

MRI IN DIAGNOSIS AND EVALUATION OF AVN OF FEMORAL HEAD IN SICKLE CELL DISEASE AND COMPARISON WITH PLAIN X RAYSatyabhuwan Singh Netam¹, Rajesh Singh², Sumit Bichpuria³, Sanjay Kumar⁴, Vishal Jain⁵**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: OBJECTIVE: To assess the role of MRI in cases of AVN of femoral head in sickle cell disease in comparison to x-ray. **MATERIAL AND METHODS:** 55 patients (110 hip joints) who were suffering from sickle cell disease (Confirmed by HB electrophoresis) & with complain' of pain in one or both hip joints, were examined by plain x-ray and 0.2 tesla MRI, using T1W (350ms/17ms), T2W (2200ms/110ms) and STIR (4000ms/80ms/90) sequences in axial, coronal and sagittal planes. **RESULTS:** study comprised of 55 patients suffering from sickle cell disease (110 hip joints). 49 of these patients confirmed changes relative to avascular necrosis of femoral head. Out of which 30 patients had bilateral involvement. 19 patients showed unilateral hip joint involvement. Therefore 79 femoral heads out of 110 hip joints showed changes of avascular necrosis in MR. Fatty marrow conversion, neck widening, marrow edema, joint effusion, abnormal signal like; band pattern, ring pattern. homogenous and inhomogenous pattern are MRI characteristics of AVN. Plain x-ray shows changes of AVN in 59 hip joints. Sclerosis, Mottling, flattening, Perthes like lesion and Destruction were the main findings in x- ray in our study. **CONCLUSION:** MRI turns out to be most sensitive for diagnosis and determination of extent of disease process. MR imaging has high degree of sensitivity in early stages of AVN as compared to x-ray. MR imaging also helps to evaluate asymptomatic contralateral hip in single setting as there is increased chances of opposite hip getting involved in AVN in sickle cell disease.

KEYWORDS: AVN of femoral head, MRI, Sickle cell disease, X-ray.

INTRODUCTION: Avascular necrosis (AVN) or osteonecrosis is a disease resulting from the temporary or permanent loss of blood supply to the bones. Sickle cell disease is most common cause of AVN in our state. MRI is the most sensitive method for diagnosing avascular necrosis in the early stages. Unlike x-ray, bone scan, and CT scan, MRI detects chemical changes in the bone marrow. MRI provides the doctor with a picture of affected area and bone rebuilding process. In addition MRI may show diseased areas that are not yet causing any symptoms. High soft tissue contrast, the ability to image in multiple planes, the ability to manipulate tissue contrast, and high sensitivity to marrow-based pathologic condition gives MRI significant advantage over other imaging techniques.

MATERIAL AND METHODS: Our study comprised of a total of 55 patients (110 hip joints) from both in and out patient department in Dr B. R. Ambedkar Memorial Hospital, Raipur (C.G.). Local resident of our state, who are suffering from sickle cell disease (Confirmed by HG electrophoresis) and with complaint of pain in one or both hip joints were evaluated by MRI. MRI is performed in Siemens, magnetom concerto 0.2 tesla permanent magnet MRI machine by using standard body coil for acquisition of images. Axial, coronal, and sagittal planes were obtained using multi-slice and multi-echo sequences with thickness of 4mm.

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The data acquisition was done using a matrix of 256 x 256.

SCANNING PARAMETERS:

Spine echo Sequences	0.2 T SIEMENS PERMANENT MAGNET		
	TR(m sec)	TE(m sec)	TI (m sec)
Ti	350-450	17-25	
T2	2200-3500	110-120	
STIR	4000	80-90	90

Protocol used for scanning:

1. T1WI and T2 WI spin echo, coronal, sagittal and axial scans of bilateral hip joint were done using body coil.
2. STIR sequences were done in coronal plane.

RESULTS: This study comprised of 55 patients suffering from sickle cell disease (110 hip joints), 49 of these patients confirmed changes relative to avascular necrosis of femoral head of which 30 patients had bilateral involvement whereas only 19 showed unilateral involvement. Total number of femoral head showing changes of AVN in MR imaging were 79 as compared to 59 true positive heads in X-Ray. Most of the hip joint with AVN show changes related to stage I with 30.3% followed by stage II and III with 22.8% each. Findings like sclerosis, mottled appearance, and perthes like lesion are usually associated with milder symptoms and were most commonly seen in younger age group (11 – 20 yrs.) while destruction, necrosis and arthrosis are associated with severe symptoms and seen in mid age group (21 – 30 yrs.) (Table no-1). Fatty marrow conversion comprised of 72% of all the affected hips with highest percentage seen in stage III AVN (88.9%). Femoral neck widening was seen in 16.5% cases with most commonly involving hip joints in stage IV (52.6%).

Amongst four patterns, band pattern was most commonly involving stage I and II, while ring pattern showed predominance in stage III and in-homogenous pattern in stage IV (Fig-1). Most common location (Segment) of AVN lesion in femoral head was superomedial aspect (50.6%) followed by superolateral aspect (32.9%). Most of the femoral head in the study showed less than 25% involvement. Similar pattern was seen in stage wise distribution except in stage IV where most of the femoral head showed more than 75% involvement. Marrow edema was the most common MR finding in whole study and it predominantly involved stage III and IV (100%). Joint effusion (Fig- 2) was seen in almost all the stages of AVN but most strikingly seen in stage IV cases (68.4%). Stage II came out as the most commonly involved stage with finding of double line sign with 77.8% hip joints followed by stage III with 66.7%.

Collapse of articular surface of femoral head was the exclusive finding of later stage of AVN (stage IV) with 100%. Joint space narrowing and acetabular involvement (Fig- 3) are exclusive for later stages of disease especially stage IV but also seen in stage III after the collapse of articular surface (Table no-2). Reduction in joints space, Sclerosis, perthes like lesions, crescent sign, mottling, Flattening of contour of head of femur, Acetabular changes and Total destruction of head of femur are the major x-ray findings (Fig -4). Sensitivity of X-Ray in diagnosing AVN in early stages (Stage I and II) is less than that of MR imaging i.e.33% and 77.8%, but in late stages (Stage III and IV) both show equal sensitivity i.e. 100% (Table no-3).

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COMPARISON OF PLAIN X-RAY WITH MR IMAGING: Because of absence of histological correlation MR findings were considered as the modality of choice for making final diagnosis of AVN and radiographs were compared with the findings of MR imaging using standard formulae to arrive at the test characteristics. **The criteria used were as following:-**

True Positive: Positive AVN changes + indeterminate AVN changes in X-ray confirmed by MR imaging as positive.

True Negative: No changes of AVN in X-ray confirmed as Negative by MR imaging.

False Positive: Positive AVN changes + indeterminate changes in X-ray confirmed by MR imaging as Negative.

False Negative: No changes of AVN in X-ray confirmed by MR imaging as Positive.

	TEST CHARACTERISTICS	X-RAY RESULTS N = 61/110
1.	SENSITIVITY	76.6
2.	SPECIFICITY	94
3.	ACCURACY	81.8
4.	POSITIVE PREDICTIVE VALUE	96.7
5.	NEGATIVE PREDICTIVE VALUE	63.3
6.	TRUE POSITIVE	59
7.	TRUE NEGATIVE	31
8.	FALSE POSITIVE	2
9.	FALSE NEGATIVE	18

DISCUSSION: In the detection of avascular necrosis of the femoral head in sickle cell disease, the advantages of magnetic resonance imaging compared with other imaging modalities are many: it is non-invasive, ionizing radiation is not used, and it allows exact determination of the location and extent of abnormality in the femoral head. Furthermore, magnetic resonance imaging has been shown to have the greatest sensitivity of all radiographic imaging modalities. Cortical bone is seen as a signal void and appears as a black line. The distribution of fatty marrow can be assessed with anatomical precision on T1-weighted images, Because of its short T1 relaxation time, fat has a high signal intensity on T1-weighted images. Increased contrast between fatty and hematopoietic marrow can be obtained with techniques that are sensitive to chemical shifts.

Coronal-plane imaging is favored for evaluating avascular necrosis of the femoral head because it allows the best assessment of the weight-bearing surface. Only T1-weighted images are necessary to exclude avascular necrosis: T2- weighted images increase diagnostic specificity. The classic characteristic of avascular necrosis of the femoral head on a magnetic resonance image is a decrease in the intensity of the signal (normally high) of the marrow of the femoral head. The unique histopathological feature of established avascular necrosis is the reactive interface between necrotic and living bone. The most specific characteristic of avascular necrosis on a magnetic resonance image is the T2-weighted image of this reactive interface. A so-called 'double-line sign' is seen: a peripheral low-signal rim with a high-signal inner border. Over the years, numerous different classification systems have been developed to evaluate patients with femoral head osteonecrosis. However, for the purpose of this study, we use the stages of ARCO classification.

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Staging system based on the consensus of the Subcommittee of Nomenclature of the International Association on Bone Circulation and Bone Necrosis (ARCO)

Stage	Clinical and Laboratory Findings
Stage 0	<ul style="list-style-type: none"> • No symptoms Normal radiographs and MR images Osteonecrosis at histology
Stage I	<ul style="list-style-type: none"> • Presence or absence of symptoms Normal radiographs Abnormal MR images Osteonecrosis at histology
Stage II	<ul style="list-style-type: none"> • Symptoms Trabecular bone changes on radiographs without subchondral bone changes. Preserved joint space Diagnostic MR findings
Stage III	<ul style="list-style-type: none"> • Symptoms Variable trabecular bone changes with subchondral bone fracture (crescent sign and/or subchondral bone collapse) Preserved shape of femoral head and preserved joint space Sub-classification based on extent of crescent, as follows: Stage III a: Crescent is less than 15% of the articular surface Stage III b: Crescent is 15%-30% of the articular surface Stage III c: Crescent is more than 30% of the articular surface
Stage IV	<ul style="list-style-type: none"> • Symptoms Altered shape of femoral head with variable joint space Sub-classification depends on the extent of collapsed surface, as follows: Stage IV a: Less than 15% of surface is collapsed Stage IV b: Approximately 15%-30% of surface is collapsed. Stage IV c: More than 30% of surface is collapsed.

The severity of hip symptoms and gait generally corresponded with that of the radiological lesions. In the present study there was a relationship between the type of radiographic lesion and the age of the patient. The younger patients tended to have the milder forms of the disease (Subchondral sclerosis and Perthes-like lesions), whereas disease of higher age group tended to be of the type with destruction or diffuse necrosis. Maximum number of cases in our study presenting with sclerosis, mottling and perthes like lesion belonged to younger age group (11–20 yrs.) whereas lesion like destruction and necrosis belonged to mid age group (21–30 yrs.). These findings were consistent with those previously experienced by C. G. Iwegbu et al 1985.¹ and Lee RE et al 1981.²

Present study revealed the presence of fatty conversion in the marrow of femoral head and intertrochanteric marrow which was most commonly involving the heads in stage III with 88.9% cases showing this finding followed by stage II (77.8%) and stage I (71%). Overall among the involved femoral heads with AVN nearly 72% cases were positive for this finding.

Other studies showing similar femoral head involvement pattern are the one from Donald G. Mitchell et al 1987³ were this very finding involved nearly 80% of cases of avascular necrosis. David J.

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Sartoris et al 1987.⁴ also noticed early conversion of normal marrow signal to fatty marrow in the patients with ischemic necrosis and remarked it to be caused by diminished vascularity. Similar study and findings were also experienced by Koo, Kyung-hoi et al 1999.⁵ and Beverly G. Coleman et al 1988.⁶

In present study neck widening was seen in 16.5% cases with most commonly involving stage IV (52.6%) followed by stage III (11.1%). Although this is the finding common before the fusion of capital femoral epiphysis associated with diffuse flattening of femoral head, in our study it was seen in age ranging from 10 – 41yrs. Presentation of this finding in middle age cases might be due to commencement of necrotic process of femoral head in their childhood. Involvement of immature capital femoral epiphysis leading to neck widening has been reported by S. V. Pathak et al 2006.⁷

Four pattern of femoral head involvement in avascular necrosis were studied in our work and were classified on the basis of stage in which band pattern was most common in stage I with 83.3% cases followed by stage II where 72.2% cases showed band pattern involvement. Ring pattern was common in stage III (77.8%) AVN and inhomogenous pattern was common in stage IV (79%). None of the stage IV femoral head showed band pattern. Similar stage wise distribution of pattern was also observed by Takashi Sakai et al 2000.⁸ and Vijay M. Rao et al 1988.⁹ Pattern based study was also performed by William G. Totty et al 1984.¹⁰ and found no correlation between pattern of involvement and stage of the disease and Thruman Gillespy iii et al 1986.¹¹ interpreted uncertainty of significance of these different patterns.

In present study, femoral head was divided into four quadrants and the involvement of quadrants were evaluated and found that it was superomedial aspect which was most commonly involved in each stage and also in whole study. Superomedial aspect involvement comprised of 50.6% of all the cases similar involvement of superomedial aspect was also seen by J. P. Hauzeur et al 1989.¹² and Yoshio Takatori et al 1992.¹³ although other author simply considered anterosuperior aspect to be most common in showing involvement rather than dividing it into medial and lateral.

They include Helena Gabriel et al 1994.¹⁴ and James J. Guerra et al 1995.¹⁵ Michael A. Mont.¹⁶ also experienced anterolateral region to be most commonly involved but also remarked that no area is necessarily spared. According to our findings the maximum numbers of cases in whole study shows 0 -25% involvement of femoral head. Similar pattern of percentage of head involvement is also seen in stage I, II and III individually. Only stage IV femoral head involvement shows 75-100% involvement pattern as the most common.

Sebastian F. Cherian et al 2003.¹⁷ also emphasized on the importance of percentage of femoral head involved with AVN and concluded it to be one of the important and reliable finding for evaluating the extent of avascular necrosis of the femoral head and thus the outcome. Jonathon A. Lee et al 2002.¹⁸ also came up with similar results and conclusion. Beltran et al 1990.¹⁹ in his study showed that number of hips undergoing collapse was directly related to percentage of femoral head involved. Larger is the head involvement more is the chances of collapse in AVN.

In the current study we found that marrow edema involving the head and neck region of femoral head was not the prominent finding of initial stages of AVN but it developed in later stages with the increased severity of the symptoms and in radiologically pre and post collapse stages (Stage III and IV). But as the patient is likely to be evaluated for AVN after the onset of pain and other symptoms, marrow edema becomes evident in first MR scan and hence it is counted as finding of an early ischemic change. Our study showed marrow edema as one of the most common finding comprising of 77.2% of all the cases. All the cases of stage III and IV (100%) showed this finding

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whereas only 83.3% cases from stage II and 37.5% cases of stage I revealed this finding. Similar observations were reported by Satoshi Lida et al 2000.²⁰ Hirata Soichiro et al.²¹ emphasized that AVN should be considered as a differential diagnosis when MR images exhibits diffuse marrow edema pattern. Some other authors with similar findings are Y. M. Kim et al 2000.²²; Neuhold A. et al 1993.²³ and Huang GS et al 2003.²⁴ in a previous MR imaging study of marrow infarct in 11 patients with sickle cell anemia, Rao et al 1986.²⁵ showed a strong direct correlation between marrow edema and pain.

In our study there was regular increase in the number of cases showing joint effusion depending upon the stage with stage IV showing maximum percentage of cases involved (68.4%) followed by stage III, II and then I. among all the hips confirmed to have AVN only 48.1% cases show this finding. Although Huang GS et al 2003.²⁴ showed stage III as the commonest stage to show joint effusion, whereas Beverly G. Coleman et al 1988.⁶; David J. Sartoris et al 1987.⁴ and Donald G. Mitchell et al 1987.³ observed effusion in advanced stages of AVN because of cartilage destruction and collapse of articular surface of femoral head acting as a synovial irritant and inducing joint effusion.

Considered to appear later in the disease process and remarked as the radiologically pre collapse stage. This sign has been described as a rim of high signal inside the low signal intensity margin on T2 sequences. It is believed to be the reactive interface between the hyperemic and ischemic bone thus helping to differentiate AVN from diffuse bone marrow edema. This sign was present in 77.8% hips in stage II representing the most commonly involved stage followed by stage III with 66.7% hips. Overall it comprise of 40.5% hips from those under study David J. Sartoris et al 1987.⁴ and Beverly G. Coleman et al 1988.⁶ also found similar findings and considered it to be pathognomic of avascular necrosis. Other author like Helena Gabriel et al 1994.¹⁴; John V. Zurlo et al 1999.²⁶ and Jenő L. Sebes 1989.²⁷ also agreed on the above discussion.

As per the natural history of avascular necrosis of femoral head in sickle cell disease there is increased likeliness of developing collapse if any treatment is not initiated in the early stages of disease. In our study collapse was the exclusive entity of stage IV of AVN and variable percentage of articular surface involvement by collapse was seen in all the cases of stage IV (100%). Collapse comprised of 24% of all the hips showing changes of AVN. Hernigou et al 2006.²⁸ also came up with similar outcome and quoted that "Untreated asymptomatic osteonecrosis of the femoral head in patients with sickle cell disease has a likelihood of progression to pain and collapse". Beltran et al 1990.¹⁹ in his study showed that number of hips undergoing collapse was directly related to percentage of femoral head involved. Larger is the head involvement more is the chances of collapse in AVN.

After the collapse of articular surface of femoral head there is synovial irritation causing joint effusion but later in the stage there is reduction in joint space and acetabular change seen in form of altered signal in MR imaging suggestive of marrow edema and ischemic changes and changes related to rapidly progressive and destructive osteoarthritis. In present study both the changes are seen near exclusively in later stage IV of AVN with few exceptions. 84.2% of cases of stage IV AVN show findings suggestive of reduction of joint space and 47.4% cases of stage IV show changes in acetabulum. Severe arthrosis was the feature of stage IV AVN though stage III also shows changes related to joint space narrowing and acetabular involvement. Similar interpretations were made by Siegfried Hofmann et al.²⁹; SV Pathak et al 2005.⁷ and T. Sakai et al.⁸

Early diagnosis and therapy are crucial for the management of avascular necrosis. Our study firmly establishes the ability of MR to allow early detection and staging of AVN of femoral head even

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in radiologically negative patients. By plain X-Ray we were able to detect only 59 hips showing one or the other finding of AVN as compared to 79 hips detected by MR imaging. Two X-Rays with positive findings showed no abnormality on MR. Most of the undiagnosed hips by X-Ray were from stage I and some from stage II. X-Ray and MR both showed equal ability to detect hips involved in Stage III and IV of AVN (100%). This confirms the earlier reports of others who have described MR as being more sensitive than plain radiography like the work done by A. Banerjee et al 1988³⁰; David J. Sartoris et al 1987.⁴; Beverly G. Coleman et al 1988.⁶ and William G. Totty et al 1984.¹⁰ in addition to above finding Donald G. Mitchell et al 1987.³ also stated that MRI is a promising modality for characterizing the extent and severity of the necrotic process and its complication.

CONCLUSION: Early fatty marrow conversion has been attributed to decreased vascularity of proximal femur thus considered as one of the earliest finding of avascular necrosis in sickle cell disease. Sclerosis, mottled appearance and perthes like lesion are seen in younger patients whereas destruction, necrosis and arthrosis are seen in mid and old age patients in x-ray. The stage and severity of MR lesion vary widely and appears to be unrelated to age of patients but related to age at the onset of hip symptoms. No correlation has been found among specific MR pattern and stage of disease. Larger is the percentage of head involved by the lesion more are the chances of collapse of articular surface of femoral head. Marrow edema is the finding of later stage when head show signs of necrosis and collapse. Severity of pain is closely related to degree of bone marrow edema and amount of joint effusion causing stretching of capsule. Double line sign considered to be highly specific for avascular necrosis occurs later in disease process after the start of osseous repair and helps to differentiate AVN from transient bone marrow edema. Untreated asymptomatic osteonecrosis of the femoral head in patients with sickle cell disease has a likelihood of progression to pain and collapse. MR imaging has high degree of sensitivity in early stages of AVN as compared to x-ray. MR imaging also helps to evaluate asymptomatic contra-lateral hip in single setting as there is increased chances of opposite hip getting involved in AVN in sickle cell disease.

RADIOGRAPHIC CHANGES	No. of Hips	AGE RANGE						SYMPTOM SEVERITY
		0 - 10	11 - 20	21 - 30	31 - 40	41 - 50	51 - 60	
SCLEROSIS	26	1	8	10	3	3	1	Minimal
MOTTLING	19	1	7	6	2	2	1	Minimal
PERTHE'S LIKE LESION	1	0	1	0	0	0	0	Mild to moderate
CRESCENT SIGN	10	1	2	3	2	1	1	Mild to moderate
FLATTENING	10	0	3	4	2	1	0	Mild to moderate
TOTAL DESTRUCTION	10	0	3	5	1	1	0	Moderate to severe
NECROSIS	11	0	3	5	1	2	0	Moderate to severe
ACETABULAR CHANGES	6	0	2	4	0	0	0	Moderate to severe
MIGRATION	7	0	2	4	1	0	0	Moderate to severe
PERIOSTEAL REACTION	7	0	3	3	0	0	1	Moderate to severe

Table 1: X-ray characteristic with age wise distribution

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MR FINDINGS		STAGE I		STAGE II		STAGE III		STAGE IV		TOTAL	
		No.	%	No.	%	No.	%	No.	%	No.	%
FATTY MARROW CONVERSION		17	71	14	77.8	16	88.9	10	52.6	57	72.1
NECK WIDENING		0	0	1	5.5	2	11.1	10	52.6	13	16.5
PATTERN	HOMOGENOUS	0	0	2	11.1	1	5.6	2	10.5	5	6.3
	INHOMOGENOUS	0	0	2	11.1	2	11.1	15	79	19	24
	RING	4	16.7	1	5.6	14	77.8	2	10.5	21	26.6
	BAND	20	83.3	13	72.2	1	5.6	0	0	34	43
SEGMENT	SUPERO-LAT	4	16.7	7	38.9	7	38.9	8	42.1	26	32.9
	SUPERO-MED	8	33.3	10	55.6	11	61.1	11	57.9	40	50.6
	INFERO-MED	0	0	1	5.5	0	0	0	0	1	1.3
% OF HEAD INVOLVED	0 - 25%	6	25	12	66.7	11	61.1	0	0	29	36.7
	25 - 50%	3	12.5	5	27.8	4	22.2	6	31.6	18	22.8
	50 - 75%	0	0	0	0	3	16.7	5	26.3	8	10.1
	75 - 100%	1	4.2	0	0	0	0	8	42.1	9	11.4
MARROW EDEMA		9	37.5	15	83.3	18	100	19	100	61	77.2
JOINT EFFUSION		8	33.3	8	44.4	9	50	13	68.4	38	48.1
DOUBLE LINE SIGN		4	16.7	14	77.8	12	66.7	2	10.5	32	40.5
JOINT NARROWING		0	0	0	0	4	22.2	16	84.2	20	25.3
COLLAPSE		0	0	0	0	0	0	19	100	19	24
ACETABULAR INVOLVEMENT		1	4.2	0	0	2	11.1	9	47.4	12	15.2

Table 2: MR characteristics with staging

Sl. No.	STAGE	No. of HIPS	X-RAY	%	MRI	%
1.	STAGE I	24	8	33.33	24	100
2.	STAGE II	18	14	77.8	18	100
3.	STAGE III	18	18	100	18	100
4.	STAGE IV	19	19	100	19	100

Table 3: Sensitivity of MRI and X-Ray in various stages of AVN

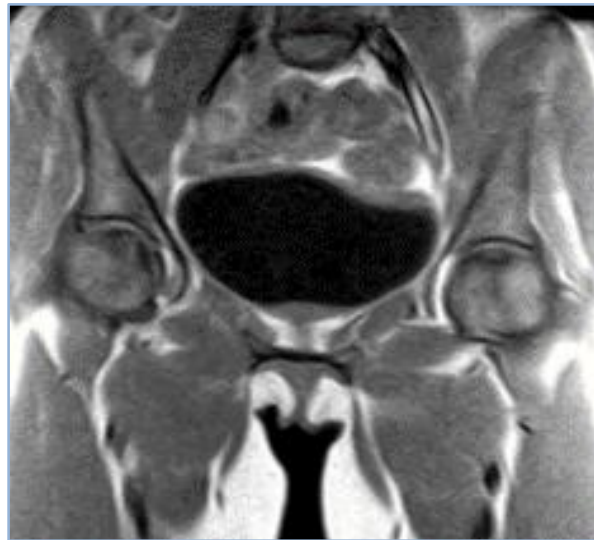


Fig. 1

Fig- 1: Coronal TIWI image showing avascular necrosis involving bilateral femoral head with hypointense band pattern on right side and ring pattern on left side

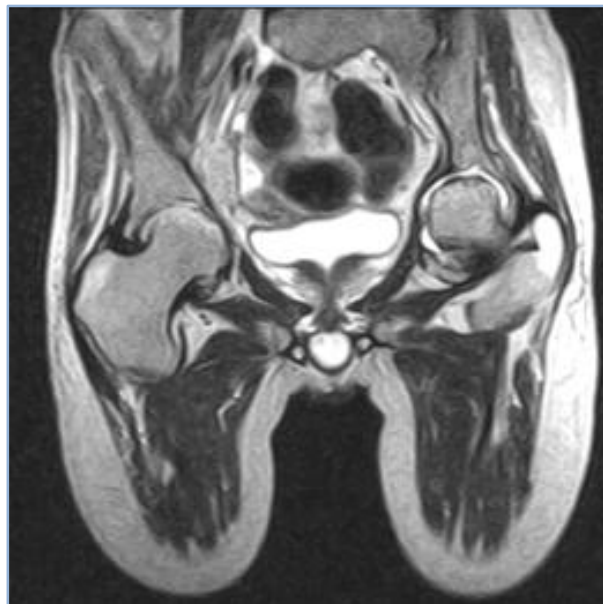


Fig. 2

Fig -2: Avascular necrosis of femoral head showing alteration of signal, joint effusion and surface irregularities. Signal changes are also seen in marrow of greater trochanter apophysis.

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Fig. 3

Fig- 3: Coronal T2WI image showing bilateral femoral head destruction with cephalad migration including acetabular changes related to AVN



Fig- 4: Bilateral avascular necrosis changes- Destruction of articular surface with collapse and flattening, mottled appearance, marked reduction in joint space leading to acetabular changes.

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