ISSN: 2457-0400

Impact Factor: 6.711

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

www.wjahr.com

Volume: 9, Issue: 12

Page N. 62-74

Year: 2025

Original Article

Coden USA: WJAMA3

SHOULDER JOINT INVOLVEMENT BY AVASCULAR NECROSIS OF THE HUMERAL HEAD IN SICKLE CELL DISEASE IN BASRAH

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Article Received: 30 October 2025 **Article Revised:** 19 November 2025 **Article Published:** 01 December 2025

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DOI: https://doi.org/ 10.5281/zenodo.17748527

How to cite this Article: *1Dr. Khaldoon H. Qasim, 2Dr. Mubder A. Mohammed Saeed, 3Dr. Basim Abdulkareem Abdulhassan Alhijaj (2025). Shoulder Joint Involvement By Avascular Necrosis Of The Humeral Head In Sickle Cell Disease In Basrah. World Journal of Advance Healthcare Research, 9(12), 62–74.

ABSTRACT

Background: Sickle cell disease is a common hemoglobinopathy in Iraq generally and Basrah specifically. It is associated with various musculoskeletal complications, particularly avascular necrosis of the hip and the shoulder joints. Although avascular necrosis is a known complication of sickle cell disease, data specifically addressing humeral-head involvement are limited. **Objectives:** To determine the prevalence, clinical features, radiological findings, and outcomes of shoulder avascular necrosis in patients with sickle cell disease presenting with shoulder pain in Basrah city. **Methods:** A Randomised prospective observational cohort study with baseline cross-sectional assessment conducted on 102 sickler patients with shoulder pain attending the Basrah Hereditary blood disease Center, Al-Sayyab Teaching Hospital and Basrah Teaching Hospital (joint arthroplasty center) from (April 2024 to May 2025). All patients underwent clinical evaluation, radiography, and selective computed scan and magnetic resounce imaging. Pain severity was assessed using the Visual Analog Scale, shoulder function was evaluated with Oxford shoulder score OSS (the old version), and functional outcomes were documented. **Results:** Avascular necrosis of the shoulder was identified in 21 patients (20.6%). The radiological staging shown by magnetic resonance imaging revealed 4 (19.04%) in stage I, 6 (28.57%) in stage II, 8 (38.09%) in stage III, and 3 (14.28%) in stage IV. Moreover, avascular necrosis was significantly associated with chronic pain (>1 month), severe pain (Visual Analog Scale 7–10), low Oxford scores, tenderness, muscle wasting, deformity, and limited movement (p value < 0.01). Additionally, sclerosis and humeral head collapse were prominent radiographic findings. At follow-up, of non- avascular necrosis patients 95.1% showed improvement in pain and function, compared to only 38.1% of avascular necrosis patients, worsening of symptoms occurring exclusively in the avascular necrosis group (23.8%). Lastly, rehospitalisation for vaso-occlusive crisis was also more frequent in avascular necrosis patients (95.2% versus 53.1%; p value = 0.001). **Conclusions:** Shoulder avascular necrosis is a frequent and disabling complication of sickle cell disease in Basrah. It is associated with distinct clinical and radiological features, prolonged pain, severe functional impairment, and poorer prognosis compared to Vasooclussive crisis-related shoulder pain. Early recognition through radiology and magnetic resonance imaging, combined with timely intervention, is essential to reduce morbidity and improve quality of life.

KEYWORDS: Avascular, Basrah, Heah, Necrosis, Sickle.

1. INTRODUCTION

Sickle Cell Disease (SCD) is a hereditary condition (autosomal recessive) caused by the substitution of valine for glutamic acid at the sixth position in the beta-peptide chain of the hemoglobin molecule.[1] Due to the spatial configuration change of the helical hemoglobin structure in low oxygen conditions, red blood cells change from their typical biconcave compressible shape to a sickle shape that is less deformable to be squeezed through the tiny capillary diameter in various

microcirculatory sites throughout the body.[1] This hemoglobinopathy's clinical consequences are mainly caused by persistent hemolysis and vaso-occlusion, which leads to endothelial damage and injuries from ischemic reperfusion.[2]

After the spleen, bones are the second most commonly affected organs by Sickle Cell Disease.[3] The most common skeletal manifestation of SCD is painful vaso-occlusive crises, which often resolve spontaneously within a few days without leaving permanent sequelae in most cases.[1] Locally there has been limited research on bony involvement in SCD, characterised mainly by osteonecrosis and osteomyelitis.[3] Despite the significance of osteoarticular involvement in SCD, these problems are still little recognised in terms of their pathophysiology.[3]

There are two primary categories of bone changes in SCD: those linked to ischemia events such as bone necrosis and its consequences, and those linked to bone marrow hyperplasia brought on by chronic anaemia.[5] Although the exact causes of the bone marrow's susceptibility to microvascular occlusion are unknown, bone marrow hypercellularity, which reduces blood flow and causes localised hypoxia, may play a role.[6-7]

Sickle cell disease can significantly affect the shoulder, most commonly through avascular necrosis (AVN) of the humeral head, which is the ball portion of the shoulder joint. This condition, also known as osteonecrosis, occurs when the blood supply to the bone is reduced, leading to bone death and potential joint damage. The shoulder can also be affected by other complications of sickle cell disease, such as painful crises, synovitis, and even dislocations.[8]

The aim of the study is to investigate the prevalence, clinical features, pathophysiology, diagnostic modalities, and management strategies of shoulder joint involvement by avascular necrosis in patients with sickle cell disease in Basrah, to improve patient's outcomes.

2. PATIENTS AND METHODS

First of all, ethical approval was granted from the Ministry of Higher Education, University of Basrah, College of Medicine, Research Ethics Committee and the Ministry of Health and Environment, Basrah Health Directorate, Training, and human resources center research unit. Informed consent from each participant was taken and all personal information was kept anonymous.

This is A Randomized prospective observational cohort study with baseline cross-sectional assessment conducted at Basrah Teaching Hospital for patients with painful shoulders and sickle cell disease (SCD) attending to Basrah Hereditary blood disease Center and, AL-Sayyab Teaching Hospital and Basrah Arthroplasty Center. The study incorporates a quantitative research questionnaire to assess functional impact and quality of life. The study period extends from the 1st of April 2024 to the 1st of May 2025. A total of 102 patients with SCD and shoulder pain aged from 5-65 years were recruited. The included patients were those who diagnosed with sickle cell disease (SCD) and confirmed by hemoglobin electrophoresis, aged between 5-65 years, having shoulder pain for ≥ 2 weeks and willing to participate and provide informed consent. While the excluded patients were those with previous shoulder trauma or surgery, patients with other inflammatory or autoimmune joint diseases (e.g., rheumatoid arthritis, lupus) or those with neuromuscular disorders affecting shoulder movement.

Follow-up frequencies were at 2 weeks, 3 months and 6 months.

Data were collected using a questionnaire and structured clinical assessments, including; patients' sociodemographic information such as age, gender and SCD genotype. Patient clinical characteristics such as frequency of vaso-occlusive crises in the past year, hemoglobin levels and hydroxyurea use, presence of other SCD complications (e.g., osteonecrosis of the hip, chronic pain, osteomyelitis). Furthermore, the questionnaire includes questions about shoulder pain and functional assessment such as; Oxford Shoulder Score (0-60) (the old version) to assess pain and daily activity limitations, VAS (is a 0 to 10 numeric rating scale used to measure pain intensity and quantitative research questionnaire assesses pain severity, daily activities, and treatment response. In addition to laboratory investigations and Imaging studies including; x-ray (All patients underwent plain radiography to assess osteonecrosis, osteoarthritis, and joint space narrowing), MRI (when clinically indicated) to evaluate avascular necrosis (AVN), rotator cuff tears, and effusions, CT scan to evaluate the extent of the condition and for planning of surgery and ultrasound for soft tissue abnormalities (e.g., synovitis, effusions).

The data analyzed using Statistical Package for Social Sciences (SPSS) version 26. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Independent t-test (two tailed) was used to compare the continuous variables according to mortality. Chi square test was used to assess the association between mortality and certain information, while functional improvement was evaluated by the Oxford shoulder score (OSS) using paired t-test. P-value < 0.05 considered statistically significant.

3. RESULTS

The study population consisted of 102 patients with a mean age of 20.78 ± 5.66 years (range 5–55). Of these, 58 (56.9%) were male and 44 (43.1%) were female. Residency was nearly evenly split, with 47 (46.1%) residing in rural areas and 55 (53.9%) in urban settings. The mean duration of SCD diagnosis was 17.32 ± 6.4

years, suggesting long-term disease exposure. Hemoglobin electrophoresis revealed that 70 (68.6%) had HbSS, while 19 (18.6%) had HbSβ-thalassemia, 12 (11.8%) had HbAS, and 1 (1.0%) had HbSF. The mean Hemoglobin level was (8.56±1.61). All these data are presented in Table 3.1.

Table 3.1: Sociodemographic and Hematological Characteristics of Patients with Sickle Cell Disease (SCD) (N=102).

Variables		Frequency (N)	Percentage %
Age	**Mean± sd Range**	20.78± 5.66 (5-55)	
Sex	**Male**	58	56.9
	Female	44	43.1
Residency	**Rural**	47	46.1
	Urban	55	53.9
Duration of SCD Diagnosis (per years)	**Mean± sd Range**	17.32± 6.4 (4-47)	
Hemoglobin type	**HBSS**	70	68.6
	Hb AS	12	11.8
	HbSβ_thalassemia	19	18.6
	Hb SF	1	1.0
Hemoglobin level	**Mean± sd Range**	8.56±1.61	

Table 3.2 shows the Clinical Presentation of Shoulder Pain and Associated Symptoms. Among the 102 patients, right shoulder involvement was observed in 43 (42.2%) cases, left in 25 (24.5%), and bilateral in 34 (33.3%). Notably, 59 (57.8%) also reported hip pain, and 43 (42.2%) had dorsolumbar spine pain. Most patients (67; 65.7%) experienced pain of less than 1 month duration, while 18 (17.6%) had pain lasting 1–6 months and 17 (16.7%) reported chronic pain for more than 6 months. Pain severity was predominantly moderate (VAS 4–6) in 63 (61.8%) patients, with 16 (15.7%) experiencing severe pain (VAS 7–10). Clinical signs included tenderness in 73 (71.6%) and limited range of motion in 59 (57.8%). Wasting was noted in 20 (19.6%), swelling in 11 (10.8%), and deformity in 4 (3.9%) patients. A high percentage, 72 (70.6%), had a history of frequent vaso-occlusive crises (VOC), and AVN was present in the hip in 23 (22.5%) and vertebrae in 20 (19.6%). The mean Oxford shoulder score was 20.98 ± 9.97 (range 12–56).

Table 3.2: Clinical Presentation of Shoulder Pain and Associated Symptoms Among Patients with SCD (N=102)

Variables		Frequency(n)	Percentage (%)
Shoulder Involvement	**Right shoulder**	43	42.2
	Left shoulder	25	24.5
	Bilateral	34	33.3
Other site pain involvement	**Dorsolumbar spine**	43	42.2
	Hip	59	57.8
Pain Duration	**< 1 month**	67	65.6
	1–6 months	18	17.6
	> 6 months	17	16.7
Pain Severity (VAS score)	**Mild pain (1-3)**	23	22.5
	Moderate pain (4-6)	63	61.8
	Severe pain (7-10)	16	15.7
Oxford shoulder score	**Mean± sd Range**	20.98± 9.97 (12 – 56)	
Presenting symptoms	**Swelling**	11	10.8
	Wasting	20	19.6
	Deformity	4	3.9
	Tenderness	73	71.6
	Limitation of Movement	59	57.8
History of frequent Vaso-occlusive Crisis		72	70.6
Other site AVN	**Hip AVN**	23	22.5
	Vertebral AVN	20	19.6

Table 3.3 shows the Stages of Avascular Necrosis (AVN). AVN of the shoulder was identified in 21 out of 102 patients (20.58%). According to radiological staging, 4 (19.04%) were in Stage I, 6 (28.57%) in Stage II, 8

(38.09%) in Stage III, and 3 (14.28%) in Stage IV. Among the remaining 81(79.41%) patients without AVN, 80 (78.4%) were diagnosed with shoulder pain due to VOC, and only 1 (0.9%) had supraspinatus tendinopathy and joint effusion.

Table 3.3: Stages of Avascular Necrosis (AVN) in the Study Population Based on Radiological Classification (N=102).

Diagnosis		Frequency(n)	Percentage (%)
AVN (N= 21) 20.58%	**– Stage I**	4	19.04
	– Stage II	6	28.57
	– Stage III	8	38.09
	– Stage IV	3	14.28
Other diagnosis (n=81) 79.41%	**Shoulder VOC**	80	78.4
	Supraspinatus tendinopathy and effusion	1	0.9

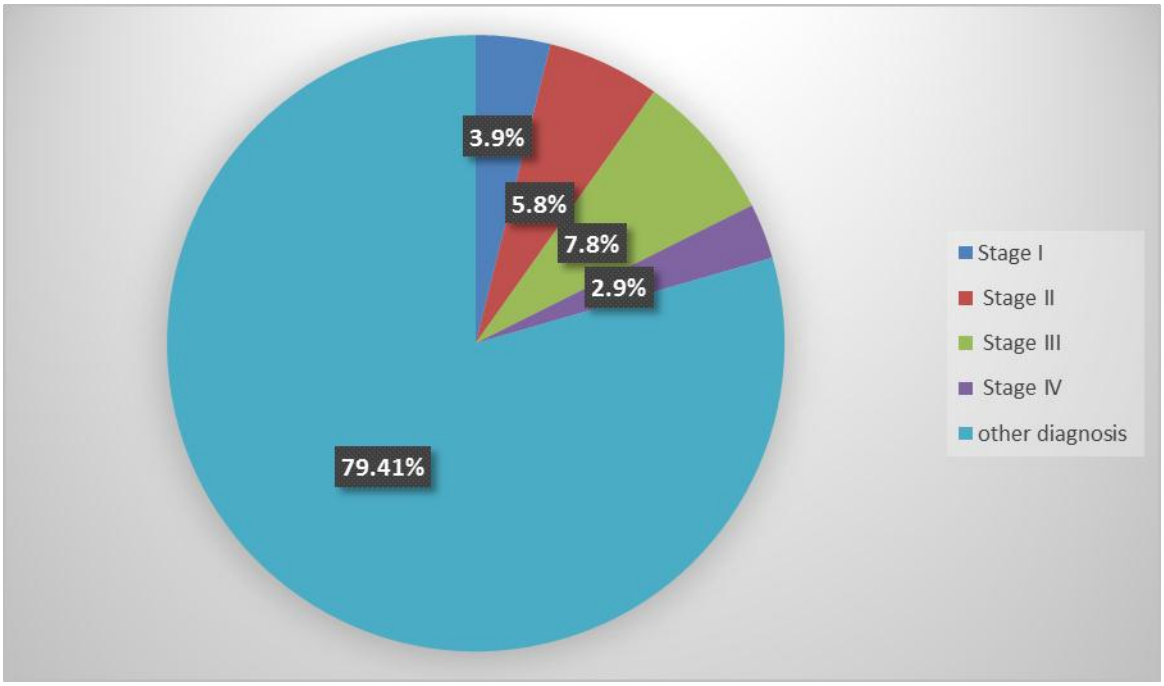

Figure 3.1: AVN distribution among study participants.

Table 3.4 shows the Radiographic Findings of the Shoulder Joint. Radiographic evaluation among SCD patients revealed that 17 (16.7%) patients had sclerosis, 14 (13.7%) had joint space narrowing, 9 (8.8%) had humeral head collapse, and 8 (7.8%) had subchondral lucency (crescent sign), all of which are consistent with features of AVN.

Table 3.4: Radiographic Findings of the Shoulder Joint Among Patients with SCD (N=102).

Xray findings	Frequency(n)	Percentage(%)
Humeral Head Collapse	9	8.8
Joint Space Narrowing	14	13.7
Sclerosis	17	16.7
Subchondral Lucency (Crescent Sign)	8	7.8

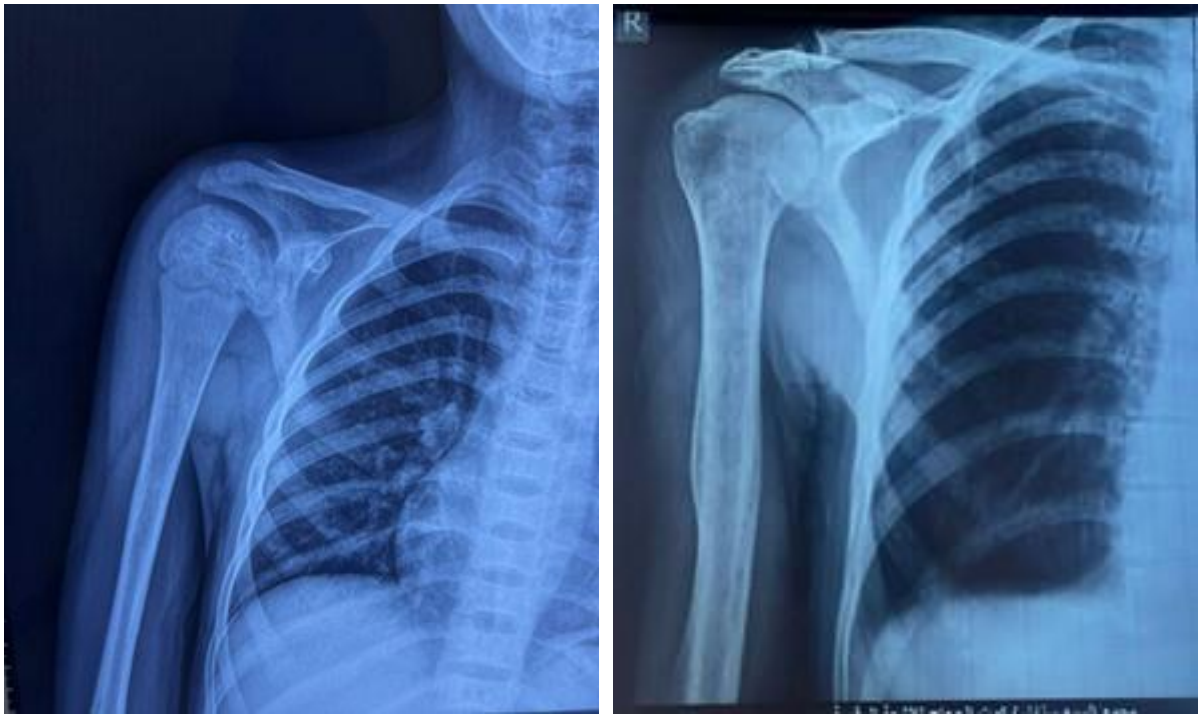

Figure (3.2): Radiographic Finding in Humeral Head AVN, (AP view shows subchondral sclerosis and osteopenia with cystic changes. The overall shape of the humeral head is preserved).

Table 3.5 shows MRI and CT Scan Findings of Shoulder Pathology. MRI was performed in only 35 (34.3%) patients. Among those imaged, 30 (85.7%) showed early marrow changes suggestive of AVN, 20 (57.1%) demonstrated bone infarcts, and 8 (22.8%) had subchondral collapse. While CT scan was performed in only 3 (2.9) patients, among those imaged 3 (2.9%) showed Sclerosis and cystic changes, 2(1.9%) demonstrated Crescent Sign and 1(0.9%) had Subchondral collapse and Glenohumeral Osteoarthritis.

Table 3.5: MRI Findings of Shoulder Pathology in Patients with SCD (N=102)

Variables		Frequency(n)	Percentage (%)
MRI Performed		35	34.3
MRI Findings	**Early marrow changes**	30	85.7
	Bone infarcts	20	57.1
	Subchondral collapse	9	22.8
	Variables	**Frequency(n)**	**Percentage (%)**
	CT Performed	3	2.9
CT Scan Findings	**Sclerosis and cystic changes**	3	2.9
	Crescent Sign	2	1.9
	Subchondral collapse and Glenohumeral Osteoarthritis	1	0.98

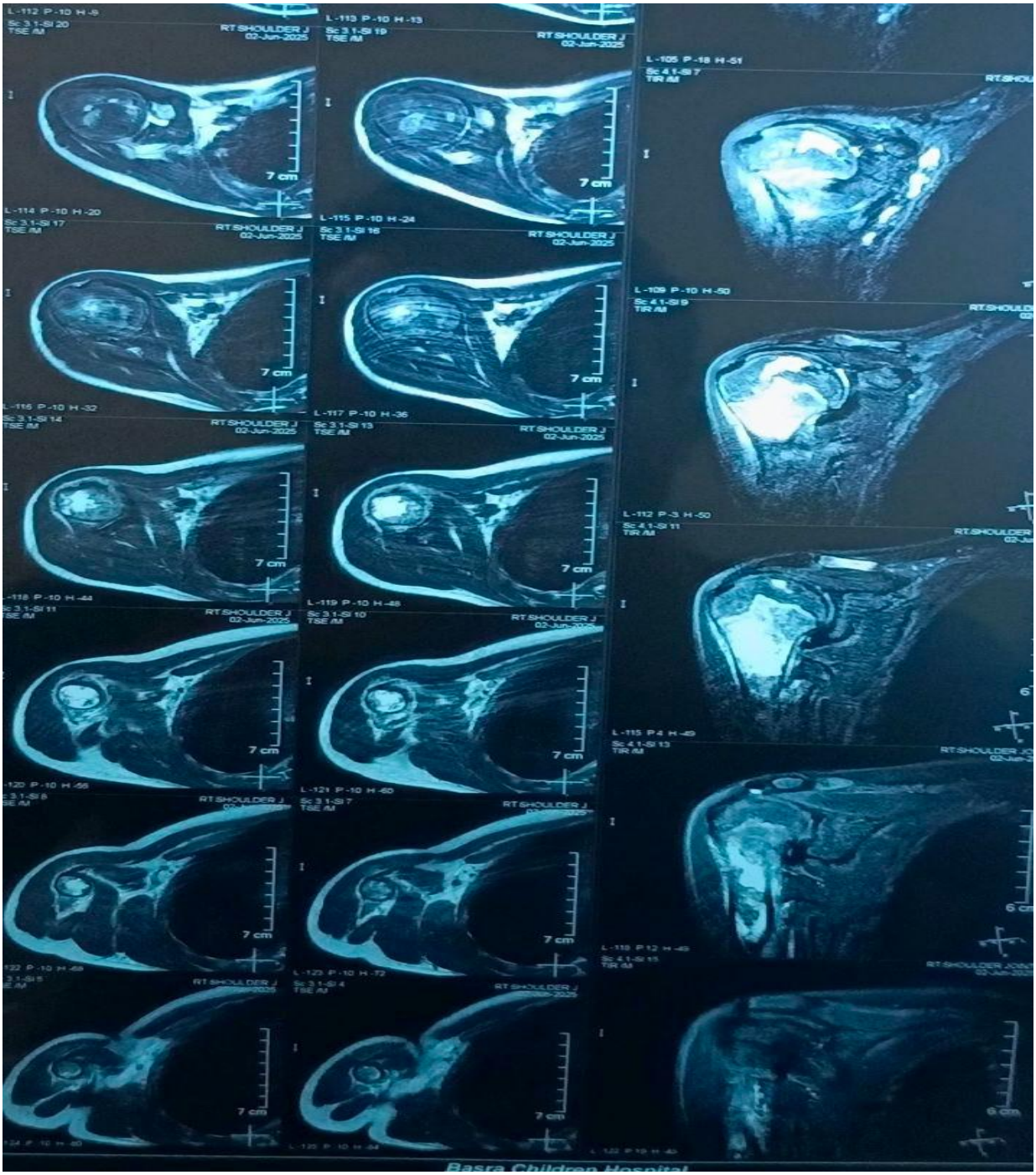

Figure (3.3): MRI Finding in Shoulder AVN (The humeral head epiphysis shows marrow edema with abnormal signal intensity, flattening and subchondral area of hypo-intense T1W signal, hyper-intense at T2 in the superior aspect of humeral head associated with mild joint effusion).

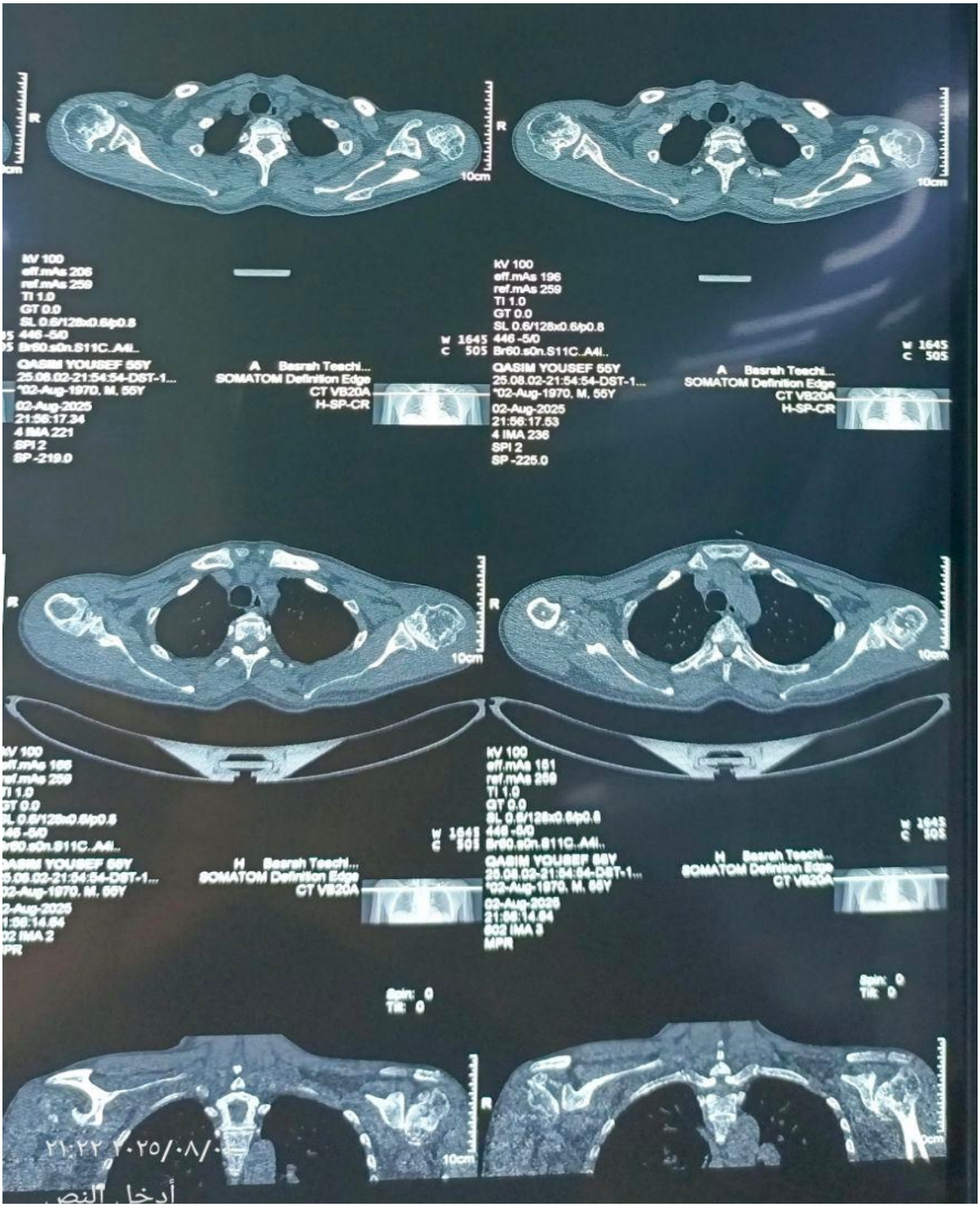

Figure (3.4): CT scan (coronal and Axial Non-contrast View) of 55 years male shows areas of sclerosis and irregularity in the humeral head with patchy mottled density and evidence of subchondral collapse, the glenohumeral joint space is relatively preserved.

Table 3.6 shows Treatment Modalities Administered. The majority of patients (100; 99.0%) received conservative treatment including analgesics and physiotherapy. Hydroxyurea was administered to 69 (67.6%) patients. Surgical intervention was with only 2 (1.9%) patients undergoing core decompression, and none receiving shoulder arthroplasty.

Table 3.6: Treatment Modalities Administered to Patients with Shoulder Pain and SCD (N=102)

Treatment Type	Frequency (n)	Percentage (%)
Conservative (analgesics, physiotherapy)	100	99.0
Hydroxyurea therapy	69	67.6
Surgical Intervention	2	1.9
– Core decompression	2	1.9

Table 3.7 shows Clinical Outcomes at Follow-up. At follow-up, 85 (83.3%) patients reported improved pain, and 78 (76.5%) had improved range of motion. However, 21 (20.6%) had no improvement, and 11 (10.8%) experienced worsening symptoms. A high rate of rehospitalization due to VOC (63; 61.8%) indicates persistent systemic disease activity.

Table 3.7: Clinical Outcomes at Follow-up (2 weeks, 3 and 6 month) Among Patients with SCD and Shoulder Pain (N=102)

Outcome at Follow-up	No.	%
Improved pain	85	83.3
Improved range of motion	78	76.5
No improvement	21	20.6
Worsening symptoms	11	10.8
Rehospitalization due to VOC	63	61.8

Table 3.8 shows the Sociodemographic and Hematologic Comparison (AVN vs. Non-AVN). Comparison between patients with AVN (n=21) and those without (n=81) revealed no significant differences in age (p=0.551), sex (p=0.977), or residency (p=0.410). Mean age was slightly higher in the AVN group (22.38 vs. 20.37 years), and mean duration of SCD was also longer (21.42 vs. 18.62 years), although not statistically significant (p=0.433). A higher proportion of AVN patients had HbSS (15; 71.4%) compared to non-AVN (55; 67.9%), and none had HbSC, though this difference did not reach statistical significance (p=0.061). The mean hemoglobin level in the AVN Patients **(**8.46±1.63) was lower than the level in non-AVN Patients (8.96± 1.5) although it's not statistically significant.

Table 3.8: Comparison of Sociodemographic and Hematological Parameters between Patients with and Without AVN.

Variables		No AVN (n= 81)	AVN (n=21)	p-value
Age	**Mean± Sd**	20.37± 1.5	22.38± 3.2	0.551
Sex	**Male**	46 (56.8)	12 (57.1)	0.977
	Female	35 (43.2)	9 (42.9)	
Residency	**Rural**	39 (48.1)	8 (38.1)	0.410
	Urban	42 (51.9)	13 (61.9)	
Duration of SCD diagnosis (years)	**Mean± sd**	18.62± 1.9	21.42 ± 2.1	0.433
Hemoglobin type	**HBSS**	55 (67.9)	15 (71.4)	0.061
	HbSC	12 (14.8)	0 (0.0)	
	HbSβ_thalassemia	14 (17.3)	5 (23.8)	
	Hb SF	0 (0.0)	1 (4.8)	
Hemoglobin level	**Mean± Sd**	8.96± 1.5	8.46±1.63	0.036

Table 3.9 shows Clinical Features and Shoulder Function (AVN vs. Non-AVN). Patients with AVN demonstrated significantly more chronic and severe symptoms. All 21 (100.0%) AVN patients had pain lasting more than 1 month, with 16 (76.2%) reporting pain duration exceeding 6 months compared to only 1 (1.2%) in the non-AVN group (p=0.001). Severe pain (VAS 7–10) was reported by 14 (66.7%) AVN patients, compared to only 2 (2.5%) in the non-AVN group (p=0.001). Oxford shoulder scores were significantly worse in the AVN group (37.76 ± 8.57 vs. 16.62 ± 3.75; p=0.001). Physical signs such as swelling (10; 47.6%), wasting (15; 71.4%), and deformity (3; 14.3%) were significantly more prevalent in AVN cases (p<0.01 for all). All AVN patients had both tenderness and limitation of movement (100.0%), in contrast to 64.2% and 46.9% in the non-AVN group (p=0.001). History of frequent VOC was also present in all AVN patients versus 63.0% without AVN (p=0.001).

Table 3.9: Comparison of Clinical Features and Shoulder Function in Patients with and without AVN.

Variables		No AVN (n= 81)	AVN (n=21)	p-value
Shoulder Involvement	**Right shoulder**	35 (43.2)	8 (38.1)	0.570
	Left shoulder	18 (22.2)	7 (33.3)	
	Bilateral	28 (34.6)	6 (28.6)	
Other site pain involvement	**Dorsolumbar spine**	43 (53.1)	0 (0.0)	0.001
	Hip	38 (46.9)	21 (100.0)	
Pain Duration	**< 1 month**	66 (81.5)	1 (4.8)	0.001
	1–6 months	14 (17.3)	4 (19.0)	
	> 6 months	1 (1.2)	16 (76.2)	
Pain Severity (VAS score)	**Mild pain (1-3)**	23 (28.4)	0 (0.0)	0.001
	Moderate pain (4-6)	56 (69.1)	7 (33.3)	
	Severe pain (7-10)	2 (2.5)	14 (66.7)	
Oxford shoulder score	**Mean± sd**	16.62± 3.75	37.76± 8.57	0.001
Presenting symptoms	**Swelling**	1 (1.2)	10 (47.6)	0.001
	Wasting	5 (6.2)	15(71.4)	0.001
	Deformity	1 (1.2)	3 (14.3)	0.006
	Tenderness	52 (64.2)	21 (100.0)	0.001
	Limitation of Movement	38 (46.9)	21 (100.0)	0.001
History of frequent Vaso-occlusive Crisis		51 (63.0)	21 (100.0)	0.001

Table 3.10 shows Radiographic Shoulder Findings (AVN vs. Non-AVN). Radiographic changes associated with AVN were significantly more common in AVN patients: humeral head collapse in 9 (42.8%) vs. none (0%) in non-AVN (p=0.001), joint space narrowing in 9 (42.8%) vs. 5 (6.2%) (p=0.001), sclerosis in 17 (81.0%) vs. none (0%) (p=0.001), and subchondral lucency in 8 (38.1%) vs. none (0%) (p=0.001).

Table 3.10: Comparison of Radiographic Shoulder Findings Between AVN and Non-AVN Groups.

Xray findings	No AVN (n= 81)	AVN (n=21)	p-value
Humeral Head Collapse	0 (0.0)	9 (42.8)	0.001
Joint Space Narrowing	5 (6.2)	9 (42.9)	0.001
Sclerosis	0 (0.0)	17 (81.0)	0.001
Subchondral Lucency (Crescent Sign)	0 (0.0)	8 (38.1)	0.001

Table 3.11 shows the MRI Findings (AVN vs. Non-AVN). MRI findings were significantly more prevalent in AVN patients: early marrow changes were seen in all 21 (100.0%) AVN cases versus only 9 (11.1%) in non-AVN (p=0.003), bone infarcts in 19 (90.5%) vs. 1 (1.2%) (p=0.001), and subchondral collapse in 9 (42.8%) vs. 0 (0.0%) (p=0.001).

Table 3.11: Comparison of MRI Shoulder Findings in AVN vs. Non-AVN Patients.

Variables		No AVN (n= 81)	AVN (n=21)	p-value
MRI Findings	**Early marrow changes**	9 (11.1)	21 (100.0)	0.003
	Bone infarcts	1 (1.2)	19 (90.5)	0.001
	Subchondral collapse	0 (0.0)	9 (42.8)	0.001

Table 3.12 shows Treatment Modalities Administered. (AVN vs. non-AVN). 80 (98.7%) of the Non-AVN Patients received conservative management and 20 (95.2%) of the AVN Patients were on conservative therapy. Regarding the use of hydroxyurea, it was higher in the AVN Patients 19(90.4%) while in the non-AVN group it was in 50(61.7%). Surgical intervention in form of Core-decompression was performed on 2(9.5) of the AVN Patients.

Table 3.12 shows Treatment Modalities Administered. (AVN vs. non-AVN).

Treatment Type	No AVN (N=81)	AVN (N=21)	P-value
Conservative (analgesics, physiotherapy)	80(98.7)	20(95.2)	0.326
Hydroxyurea therapy	50(61.7)	19(90.4)	0.009
Surgical Intervention (Core decompression)	0(0.00)	2(9.5)	0.125

Table 3.13 shows a Comparison of Clinical Outcomes between Patients with and Without Avascular Necrosis (AVN). The clinical outcomes at follow-up showed a marked difference between patients with and without avascular necrosis (AVN), with statistically significant disparities across all measured parameters (p = 0.001 for each). Among those without AVN (n=81), 77 (95.1%) reported improved pain, compared to only 8 (38.1%) in the AVN group (n=21). Similarly, improvement in range of motion was achieved in 74 (91.4%) non-AVN patients but in only 4 (19.0%) AVN patients. Conversely, the rate of no improvement was significantly higher among AVN cases, affecting 15 (71.4%) versus just 6 (7.4%) in the non-AVN group. Worsening symptoms were reported exclusively in the AVN group (5 patients; 23.8%), while none of the non-AVN patients experienced worsening (0.01%). Additionally, rehospitalization due to vaso-occlusive crisis (VOC) was more frequent in the AVN group, occurring in 20 (95.2%) compared to 43 (53.1%) in those without AVN.

Table 3.13: Comparison of Clinical Outcomes Between Patients with and Without Avascular Necrosis (AVN)

Outcome at Follow-up	No AVN (n= 81)	AVN (n=21)	p-value
Improved pain	77 (95.1)	8 (38.1)	0.001
Improved range of motion	74(91.4)	4 (19.0)	0.001
No improvement	6 (7.4)	15 (71.4)	0.001
Worsening symptoms	0 (0.01)	5 (23.8)	0.001
Rehospitalisation due to VOC	43 (53.1)	20 (95.2)	0.001

4. DISCUSSION

Sickle Cell Disease (SCD) is a common haemoglobinopathy in Basrah, southern Iraq, and both variants, whether homozygous (HbSS) or heterozygous (HbAS), that is formerly known as the Sickle Cell Trait, are prevalent in our locality. The incidence of sickle cell disease in Basrah is reported in one study to be up to 7%.[9] Hence, it is a widespread disease in Iraq, particularly in Basrah.

Bone changes in Sickle cell disease are usually due to marrow hyperplasia, tissue ischemia and infarction due to vaso-occlusive crisis, and the increasing susceptibility to infection. Almost all patients with sickle cell disease will end up with some sort of skeletal complications, irrespective of their age, for that reason, clinical awareness, early diagnosis, aggressive treatment and close follow up are always necessary to reduce the expected disabling complications.[10]

To the best of our knowledge and according to the literature search for data published from Iraq, this study is the first study with such a design to look for shoulder joint involvement among sickle cell patients in Basrah; Although, there are reported cases by Hamdan TA. et al., a study conducted in Basrah between 1988 and 1998 on 280 patients with SCD, 20(7.14%) of them had avascular necrosis of the humeral head.[10]

In the current study, we evaluated the shoulder joint in 102 patients with sickle cell disease and painful shoulder, with a mean age of 20.78 ± 5.66 years ranging from 5 to 55 years, the frequency of shoulder AVN among these patients was 21(20.58%) and this is consestant with the

British study in 1993 by David H. Et al.[11] (The shoulder in sickle cell disease) shoulder AVN were found in 28% of the 138 patients.

And this finding differ from that reported by Casale M et al.[12] in which shoulder AVN is equal to (6%) and Milner PF et al.[13] that was equal to (5.6%), the defference in our finding may be due to that we took only SCD patients with symptomatic shoulder pain.

There was a slight male predominance (56.9% male vs. 43.1% female). and near-equal distribution between rural (46.1%) and urban (53.9%) residency may reflect healthcare access disparities, with mean SCD duration of (17.32 ± 6.4) years and the mean SCD duration among patients with AVN was (23.42 ± 2.1) suggesting AVN is a late complication of chronic vaso-occlusion. these findings are consistent with a multicenter study by (Casale M et al., AVN in SCD, 2025)[12] (n=47 SCD patients with AVN) reported a median age of 35.9 years at AVN diagnosis, with 51% females and 49% males and A recent local study by Hamood et al. (2024)[14] report that the age of patients with AVN was significantly higher than those without AVN.

While other study by (Healthline Editorial Team, AVN IN SCD, 2024)[15] reports male predominance in AVN risk (e.g., due to higher disease severity or hormonal factors). and other studies show no sex difference.[12]

Regarding participants ' hemoglobin type, 70 (68.6%) had SCD (Hb SS) and 19 (18.6%) had sickle thalassemia and 12 (11.8%) had (Hb AS), The majority of AVN cases in the our study were reported in patients with homozygous mutations(Hb SS) 15 of 21 (71.4%) while 5 (23.8%) for sickle thalassemia HbSβ_thalassemia, and 1 (4.8%) (Hb SF), this is consestent with a paper published in Saudi Arabia by Zenat KH. Et al.[16] with 78.6% of the patients had SCD and 21.4% had Sickle thalassemia and a study done in Basrah by Hamood et al. (2024)[14] Homozygous HbSS was found to be an independent risk factor for AVN in this study. while Adekile et al.[17], in Kuwait, did not report a significant difference in the frequency of AVN and among patients with SCA, S/β thalassemia, and S/D genotypes.

In the current study, among the 102 patients, right shoulder involvement was observed in 43 (42.2%) cases, left in 25 (24.5%), and bilateral in 34 (33.3%). Notably, 59 (57.8%) also reported hip pain, and 43 (42.2%) had dorsolumbar spine pain. We use the Visual Analog Scale (VAS) for classification of severity. the majority fit within the range of moderate (VAS 4–6) in 63 (61.8%) patients to 16 (15.7%) experiencing severe pain (VAS 7–10). Of these Severe pain (VAS 7–10) was reported by 14 (66.7%) AVN patients, compared to only 2 (2.5%) in the non-AVN group (p=0.001), and this reflect the severity of the symptoms among patients with AVN.

Limited range of motion was noted in 59 (57.8%). And this may be due to high percentage, 72 (70.6%), of these patients had a history of frequent vaso-occlusive crises (VOC), History of frequent VOC was present in all AVN patients versus 63.0% without AVN (p=0.001), this is consistent with the study by Tran H. et al. recurrent vaso-occlusive crisis in sickle cell disease are a major cause of severe pain and limited movement for patients and a risk factor for AVN in sickle cell disease patients.[18]

In our study the cause of limitation of movement in the shoulder joint in addition to the painful crisis was avascular necrosis of the humeral head, 21 (100.0%) AVN patients had pain lasting more than 1 month, with 16 (76.2%) reporting pain duration exceeding 6 months compared to only 1 (1.2%) in the non-AVN group (p=0.001). Severe pain (VAS 7–10) was reported by 14 (66.7%) AVN patients, compared to only 2 (2.5%) in the non-AVN group (p=0.001).

We use the old Oxford shoulder score (OSS) which is a 12-item questionnaire that evaluates pain and daily function related to the shoulder over the past 4 weeks. The mean Oxford shoulder score for the study population was 20.98 ± 9.97 (range 12–56). While Oxford shoulder scores were significantly worse in the AVN group (37.76 ± 8.57 vs. 16.62 ± 3.75; p=0.001). which is the same reported by Casale M et al.[12] that AVN is a frequent, early, progressive and worsening complication in SCD.

Regarding radiological evaluation of the shoulder joint in SCD, according to Hernigou P et al.[19] If history and physical examination findings are suspicious for shoulder osteonecrosis, plain radiography is the next step in diagnosis. Although very early shoulder osteonecrosis may be undetectable on plain radiography, early shoulder osteonecrosis shows cystic and/or sclerotic changes in the humeral head. The term “crescent sign” is used to describe an area of subchondral lucency in the humeral head that indicates subchondral fracture due to bone necrosis and subsequent attempts at repair. Shoulder osteonecrosis at a later stage shows humeral head flattening, collapse, and degenerative changes.

In the current study we found that radiographic changes associated with AVN were significantly more common in AVN patients: humeral head collapse in 9 (42.8%) vs. none (0%) in non-AVN (p=0.001), joint space narrowing in 9 (42.9%) vs. 5 (6.2%) (p=0.001), sclerosis in 17 (81.0%) vs. none (0%) (p=0.001), and subchondral lucency in 8 (38.1%) vs. none (0%) (p=0.001).

Overall, the radiographic changes among our study population were 47(46%) and this align with Hernigou P. et al. 2020 a study for 110 adults with sickle cell anemia were radiographic abnormality noted in (48.2%).[19]

By MRI AVN of the shoulder was identified in 21 (20.6%) patients with most cases in Stage II 6 (28.57%) and 8 (38,09%) in Stage III, this is consistent with the

finding by Hamood et al. (2024)[14] who reported that most patients with AVN were diagnosed during stage II, followed by stage III. Similarly, by Mallet et al.[20] who reported stage III in (52%) of patients, followed by stage II (36%).

While Elalfy et al. studied patients with SCD and AVN in Egypt and Oman and found that 19.1% had stage II, 20.6% had stage III, and 25% of patients were at stage IV disease.[21] In Nigeria, Akinyoola et al. found that most patients have stage IV AVN (52%), followed by stage II disease (28%)[22] and Ofakunrin et al. reported that 75.8% of the children were diagnosed at late stages of the disease.[23] The difference can be explained by the different screening tools used in different study populations (plain radiography, MRI, or both), different scoring systems, and whether different centers screen children with SCD for AVN early and routinely.

Among the remaining 81 patients without shoulder AVN, 80 (78.4%) were diagnosed with shoulder pain due to VOC, hip AVN in 23 (22.5%) of patients, 20 (19.6%) with vertebral osteonecrosis while only 1 (0.9%) had supraspinatus tendinopathy, and no infection was observed during the study period. The reason why among the 102 patients in our study no cases were diagnosed with infection or osteomyelitis is not entirely clear, which does not fit with the findings of Hamdan et. al. a study in Basrah in 1998 for 280 patients when 4(1.4%) of them were diagnosed with shoulder osteomyelitis and 3(1.07%) with pyogenic arthritis[10] the difference in our finding may be due to improved prophylaxis and vaccination and due to the use of better antibiotics and earlier treatment.

Lee WQ. et al. suggest that MRI should be done for patients with shoulder pain and underlying risk factors for humeral head AVN with unremarkable or early stage AVN radiographs. This allows early stage (I/II) AVN to be detected and some form of prognostication of future progression. Conservative therapy (rest, physiotherapy, analgesia) should be pursued initially. The eventual management will then be guided by the stage of AVN on diagnosis and eventual progression.[24]

Regarding Treatment Modalities Administered, most patients in this study (100; 99.0%) received conservative treatment including rest, analgesics and physiotherapy. Hydroxyurea was administered to 69 (67.6%) patients. Surgical intervention was rare, with only 2 (1.9%) patients undergoing core decompression, and none undergoing shoulder arthroplasty.

The clinical outcomes at follow-up showed a marked difference between patients with and without avascular necrosis (AVN), with statistically significant disparities across all measured parameters ($p = 0.001$ for each). Among those without AVN (n=81), 77 (95.1%) reported improved pain, compared to only 8 (38.1%) in the AVN group (n=21). Similarly, improvement in range of motion was achieved in 74 (91.4%) non-AVN patients but in only 4 (19.0%) AVN patients. Conversely, the rate of no improvement was significantly higher among AVN cases, affecting 15 (71.4%) versus just 6 (7.4%) in the non-AVN group. Worsening symptoms were reported exclusively in the AVN group (5 patients; 23.8%), while none of the non-AVN patients experienced worsening. Additionally, rehospitalization due to vaso-occlusive crisis (VOC) was more frequent in the AVN group, occurring in 20 (95.2%) compared to 43 (53.1%) in those without AVN.

This corresponds to Casale M. et al. found that a high rate of compromised joint function and pain was observed 10 years after diagnosis of AVN regardless of the type of treatment, indicating the need to improve the management strategies of this sickle-related complication.[12]

During follow-up of the two patients with core decompression, one was lost to follow-up (LTFU) after discontinuing communication (phone contact terminated). While the other one showed valuable improvement in pain and increased range of motion with an Oxford shoulder score (OSS) of 21 at 6 months postoperatively compared to preoperative OSS score of 34, although toward clinical benefit was observed, the small number of cases limits the strength of this finding.

The limitations of the study were; the possibility of recall bias in VOC history and functional assessments. Secondly; MRI availability limitations, leading to reliance on X-ray for some diagnoses. The third limitation was the short follow-up period (1 year) may not capture long-term joint deterioration.

5. CONCLUSIONS

This study demonstrates that avascular necrosis of the shoulder is a notable complication in patients with sickle cell disease in Basrah, with a prevalence of 20.5% among those presenting with shoulder pain. Radiological evaluation proved essential for diagnosis, MRI was particularly valuable for identifying early marrow changes and bone infarcts, allowing for earlier recognition of the disease process. Clinically, AVN patients exhibited significantly higher rates of symptomatic pain and limitation of movement, reflecting a profound impact on daily activities and quality of life. These findings underscore that AVN is a disabling complication of SCD. Early recognition and timely management are crucial to improving patient outcomes and preventing long-term disability.

For Clinical Practice; implement early radiological and MRI evaluation in all SCD patients with persistent shoulder pain, especially when symptoms exceed one month, adopt multidisciplinary care involving hematologists, orthopedic surgeons, and radiologists for comprehensive management and ensure early referral for physiotherapy and surgical evaluation in advanced stages

of AVN. Conduction of larger multicenter studies to better define the prevalence, risk factors, and natural history of shoulder AVN in SCD across Iraq, explore genetic and hematological predictors associated with AVN development and evaluate long-term outcomes of conservative versus surgical management strategies.

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