



Prevalence Study of Femoral Head Avascular Necrosis and Evaluating Mutual Connection between Injury and Viral Infections: Clinical Analysis and Brief Review

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Authors' contributions

This work was carried out in collaboration among all authors. Author AY, MM, ASE, MM and BO made substantial contributions to conception and design, analysis and interpretation of data and contributed to sample collection. All authors were involved in drafting the manuscript and revising it. All authors read and approved the final manuscript.

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ABSTRACT

Avascular necrosis (AVN) could remain with negligible clinical symptoms, but it would get worsen over the time if it's left untreated and at the most cases will require surgical treatment. Prevalence of femoral head AVN is almost 0.45% among HIV patients which is approximately 45 times more than the rest of Society. AVN occurs 0.088%-1.33% annually among HIV victims. Avascular necrosis of the femoral head is a bone deteriorating plight. At this study, the clinical prevalence of it has been analyzed among a group of 180 patients at Rasool-e-Akram Hospital (Iran, between 2008 and 2016). Patients were including 121 men and 59 women. Analysis results showed that the prevalence of HCV, HBV, and HIV was 1.7%, 1.1%, and 1.1% respectively. It was found that 63%

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of patients was currently using immunosuppressive drugs. 17% had a history of drug abuse among which 3.3% were using IV drugs. It was concluded that femoral head AVN is more common among hepatitis and HIV patients.

Keywords: Avascular bone necrosis; femoral head; human immune deficiency virus; hepatitis; hip arthroplasty.

1. INTRODUCTION

After the pioneer studies and introducing the subject of avascular bone necrosis by Alexander Murno [1], lots of efforts have been taken to in-depth exploration of contributing factors to femoral head AVN (AVN stands for avascular necrosis) [2]. Femoral head AVN is a bone deteriorating condition which is due to compromised blood supply to femoral head which renders its tissue in an ischemic condition [2,3]. This ischemic condition will further antecedent toward osteocell death and necrosis of bone and surrounding tissue and renders patients in a debilitating situation [4]. When this avascular phenomenon continues, femoral head will become cracked and crumbled and multiple bone fracture will cause collapsing and mobility will be restricted [5]. Femoral head AVN usually needs partial or total hip joint replacement. Although most often AVN occurs at femoral head, but it also could be happening at any other joints including knee, elbow, foot, wrist and shoulder [6]. Avascular necrosis could remain with negligible clinical symptoms, but it would get worsen over the time if its left untreated and at the most cases will require surgical treatment [7].

Femoral head AVN is considered to be a common cause of musculoskeletal weakening and is a major diagnostic and remedy challenge [8,9]. Its estimated that almost 50% of patients with femoral head AVN will experience extreme joint deterioration and around three years after the initial diagnosis they will require a hip arthroplasty which is known as a major surgical procedure [10,11].

AVN of head of femur has different levels [12], and could happen due to various reasons including trauma and drugs including steroids like Corton or long and heavy alcohol intake, systematic diseases like diabetes, systemic lupus erythematosus [13,14], sickle cell anemia (SCA). Recently using Unauthorized drugs in bodybuilding specially steroids has become a

new concern that may incite femoral head AVN [15,16].

Femoral head AVN is an up growing issue among HIV patients [17]. Prevalence of femoral head AVN is almost 0.45% among HIV patients which is approximately 45 times more than the rest of Society. AVN occurs 0.088%-1.33% annually among HIV victims. Diagnostic tools like Magnetic Resonance Imaging (MRI) have improved recognizing patient with underlying AVN [18]. Considerable efforts have been devoted to recognize different aspects of this phenomenon.

Current study is focusing on three root causes of femoral AVN which includes HIV, Hepatitis, and substance intake (both drugs and alcohol consumption).

2. REVIEWING PREVIOUS STUDIES

2.1 Human Immune Deficiency Virus

Metha et al. (2011) studied femoral head AVN among HIV patients. Among 6487 members of members of surveyed society who were all suffering from HIV (2007-2010), AVN patients were recognized by Magnetic resonance imaging (MRI). Results revealed that 19 males and 3 females had underlying femoral head AVN (0.34% incidence; 95% CI, 0.2-0.48%). According to their study 68 percent of these patients had multiple joint deterioration and 73% had more than two risk factors for AVN including Highly Active Antiretroviral Therapy (HAART)(91%), protease inhibitors (68%), hypercholesterolemia (59%), corticosteroids (55%), hypertriglyceridemia (45%), smoking (45%), alcohol intake (27%), and CD4 <200 cells/ μ L (23%). An average CD4 cells count among this group was 52 cells/ μ L. It should be mentioned that only 9% of all patients were considered as idiopathic. According to data provided by designated study it is implicated that AVN is one of the most common multifactorial complications of musculoskeletal at HIV infected population which usually affects more than one joint.

Provided having a better knowledge of every possible risk factors, appropriate preventive measurements must be taken into consideration, and when an HIV patient presents with painful joints AVN should be evaluated. On the other hand, when someone is complaining about multiple joint sore, HIV should be suspected [19].

Yombi et al. (2009) who studied femoral head AVN among HIV type 1 patients reported that osteonecrosis of femoral head (ONFH) usually occurs among young and socially active people who are socially and economically active and reduces their effectiveness. Among HIV patients this condition is a growing health issue [20]. They studied 815 AIDS patients among which 6 patients suffered from femoral head bone necrosis (0.74%) and no gender difference was considered (sex ratio equal to one). In that study 2 out of 6 patients had no risk factor for AVN (33.3%). One of patients had 3 risk factors including corticosteroids intake, chemotropic agent absorption and radiotherapy. The time from beginning of femoral head AVN was short at these patients. All available antiviral drugs were used at this population. Due to concurrent use of different drugs it was impossible to focus on each drug.

Chokotho et al. (2013) studied risk factors of AVN among HIV positive patients and healthy ones, and evaluated initial response to Total Hip Arthroplasty (THA) in normal patients and HIV positive patients [21]. At their study 26 AVN patients with total 37 joint disruptions and receiving surgery were studied. They mentioned that 15 cases were males and 11 patients were females. Mean age of all patients was 47.1 ± 8.0 and population was ranging 33-66 years old. 12 patients were HIV positive and 11 were HIV negative and 3 patients were not discriminated about HIV. Use of alcohol was a common risk factor of AVN among all patients. It was witnessed that 58% of patients had more than 1 risk factor for AVN and only 2 patients out of 12 patients had no other risk factor except being HIV positive. At their analysis 17% of surgeries had no early Surgical complication.

AVN has a multifactorial etiology even among HIV positive patients. Another study showed that irrespective of being HIV positive, surgery usually provides patients with an immediate positive outcome [22].

2.2 Hepatitis

Currently HCV is a worldwide complaint in healthcare services [23]. Prevalence of HCV is less than 1% in Iranian population, but it has an increasing rate at this society. HCV is especially more common among IV drug addict patients. Studying HCV sufferers has showed that comparing with healthy ones AVN could be lot more common among infected community. One specified reason that brings up suspicion is treatment with PEGylated interferon and ribavirin [24].

Landerreche et al. (2015) studied bilateral avascular necrosis of the femoral head. Causes including vascular diseases, malignancies, hypercoagulability states, long-term steroid treatment were inspected. In this study 5 patients were involved including four men and one woman. This study mentioned that some patients had a history of Hepatitis C infections treated with PEGylated interferon and ribavirin. Diagnosis was reconfirmed by pathology assessment after arthroplasty surgery [24]. This study also implies a connection between hypercoagulability and disruption in retinacular blood supply of femoral head. It also has been suggested that viral infection can cause an autoimmune response ending in transient vasculitis in these patients [25-27]. As reported by Zangari M et al., infections with HCV, HBV and HIV viruses may induce hypercoagulability which causes an autoimmune response resulting in transient vasculitis and consequent femoral head AVN[28].

2.3 Substance Intake

Previous studies have shown that there is a direct link between alcohol intake and progress of femoral head AVN [29]. Regarding religious and social bans on alcohol in Iran, it was impossible for us to provide conclusive data on current subject from our country, but there is no doubt that lots of cases as a result of alcohol intake had gone unreported.

The 15-45 years old Iranian population was 50 million in 2011 [30]. The number of drug addict people is estimated to be one million and 300 thousand among which a large number of them are using IV substances [31]. It's worthy to mention that most of drug abusing patients in Iran are male and women constitute a smaller portion of IV drug abusers.

There are also reports of connection between taking interferon because of multiple myeloma and increased risk of avascular necrosis of femoral head. It was suggested that using PEGylated interferon 2B to treat viral infections (most notably HIV, HBV and HCV) could be another reason of non-traumatic AVN [28].

3. METHODS

Current study is a cross sectional study carried out to evaluate the prevalence of HIV, HBV and HCV among 180 patients who were suffering from avascular necrosis of femoral head. This study has been performed and includes data from 2008 till 2016. AVN cases were diagnosed by simple radiography with anterior-posterior (AP) and lateral view, bone scanning and MRI. Results were confirmed by pathology investigation after surgery. Studied cases were not having any history of hip surgery, and didn't have a history of fracture around hip. Exclusion criteria were having a history of hip surgery, history of acetabulum fracture, and a history of femoral head fracture. Due to prohibition on alcohol in Iran, this risk factor was not considered in the present study. Informed written consents were taken from those who voluntarily agreed to participate at this study and moral committee of Hospital supervised the entire procedure. Participants included both sexes.

Investigated factors included age and gender of patient, drug intake, being infected with HIV, HCV, and HBV viruses. Information was driven from patients' documents and collected using a check list. Data were statistically analyzed using SPSS software version 24. Measures of dispersion including mean, minimum, maximum, variance & standard deviation and frequency were calculated for quantitative and qualitative variables.

4. RESULTS

In the current study mean of age was 32.83 with minimum 18 and maximum 58 years. 90% of patients were at range of 18-42 years old. Among these 180 patients group, 67.2% were men and 32.8% were women.

Prevalence of HCV, HBV and HIV was 1.7%, 1.1%, and 1.1% respectively. It was found that 1.1% of cases had 2 concurrent risk factors. It was found that HCV appears to be more prevalent among AVN bone necrosis patients.

There was only one case older than 50 years and most patients were at 18-42 years of their life. It was revealed that 63 percent of this cohort was using immunosuppressive drugs. Results showed that 17 % of patients were drug addicted (opioid addiction) and 3.3% had a history of intravenous (IV) drug abuse most occurring out of hospital morphine dependence. The biggest portion of drug addicts was male and women didn't report any serious opioid addiction except using legal tranquilizers including acetaminophen. Those drug addicts that were taking corton, immunosuppressive drugs and specially those were taking opioid alternative drugs were found to have worse prognosis. Data are summarized in Table 1.

Table 1. Demographic data and prevalence of studied variable

Variable	N=180, prevalence (%)
Mean age (years)	32.83
Gender (M: F) (%:%)	121:59 (67.2%: 32.8%)
HCV (%)	1.7
HBV (%)	1.1
HIV (%)	1.1
Concurrent Risk factors (%100)	2 (1.1%)
Using immunosuppressive drugs	114 (63%)
Opioid addiction	30 (17%)
IV drug addiction	6 (3.3%)

Information about alcohol intake was not conclusive because patients were not willing to inform healthcare providers about this habit due to religious and governmental ban on alcohol. We also found that those who had a history of taking steroid drugs at gym also had a faster progress of AVN causing worse condition to patients.

5. DISCUSSION

Previous studies have suggested that AVN is a multifactorial anomaly which could be influenced by a variety of factors [32]. It has been proposed that factors other than trauma including drug, alcohol and viral infection can impinge normal blood supply to head of femur [33-37].

There is no doubt that these condition are getting widespread in many societies. Recent reports from Iran are implying that HIV and hepatitis are raising more concerns [38]. According to Taherkhani et al. (2015) prevalence of HIV and

HCV in Iran are respectively 0.2% and 0.14% and our current study showed that this prevalence had a meaningful statistical connection with AVN (P value<0.05) [39]. On the other hand, we should take it into consideration that drugs availability also is giving raise to this problem. Based on provided evidence we assume that apart from current drug addiction, taking alternative drugs by addicted patients at hospital, especially steroid base drug, appears to augment the prevalence of femoral head AVN. Although there are previous studies concerning AVN that have clearly proved the role of corticosteroids in femoral head AVN, causing AVN by alternative drugs given to drug dependent patient is still a theory and needs further investigation [40].

Since the earlier diagnosis can contribute to better prognosis of the patients it is suggested to investigate AVN bone necrosis among patients with mentioned risk factors. New diagnostic tools like imaging devices including X-Ray imaging, bone scanning and topographic devices, and MRI can improve diagnosing of underlying AVN bone necrosis in suspected patients. On the other hand, physicians should also become suspicious of viral infections when a patient is presenting with multiple joint deterioration due to avascular necrosis [41].

6. CONCLUSION

Infection with HIV, HBV and HCV will increase the risk of avascular bone necrosis. Currently the rate of these infections is accelerating in Iran. AVN sufferers should better be screened for HIV, HCV and HBV and also be warned of alcohol usage. The earlier diagnosis through screening can result in a better prognosis for the patients.

CONSENT

Informed written consents were taken from those who voluntarily agreed to participate at this study and moral committee of Hospital supervised the entire procedure.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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