Original Article

Epidemiological Profile of Femoral Head Osteonecrosis in the North Indian Population

Abstract

Background: There are limited studies on the epidemiology of femoral head osteonecrosis in Indian population. This study was designed to look for the risk factors of osteonecrosis hip and to assess the severity as per radiological staging (Association Research Circulation Osseous [ARCO]) and clinical score (Harris hip score [HHS]). **Materials and Methods:** 249 patients (382 hips) of osteonecrosis femoral head (ONFH) who were evaluated at our center between January 1, 2005, and June 30, 2013, were included in this retrospective study. The details of history, clinical examination, radiological grading, and HHS were entered into a proforma. **Results:** The mean age was 34.71 years (range 14-70 years) and 70.28% (n=175) patients were between 20 and 40 years. Male to female ratio was 5:1. Bilateral ONFH was observed in 53.41% (n=133) patients. In atraumatic conditions, bilateral involvement was seen in 61.61% (130/211) patients. Steroid administration (37.3%, 93/249) was most commonly observed in the patients followed by idiopathic in 21.3% (53/249) patients, chronic alcohol consumption in 20.1% (50/249) patients, and trauma in 15.3% (38/249) patients. There were 48% (185/382) hips in ARCO Stage 2 followed by 33% (125/382) in Stage 3 and 16% (61/382) in Stage 4. The mean HHS was 80.97 ± 14.35 in unilateral ONFH. The mean HHS was 72.79 ± 14.43 and 80.07 ± 13.52 in more involved hip and in less involved hip, respectively, in bilateral ONFH. The ARCO staging had statistically significant correlation with HHS (Pearson's correlation coefficient $r = -0.783$, $P < 0.01$) in unilateral ONFH patients and more severely affected hip in bilateral (Pearson's correlation coefficient $r = -0.654$, $P < 0.01$) ONFH, but it did not show any association with less involved hip in bilateral cases. **Conclusion:** ONFH in the North Indian patients is a disease of young individuals with male predominance. Steroid intake is most commonly observed in these patients followed by idiopathic, chronic alcohol consumption, and trauma.

Keywords: *Avascular necrosis, osteonecrosis, femoral head, hip joint, risk factor, total hip replacement*
MeSH terms: *Femur head, osteonecrosis, epidemiology, hip joint*

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Introduction

Osteonecrosis of the femoral head (ONFH) is a disabling condition of the hip joint that primarily affects the young individuals. The etiology, natural history, and epidemiology of ONFH have not been fully elucidated. There are associations of many diseases and drugs with ONFH.[1] Mont *et al.* believe that ONFH is multifactorial that is associated with genetic predilection and exposure to certain risk factors.[2-6] These risk factors include chronic corticosteroid administration, chronic alcohol ingestion, smoking, and various chronic diseases (renal disease, hematological disease, inflammatory bowel disease, postorgan transplantation, hypertension, and gout).[7-9]

Literature from the western world and Asian countries report chronic alcohol consumption and steroid administration as the most common aetiologies.[2-18] However, there is no report from Indian subcontinent about the risk factor and epidemiological profile of ONFH. This study was designed to evaluate the risk factors of ONFH in Indian population. Being the tertiary care hospital and as a referral hospital for six states of North India, it represents the epidemiology of ONFH in Northern India.

Materials and Methods

249 patients (382 hips) who were diagnosed with ONFH at our center between January 1, 2005, and June 2013 were included to look for the diseases/habits associated with ONFH. The details of the diseases/habits were obtained from the clinical records and these patients were recalled to collect any missing data. This study was started after obtaining approval from the ethics committee.

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The details of history, clinical examination, radiological examination and Harris hip score (HHS) were entered into a proforma. The patients were evaluated radiologically with anteroposterior and lateral radiographs of the hip joint and magnetic resonance imaging. In patients with hardware inside the hip joint, bone scan was performed for diagnosis. The diagnosis of ONFH was based on the revised criteria proposed by Research Committee on Idiopathic ONFH in Japan.[19] To be labeled as ONFH, a patient has to fulfill two of the five criteria. The staging of ONFH was based on Association Research Circulation Osseous (ARCO)[20] classification. The severity of disease in bilateral cases was categorized as "more involved hip," and "less involved hip" based on their HHS. The HHS was available for 167 patients (81 unilateral hip affected patients and 86 bilateral hip affected patients).

All patients of ONFH of both traumatic or atrumatic etiologies were included in this study. In patients with history of alcoholism, detailed information of the amount and duration of alcohol intake was recorded. In those on steroids, precise information was obtained about the indication, regime, dosage, and adverse event or complications. The patients were asked about smoking, lifestyle, specific family history, and associated systemic illness. In posttraumatic conditions, the details of injury, duration of injury to surgery/intervention, surgical procedure, and modalities of evaluation for ONFH were collected. Routine laboratory investigations such as complete blood count, renal function test, liver function test, lipid profile and coagulation profile (such as prothrombin time, clotting time, and activate partial thromboplastin time) were performed for all patients. The patients with suspected condition or specific disease that might have led to ONFH were further evaluated with specific laboratory and radiological investigations, for example, serum acid phosphatase for Gaucher's disease, serum electrophoresis for hemoglobinopathies, antiphospholipid antibody for systemic lupus erythematosus, and serum uric acid for gout. Patient without any abnormality was labeled as idiopathic.

Of 382 affected hips in 249 patients, 278 hips (101 bilateral ONFH and 76 unilateral ONFH) were surgically treated (106 total hip replacement, 144 core decompression, 20 nonvascularized fibular grafting and 8 vascularized fibular grafting). Remaining 72 patients (32 bilateral ONFH and 40 unilateral ONFH, 104 hips) refused surgery.

The statistical analysis was carried out using statistical package for social sciences (SPSS Inc., Chicago, IL, Version 17.0 for Windows). All quantitative variables were described using measures of central tendencies (mean, median) and measures of dispersion (standard deviation and standard error). Normality of data was evaluated by measures of skewness and Kolmogorov–Smirnov tests of normality. For normally distributed data, means were compared using Student's *t*-test for two groups. For skewed data Mann–Whitney test was applied. For time-related comparison, paired *t*-test or Wilcoxon signed rank test was applied. Qualitative or categorical variables were described as frequencies and proportions. Proportions were compared using Chi-square or Fisher's exact test whichever was applicable. To see correlations for different variables, Pearson's correlations were calculated. All statistical tests were two-sided and performed at a significance level of $\alpha = 0.05$.

Results

Epidemiology and associated disease conditions/habits

The mean age of the patients was 34.71 years (95% confidence interval 24.71–44.71, range 14–70 years). Male to female ratio was 5:1. Bilateral ONFH was observed in 133 (53.41%) patients. In atraumatic conditions, bilateral involvement was seen in 61.61% of patients. Chronic steroid administration was observed in 37.3% patients followed by idiopathic in 21.3%, chronic alcohol intake in 20.1% and trauma in 15.3% [Table 1 and Figure 1].

ONFH in patients taking steroid was 37.3% (*n*=93) of the total patients while among the nontraumatic patients, it was observed in 44% of the patients [Figure 2]. The mean daily administration of prednisolone in unilateral and bilateral ONFH was 28 mg/day (70% of patients had administered >2 g prednisolone in 2 months) and 28.8 mg/day (86% of patients had consumed >2 g prednisolone

Table 1: Distributions of the osteonecrosis femoral head patients as per their age, sex, side involvement and aetiology

Aetiology	Number of patients *n* (%)	Age (years), *n* (%)			Sex, *n* (%)		Side affected, *n* (%)	
		<20	20-40	>40	Male	Female	Unilateral	Bilateral
Steroids	93 (37.3)	8 (3.21)	66 (26.51)	19 (7.63)	70 (28.11)	23 (9.24)	30 (12.05)	63 (25.30)
Alcohol + steroid	7 (2.8)	0 (0.00)	6 (2.41)	1 (0.40)	7 (2.81)	0 (0.00)	0 (0.00)	7 (2.81)
Alcohol	50 (20.1)	0 (0.00)	36 (14.46)	14 (5.62)	50 (20.08)	0 (0.00)	20 (8.03)	30 (12.05)
Trauma	38 (15.3)	6 (2.41)	23 (9.24)	9 (3.61)	32 (12.85)	6 (2.41)	35 (14.06)	3 (1.20)
Idiopathic	53 (21.3)	2 (0.80)	38 (15.26)	13 (5.22)	48 (19.28)	5 (2.01)	28 (11.24)	25 (10.04)
Pregnancy	4 (1.6)	0 (0.00)	4 (1.61)	0 (0.00)	0 (0.00)	4 (1.61)	2 (0.80)	2 (0.80)
Drug induced	3 (1.2)	0 (0.00)	2 (0.80)	1 (0.40)	1 (0.40)	2 (0.80)	1 (0.40)	2 (0.80)
Aplastic anemia	1 (0.4)	0 (0.00)	0 (0.00)	1 (0.40)	1 (0.40)	0 (0.00)	0 (0.00)	1 (0.40)
Total	249	16 (6.43)	175 (70.28)	58 (23.29)	209 (83.94)	40 (16.06)	116 (46.59)	133 (53.41)

in 2 months) respectively. Thirty three patients had taken steroid for <3 months, 28 had taken for 3–6 months, and 34 patients had taken for more than 6 months. The underlying causes of steroid administration included systemic lupus erythematosus (*n*=35, 37.6%), chronic painful joint pathologies (*n*=17, 18.3% with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and other inflammatory arthropathies), skin lesions (*n*=14, 15.1%), lung diseases (*n*=13, 14% with asthma, interstitial lung diseases, sarcoidosis, etc.), and miscellaneous problems (*n*=14, 15% with steroid administration for organ transplantation, for bodybuilding, prescription by local physician, or quack without specific cause, etc.). ONFH in patients with alcohol consumption was observed in 20.1% (*n*=50) patients and it was 23.7% (50/211) among nontraumatic ONFH. The mean alcohol consumption in unilateral and bilateral diseases was 520 ml/week (range 260–780 ml/week) and 926 ml/week (range 350–1850 ml/week), respectively. The mean duration of alcohol ingestion in unilateral and bilateral ONFH was 75 months and 88 months, respectively. ONFH associated with alcohol or alcohol and steroid administration was seen only in male patients. Among atraumatic ONFH in male patients, 39.5% (70/177) had steroid administration, 28.24% (50/177) had alcohol intake, and 27.11% (48/177) were idiopathic, whereas, in female patients, 67.64% (23/34) had steroid administration and 14.7% (5/34) were idiopathic.

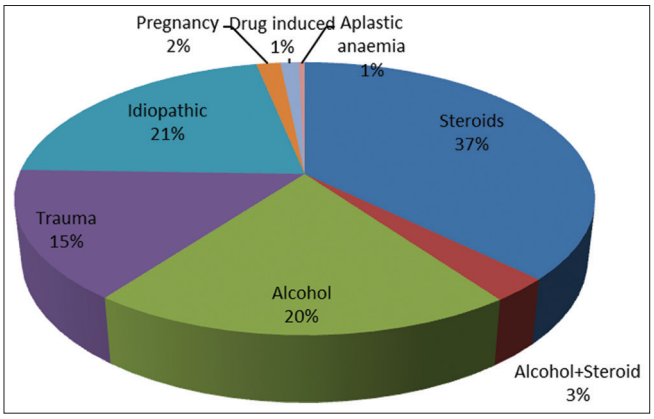

Figure 1: Pie diagram showing risk factor association in osteonecrosis of the femoral head

There was no significant association ($P > 0.05$) of gender on age-wise distribution of the disease and side involvement. Male ONFH had significant association with alcohol intake and there is no difference between male and female patients when trauma and steroid intake were considered. Regarding involvement of the disease whether unilateral or bilateral, there was no significant association of age, sex, and etiology. However, in atraumatic conditions, alcohol-induced (60% of alcohol-induced ONFH are bilateral) and steroid-induced (67.74% of steroid-induced ONFH are bilateral) ONFH were bilateral ($P < 0.05$), whereas equal incidences of unilateral (52.83%) and bilateral (47.17%) diseases were observed in idiopathic ONFH [Figure 3].

Association Research Circulation Osseous staging

Two hundred and forty-nine patients with 382 osteonecrotic hips were distributed as per their severity of involvement

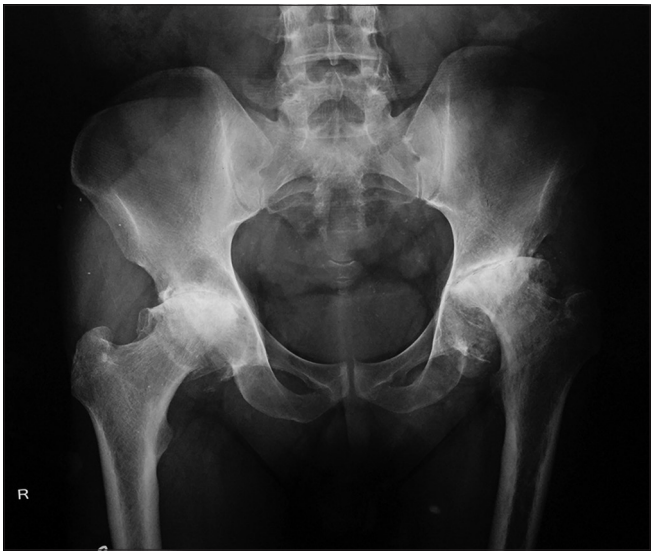

Figure 2: X-ray pelvis showing both hips anteroposterior view showing secondary arthritis of bilateral hip joints due to steroid-induced osteonecrosis of the femoral head

Table 2: Severity of the disease (association research circulation osseous staging) among patients of different etiology

Etiology	Number of patients, *n* (%)	Number of osteonecrotic hip, *n* (%)	ARCO staging, *n* (%)			
			1	2	3	4
Steroids	93 (37.3)	156 (40.84)	3 (0.79)	80 (20.94)	49 (12.83)	24 (6.28)
Alcohol + Steroid	7 (2.8)	14 (3.66)	0	5 (1.31)	6 (1.57)	3 (0.79)
Alcohol	50 (20.1)	80 (20.94)	3 (0.79)	37 (9.69)	29 (7.59)	11 (2.88)
Trauma	38 (15.3)	41 (10.73)	0 (0)	18 (4.71)	14 (3.66)	9 (2.36)
Idiopathic	53 (21.3)	78 (20.42)	5 (1.31)	37 (9.69)	22 (5.76)	14 (3.66)
Pregnancy	4 (1.6)	6 (1.57)	0	5 (1.31)	1 (0.26)	0
Drug induced	3 (1.2)	5 (1.31)	0	3 (0.79)	2 (0.52)	0
Aplastic anemia	1 (0.4)	2 (0.520	0	0	2 (0.52)	0
Total	249	382 (100)	11 (2.88)	185 (48.43)	125 (32.72)	61 (15.97)

ARCO=Association research circulation osseous staging

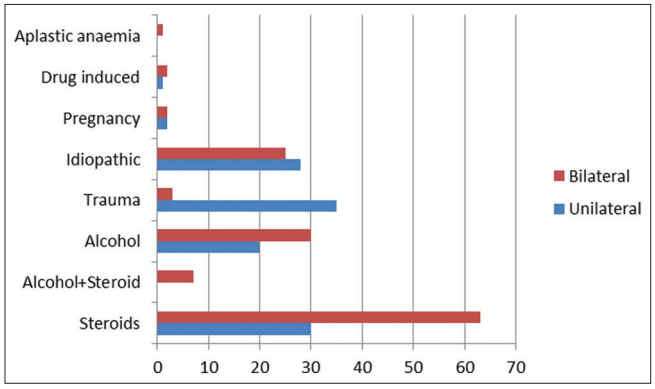

Figure 3: A bar diagram showing unilateral and bilateral involvement of the disease among different etiologies

by ARCO staging in Table 2. There were 48% (n=185) hips in Stage 2 followed by 33% (n=125) in Stage 3 and 16% (n=61) in Stage 4. Of all patients in steroid-induced ONFH, 46.79% (73/156) hips were in stage 3/4. Accordingly, 50% (40/80) in alcohol group and 46.15% (36/78) in idiopathic group were in Stage 3/4 [Table 2]. There was statistically no difference ($P > 0.05$) in ARCO staging of patients in relation to their age, sex, etiology, or side of involvement.

Harris hip score

The mean HHS was 80.97 ± 14.35 in unilateral ONFH. The mean HHS was 72.79 ± 14.43 and 80.07 ± 13.52 in more involved hip and in less involved hip, respectively, in bilateral ONFH [Table 3]. The disease severity based on ARCO staging had statistically significant correlation with HHS in unilateral ONFH (Pearson's correlation coefficient $r = -0.783$, $P < 0.01$) and more severely affected hip of bilateral ONFH patients (Pearson's correlation coefficient $r = -0.654$, $P < 0.01$), but it did not show correlation with less involved hip in bilateral diseases.

Discussion

There is no study on epidemiological profile of ONFH in Indian population. However, in the United States, 10,000–20,000 new cases of ONFH are diagnosed every year.[20,21] It has been reported that the need of arthroplasty in these patients is increasing.[22] Fukushima *et al*. from Japan[12] reported that ONFH was seen commonly in the male patients in their 40s and in females in their 30s. However, Kang *et al*. from Korea reported the peak age group to be slightly higher, i.e., 40–59 years.[13] The mean age of patients presenting with ONFH in a series by Sugano *et al*.[19] was about 44 years. Wang *et al*.[23] from China reported mean age of ONFH to be 48 years with majority of their patients were between 30 and 50 years among males (peak age 40 years) and 20 and 60 years among females (peak age 50 years). The age profile in present series (mean age 35 years) is not very different from these Asian studies. However, Cooper *et al*.[11] from

Table 3: Clinical (Harris hip score) and radiological (Association Research Circulation Osseous Staging) association among osteonecrosis of the femoral head patients

Score	ARCO staging in unilateral hip					ARCO staging in bilateral hip (more affected)					ARCO staging in bilateral hip (less affected)				
	Stage 1, *n* (%)	Stage 2, *n* (%)	Stage 3, *n* (%)	Stage 4, *n* (%)	Total, *n* (%)	Stage 1, *n* (%)	Stage 2, *n* (%)	Stage 3, *n* (%)	Stage 4, *n* (%)	Total, *n* (%)	Stage 1, *n* (%)	Stage 2, *n* (%)	Stage 3, *n* (%)	Stage 4, *n* (%)	Total *n* (%)
HHS															
<70	0	4 (1.58)	6 (2.37)	6 (2.37)	16 (6.32)	0	5 (1.98)	16 (6.32)	13 (5.14)	34 (13.44)	0	2 (0.79)	7 (2.77)	6 (2.37)	15 (5.93)
70-79	0	7 (2.77)	6 (2.37)	3 (1.19)	16 (6.32)	0	10 (3.95)	14 (5.53)	4 (1.58)	28 (11.06)	0	6 (2.37)	13 (5.14)	5 (1.98)	24 (9.49)
80-89	2 (0.79)	10 (3.95)	9 (3.58)	2 (0.79)	23 (9.09)	0	3 (1.19)	3 (1.19)	3 (1.19)	9 (3.58)	3 (1.19)	5 (1.98)	7 (2.7)	6 (2.37)	18 (7.11)
>90	2 (0.79)	18 (7.11)	5 (1.98)	1 (0.4)	26 (10.28)	0	9 (3.56)	5 (1.98)	1 (0.4))	15 (5.93)	2 (0.79)	14 (5.53)	11 (4.35)	4 (1.58)	29 (11.46)
Total	4 (1.58)	39 (15.42)	26 (10.28)	12 (4.74)	81 (32.01)	0	27 (10.67)	38 (15.02)	21 (8.3)	86 (33.99)	5 (1.98)	50 (19.76)	17 (6.72)	14 (5.53)	86 (33.99)

ARCO=Association research circulation osseous staging, HHS=Harris hip score

the UK reported the mean age of 57.6 years in their patients. It seems the disease is quite prevalent in the young Asian individuals during their active period of life.

The studies from Japan, Korea, China, and UK reported 58.28%, 77.76%, 73.91%, and 47% male patients suffering from osteonecrosis.[11-13,23] Our study had 83.1% male patients. No specific cause could be elucidated for such a difference in gender variation. However, it is quite evident that in Asian subcontinent, male patients are more commonly affected than females.[11-13] We observed 62% bilateral involvement of the hip. Sugano *et al*.[19] from Japan reported 67% bilateral ONFH. Wang *et al*. found 49% bilateral involvement in Chinese, and Kang *et al*. from Korea found 37% of their patients with bilateral disease.[13,23] This discrepancy was due to noninclusion of the asymptomatic contralateral hip.

Among different causes of ONFH, alcohol intake (20%–40%), corticosteroid therapy (35%–40%), and idiopathic (20%–40%) are common causes in the United States.[20,21] The most common cause of ONFH in Japan was corticosteroid (51%) followed by chronic alcohol intake (31%).[12] In England, the most important risk factor involved in the development of avascular necrosis of the femoral head is trauma.[24] In North Indian population, steroid intake was observed in37.3% of patients with ONFH, followed by chronic alcohol intake (20.1%), trauma (15.3%) and miscellaneous conditions. No identifiable risk was observed in 21.3% of patients.

As per Mont *et al*.,[6] corticosteroid administration is one of the most common risk factors for ONFH, but the true extent of its use that constitutes a risk factor is still under debate. Although patients receiving corticosteroids have at least one other confounding factor, multivariate analysis has suggested that corticosteroid use, especially in high doses, is an independent variable.[6] Dosages typically considered to be associated with the disease are >2 g of prednisone, or its equivalent, within a period of 2–3 months. The risk period for development of ONFH following corticosteroid therapy has been more exactly defined to be 12 months or less for the majority of patients receiving corticosteroids.[6] Even in the current study, nontraumatic ONFH associated with steroid intake was accounted for 44% patients. The mean daily intake of prednisolone in unilaterally affected patients was 28 mg (70% of patients had consumed >2 g prednisolone intake in 2 months), and with bilateral involvement, the mean intake was 28.8 mg per day (86% of patients had consumed >2 g prednisolone intake in 2 months). Fukushima *et al*.[12] had defined steroid induced ONFH by a history of taking 1800 mg prednisolone or an equivalent over 4 weeks or by a history of continuous corticosteroid medication for at least 2 months. In the study of Fukushima *et al*.,[12] systemic steroid administration (steroid induced) accounted for 51%. Thus, there is not much difference in this profile. However, this is in contrast with the study by Kang *et al*.[13] where only 14.6% were related to steroid intake. Although these data were comparable to those reported previously in Korea,[13] they are quite different from France where 30% ONFH were secondary to steroid intake.[13]

Alcohol intake is another important factor contributing to ONFH. Mont *et al*.[6] reported a clear dose–response relationship in patients with ONFH secondary to alcohol intake, with relative risks of 3.3, 9.8, and 17.9 for current drinkers consuming <400, 400–1000, and ≥1000 ml/week of alcohol (ethanol), respectively. In our study, ONFH with associated alcohol intake was seen in 20.1% of patients, and in nontraumatic ONFH, it was observed in 24% of patients. The mean alcohol intake in patients with unilateral involvement is 520 ml/week, and in patients with bilateral involvement the mean intake is about 926 ml/week. The mean duration of intake of alcohol in unilaterally affected patients is 75 months; in patients with bilaterally involved patients, mean duration is about 88 months. Though there is difference, it is not significant. In the study of Fukushima *et al*.,[12] the habitual use of alcohol accounted for 31%. Thus, there is not much difference in the etiologic profile secondary to alcohol intake. In the study of Kang *et al*.,[13] 32.4% of patients had history of alcohol abuse. The proportion of alcohol induced ONFH in our study is comparable to the above mentioned studies. In the present study, all patients with ONFH secondary to alcohol intake were males. This is because of the well accepted social characteristics of Indian culture where alcohol intake is not common among females.

In the current study, 21.3% patients were idiopathic, where there was no identifiable risk found. In the study of Fukushima *et al*.,[12] idiopathic ONFH accounted for 15% of total cases. Thus, there is not much difference in the distribution of this etiological profile.

ARCO's international classification[25] of osteonecrosis has been accepted as a standard protocol for clinical research. Hence, we had used ARCO staging for quantification of the disease. There were 43 of 81 hips (53%) in stage 1 or 2 in unilateral ONFH and 54 of 172 hips (31%) in Stage 1 or 2 in bilateral ONFH. This study shows that patients with unilateral involvement presented at an early stage of the disease whereas patients with bilateral involvement presented at an advanced stage. A possible explanation for advanced disease in bilateral ONFH may be explained on aggressively progressive nature of bilateral disease compared to unilateral so that patients have less time in seeking health care. There were 48% hips in Stage 2 followed by 33% in Stage 3 and 16% in Stage 4. Of all patients in steroid-associated ONFH, 46.79% hips were in Stage 3/4. Accordingly, 50% in alcohol group and 46.15% in idiopathic group were in Stage 3/4. North Indian patients usually present in Stage 2 or 3 (87%). Almost 50% of hips were in advanced stage of the disease in steroid associated ONFH, alcohol associated ONFH, and idiopathic ONFH.

This study confirmed that ARCO staging has no association with age, sex, etiology, or unilateral/bilateral disease.

However, the functional status of the hip as evaluated by HHS shows high correlation with ARCO staging in unilateral ONFH and more severely affected bilateral ONFH. ARCO staging and HHS have no correlation in bilateral cases with less involved hip. The functional part of HHS varies in cases with bilateral involvement. In patients with bilateral ONFH, some patients have complaints with one side and they are asymptomatic on the other side, some patients have one hip being more symptomatic than the other, and in some patients, both hips are equally affected. Hence, in the current study, in patients with bilateral involvement, both the hips were scored individually. There was significant correlation found between HHS and the stage of disease. Patients with early stage of disease have good to excellent hip functions in unilateral ONFH. As the disease progresses, the functional status of the hip tends to decline.

Conclusion

Steroid administration (37.3%) is most commonly observed cause among North Indian patients suffering from ONFH followed by chronic alcohol intake (20.1%) and trauma (15.3%). No identifiable risk was observed in 21.3% of patients. The steroid- and alcohol-associated ONFH are usually bilateral, whereas idiopathic ONFH has equal incidence of unilateral and bilateral involvement.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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