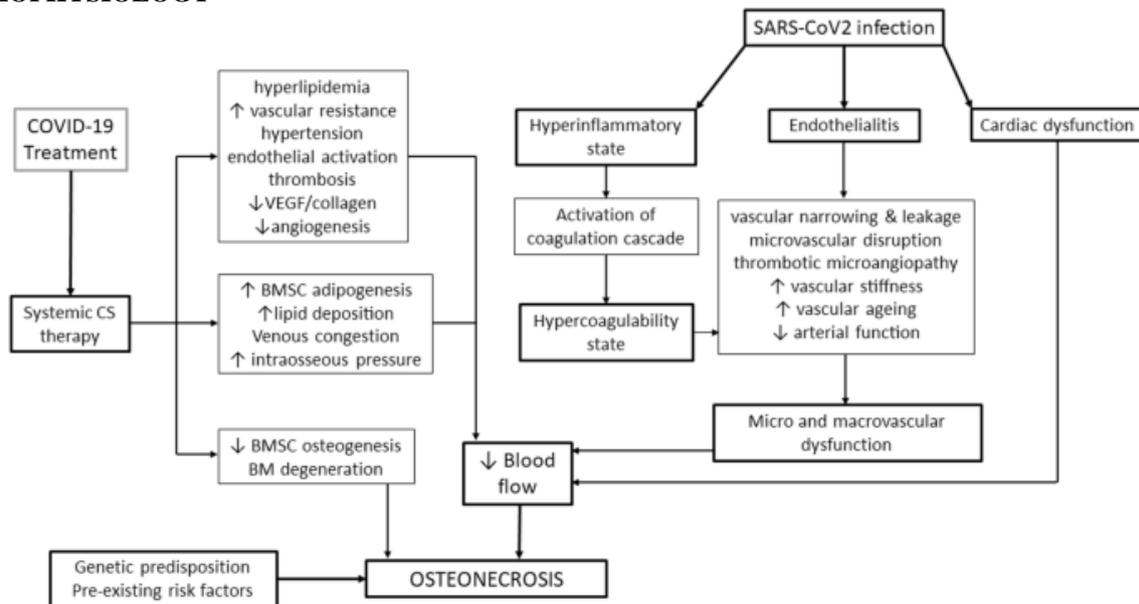
PATHOPHYSIOLOGY ^[6]

Fig. 2. Pathogenesis of osteonecrosis in COVID-19 through different pathways. COVID-19—coronavirus disease 2019; SARS-CoV-2—severe acute respiratory syndrome coronavirus-2; CS—corticosteroid; VEGF—vascular endothelial growth factor; BMSC—bone marrow stem cell; BM—bone matrix.

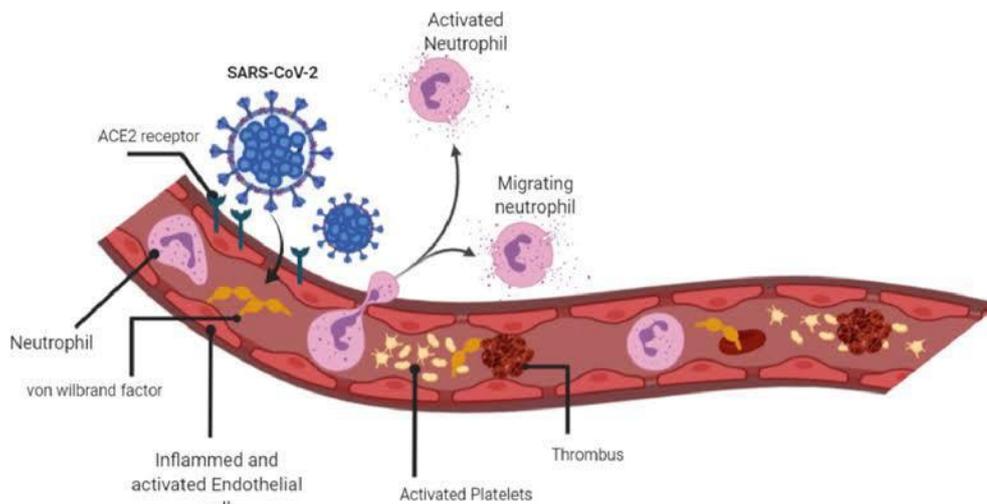


Fig. 3: Effects of SARS-CoV-2 on endothelial cells and thrombus formation.^[7]



Fig. 4: The above figure indicates the X-ray of Avascular necrosis due to long-term corticosteroid use.^[8]

COMPLICATIONS ^[9]

Infections at the surgical site, issues with prostheses, and neurovascular impairment are typical postoperative consequences for avascular necrosis. As the condition progresses despite surgical intervention, high failure rates happen. For instance, 90% of patients who had treatment for AVN of the hip saw disease progression despite core decompression.

Complication rates are also significantly influenced by patient comorbidities. For instance, prolonged hospital admissions, a higher risk of acute renal injury, implant failure, pulmonary embolism, deep vein thrombosis, myocardial infarction, and an overall higher mortality

rate were all present in sickle cell disease patients receiving total joint replacement for AVN.

SYMPTOMS ^[10]

Many individuals with COVID recovery have reported of having AVN. Young adults between the ages of 30 and 50 make up the majority of AVN sufferers. Hip or groin pain, oedema and inflammation, joint stiffness, and loss of movement are all signs of AVN.

Early stages frequently show no symptoms. The most typical presenting symptoms are hip and groin discomfort, which typically denote late-stage development. Referred pain to the thigh and buttocks is one of the accompanying symptoms. Most people experience pain while at rest. Stiffness and modifications to gait are some more.

The condition grows more painful as it worsens. At initially, pressing on the damaged bone can be the only thing that hurts. The pain could then become ongoing. Then the patient could experience excruciating agony that makes you immobile if the surrounding joint and bone collapse. Depending on the joint, it takes from a few months to over a year for the progression from the early stage to complete bone collapse.

DIAGNOSIS ^[11]

The patient in addition to a thorough medical history and physical examination, requires one or more of the following tests such as **X-ray, CT (computerised tomography) scan, Imaging with magnetic resonance (MRI), Bone scan using radionuclides** - this test reveal both blood flow to the bone and cell activity, **Biopsy, Bone functionality assessment**- Tests to detect the pressure inside the bone that typically require surgery.

TREATMENT

Early detection is the primary goal to retard progression in AVN which is possible through MRI. Treatment objective in AVN is to obtain pain relief, retard disease progression, prevent collapse and restore joint function. Multitude treatment options are available for managing AVN ranging from conservative, medical to surgical modalities, however no standardised protocol exists. Various medical therapies tried in the past including iloprost, nifedipine and hyperbaric oxygen therapy have not shown significant benefits. Therefore, arthroplasty remains the mainstay of treatment. Although it provides good outcome but when performed at a young age will necessitate at least one revision in the future. Successful use of bisphosphonates for the treatment of AVN in adults was first reported by Agarwala *et al.* It has been observed that bisphosphonates not only give good clinical outcome but also retard progression of the disease and the need for a surgery. Subsequently, supplemental therapy with vitamin D and calcium in addition to bisphosphonates is beneficial.^[12,13]

MEDICATIONS

As avascular necrosis progresses, some drugs may help relieve symptoms:

Non-steroidal anti-inflammatory medications (NSAIDs): Ibuprofen or naproxen sodium, may ease the discomfort brought on by avascular necrosis.

Drugs for osteoporosis: bisphosphonates, alendronate, risedronate drugs might slow the development of avascular necrosis.

Drugs for lowering cholesterol such as statins are used to lower the blood cholesterol and fat levels which are responsible for Blood vessel obstructions that can result in avascular necrosis.

Drugs that dilate blood arteries such as ACE inhibitors, ARBs, CCBs, Hydralazine, iloprost may provide more blood flow to the damaged bones in AVN.

Clotting agents: Blood thinners, such as warfarin, may be able to treat clotting abnormalities and avoid clots in the blood vessels supplying the bones.

THERAPY

A practitioner in healthcare management might state:

Rest: The deterioration of the bones may be slowed by limiting physical activity or by using crutches for a while to take weight off the joint.

Exercises: Exercises to assist maintain or enhance the range of motion in the joint can be taught by a physical therapist.

The stimulation of electricity: To replace the broken bone, the body may be encouraged by electrical currents to create new bone. During surgery, electrical stimulation can be used to treat the injured area directly. Instead, it can be given using electrodes affixed to the skin.

SURGERY AND OTHER PROCEDURES

The physician could advise surgery because most people don't show symptoms until avascular necrosis has advanced. Among the choices include-

Core decompression: A portion of the inner layer of bone is removed by a surgeon. The additional room inside the bone not only eases pain but also encourages the growth of healthy bone tissue and new blood vessels.

Bone replacement (graft): The avascular necrosis-affected bone region can be strengthened with the help of this technique. A healthy bone fragment from another area of the body is used as the graft.

Bone remodelling (osteotomy): In order to help take pressure off the injured bone, a wedge of bone is removed above or below a weight-bearing joint. Joint replacement may be delayed with the aid of bone contouring.

Replacement of a joint: Surgery can replace the injured joint components with plastic or metal ones if the affected bone has collapsed or other therapies aren't working.

Treatment with regenerative medicine: A relatively novel surgery called bone marrow aspiration and concentration may be able to help hip avascular necrosis in its early stages. The surgeon takes a piece of dead hipbone during surgery and replaces it with bone marrow-derived stem cells. This might enable the growth of new bone. Further research is required.^[14]

CONCLUSION

Although steroids are one of the life-saving drugs used to control COVID-19, they should be administered with extreme caution. Using the smallest therapeutic doses and cutting the duration of steroids are essential to maintaining clinical efficacy and lowering the risk of side effects. Individuals getting steroids for the treatment of COVID-19 should be informed about their side effects and urged to keep an eye out for the development of symptoms. As it is crucial for lowering morbidity and enhancing a person's quality of life, early detection is the key to preventing the advancement of avascular necrosis of the hip in long COVID-19 and starting care of AVN according to the patient's situation. With the current global outbreak, it is crucial to discuss the use of corticosteroids, the dosage and length of treatment, as well as strategies for the prevention, early detection, and prompt intervention of steroid-induced avascular necrosis.

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