Is Magnetic Resonance Imaging Play a role in aiding the diagnostic value of COVID-19 Musculoskeletal induced pathologies?

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Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the seventh strain identified within the coronavirus family capable of infecting humans, is responsible for the onset of COVID-19 infection. Although musculoskeletal (MSK) manifestations frequently emerge as among the initial symptoms of COVID-19, their documentation remains comparatively limited, possibly resulting in their under recognition. Acute MSK symptoms, which manifest within a span of four weeks post-infection, typically encompass generalized fatigue and myalgia, exhibiting nonspecific characteristics.

Objectives: This study's goal is the use of MRI examination for evaluation of the different musculoskeletal pathologies in complaining COVID-19 patients.

Patients and Methods: In this prospective study, which included 30 patients confirmed with COVID-19 through December 2023 to May 2024, MRI was tailored based on the area of interest depending on patient's complaint.

Results: Among the enrolled patients, myalgia was the most common presentation (36.7%), the most common MRI finding was synovitis and effusion (33.3%), and the least common was bone infarction (10%), with knee joint being the most commonly affected joint.

Conclusion: Magnetic resonance (MR) imaging, either with or without contrast can help diagnosis and assessment of COVID-19 symptoms and consequences affecting the musculoskeletal system.

Keywords: MRI; COVID-19; Musculoskeletal pathologies.

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) is the seventh member of the family of coronaviruses that infects people and causes infection with COVID19. **(Zhu et al., 2020).**

Initial descriptions of this disease focused on respiratory manifestations and hematologic disorders, which result in the greatest morbidity and mortality, although infection often involves numerous organ systems, resulting in multisystem organ failure and ultimately death. **(Revzin et al., 2020).**

Musculoskeletal (MSK) manifestations are commonly among the earliest presenting symptoms of COVID-19 but have been much less widely reported and may be under recognized for several reasons. Acute MSK symptoms, which occur within 4 weeks of infection, including fatigue and myalgia, are nonspecific. **(Tuzun et al., 2021).**

Moreover, patients who are critically ill and often undergo sedation and intubation may be unable to report MSK symptoms. Finally, other MSK symptoms may manifest after the initial infection has resolved, either in the early post-acute period or in the weeks to months following the original infection, often referred to as post-COVID condition or long COVID. (**Bakılan et al., 2021).**

In COVID-19 patients, systemic inflammation is significant for bone pathologies, joint and muscular tissues. Cytokines, stimulated by the virus, have been shown to have a detrimental effect on musculoskeletal tissue. Furthermore, the use of corticosteroids, which are commonly administered to hospitalized COVID-19 patients, may also negatively impact bone tissue. **(Sinha et al., 2023).**

Magnetic resonance (MR) imaging, either with or without contrast can support diagnosis and evaluation of musculoskeletal manifestations and iatrogenic complications of COVID-19. **(Paliwal et al., 2020).**

Magnetic resonance imaging (MRI) represents the most advanced imaging in diagnosis of MSK abnormalities which can be used to accurately detect the anatomical extent of lesion because it has higher resolution , tissue contrast and better multi-planar capabilities, than other imaging modalities (ultrasound, X-ray and CT). **(Miwa et al., 2017).**

Diffusion-weighted imaging (DWI) is the technique which allows measurement of the Brownian motion of water in the tissue micro-environment depending on the organization of the tissue, integrity of cell membranes and tortuosity of extracellular space. Apparent Diffusion Coefficient (ADC) is a numerical parameter which is calculated from DWI. (**Hassanien et al., 2018).**

DW-MRI with ADC mapping is a rapidly, valuable, non-invasive, non-contrast tool for reliably recognize the MSK abnormalities. (**Hassanien et al., 2018).**

This study's goal is the use of MRI examination for evaluation of the different musculoskeletal pathologies in complaining COVID-19 patients.

Patients and Methods

The present cross-sectional cohort study involved 30 patients, spanning from December 2023 to May 2024. Prior to participation, written informed consent was obtained from patients or their legal representatives following a comprehensive explanation of the study's potential benefits.

The research was conducted with

the approval of the Tanta University Hospitals Ethical Committee approval code: 36264PR470/12/23.

Inclusion criteria: The study cohort comprised individuals who tested positive for SARS-CoV-2 via RT-PCR and exhibited musculoskeletal signs and symptoms, including fatigue, spine pain, myalgias, and arthralgias.

Exclusion criteria: Patients presenting with contraindications for MRI, such as metallic prostheses, cardiac pacemakers, or intraocular metallic foreign bodies, were excluded from the study. Additionally, individuals exhibiting claustrophobia were also excluded from participation.

The enrolled patients were subjected to:

- History taking: including onset of musculoskeletal symptoms and the affected region as well.
- Laboratory investigations for COIVD infection: including CBC (white blood cells count) and D-dimer.
- MRI for the affected joint.

MRI Protocols

The process of obtaining images was carried out using a 1.5-Tesla MRI device. The used MRI sequences were tailored for each patient based on the site of myalgia or arthralgia, and so each region protocol was chosen accordingly; generally included:

- T1-weighted spin-echo sequence: TE minimum, TR 400-750 (pre contrast and post contrast in few selected cases (in 3 cases with septic arthritis)
- T2-wighted spin-echo sequence: TE 70-85, TR 3000-6000
- PD F/S: TE 20-35, TR >2000
- STIR images: STIR: TE 35 (TI 150), TR 3000-6000
- Diffusion and ADC (b= 50, 400, 800) (in 3 cases with septic arthritis)

Statistical analysis

Statistical analysis was performed using SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were expressed as mean and standard deviation (SD), while qualitative variables were presented as frequency and percentage (%)

Results

The mean value (± SD) of age was 50.1(± 12.04) years, ranging from 32-65 years. Sex was male in 11 (36.67%) patients and female in 19 (63.33%) patients. 17 (56.67%) patients received steroids. Covid-19 was mild (including symptoms as; fever, fatigue, cough, sore throat, runny nose and sneezing) in 11 (36.67%) patients, moderate (including symptoms as; persistent fever; initially dry then productive and chest wheezing) in 14 (46.67%) patients and severe (including gastroenteritis symptoms as diarrhea, respiratory deterioration with dyspnea and hypoxemia) in 5 (16.67%) patients. As shown in (**Table.1**).

Table 1. Demographic data and covid-19 severity of the studied patients

Variables		(n=30)
Age (years)		50.1 ± 12.04
Sex	**Male**	11 (36.67%)
	Female	19 (63.33%)
Patient received steroids		17 (56.67%)
Covid-19 severity	**Mild**	11 (36.67%)
	Moderate	14 (46.67%)
	Severe	5 (16.67%)

Data are presented as mean ± SD or frequency (%).

Regarding to MSK symptoms, muscle pain was present in 11 (36.67%) patients, arthralgia was present in 9 (30%) patients, limitation of movement was present in 7 (23.33%) patients and fever and limitation of movement was present in 3 (10%) patients. Regarding to time of appearing symptoms, 12 (40%) patients had symptoms during illness and 18 (60%) patients had symptoms after 14 days from illness. As shown in **(Table.2**).

Table 2. Symptoms and timing of appearing MSK symptoms of the studied patients

Variables		(n=30)
Symptoms	**Muscle pain**	11 (36.67%)
	Arthralgia	9 (30%)
	Limitation of movement	7 (23.33%)
	Fever and limitation of movement	3 (10%)
Time of appearing symptoms	**Symptoms during illness**	12 (40%)
	Symptoms after 14 days from illness	18 (60%)

Data are presented as frequency (%).

Regarding laboratory findings, leukopenia was mild in 14 (46.67%) patients, moderate in 8 (26.67%) patients and severe in 3 (10%) patients. D.dimer was elevated in 11 (36.67%) patients. As shown in (**Table.3**).

Table 3.Laboratory findings of the studied patients

Variables		(n=30)
Leukopenia	**Mild**	14 (46.67%)
	Moderate	8 (26.67%)
	Severe	3 (10%)
D-dimer	**Elevated**	11 (36.67%)

Data are presented as frequency (%).

Regarding MRI findings, myositis was found in 5 (16.67%) patients, synovitis and effusion were found in 9 (30%) patients, AVN hip was found in 4 (13.33%) patients, bone infarction was found in 3 (10%) patients, adhesive capsulitis was found in 5 (16.67%) patients and septic arthritis was found in 3 (10%) patients. As shown in (**Table .4**) and (**Figs. 1-4**).

Regarding joint affection, shoulder affection was present in 8 (26.67%) patients, sacroiliac affection was present in 2 (6.67%) patients, hip affection was present in 4 (13.33%) patients, knee affection was present in 11 (36.67%) patients, ankle affection was present in 2 (6.67%) patients, wrist affection was present in 2 (6.67%) patients and elbow affection was present in 1 (3.33%) patient. As shown in (**Table.4**) and and (**Figs. 1-4**).

Regarding T1WI, all lesions detected at the enrolled 30 patients elicit low T1WI signal. However, regarding T2WI, 5 (16.67%) lesions elicit low signal and 21 (70%) lesions elicit high signal. Also all lesions show hyper-intense signal at STIR/PD fat saturation. Whereas DWIs and ADC were done for only 3 lesions (septic arthritis) and found to show true restriction (bright signal on DWIs and low ADC signal) at them, also post-contrast series were done for the same 3 lesions showing post-contrast enhancement as well. As shown in (**Table.5**).

Table 4.MRI findings and joint affection of the studied patients

Variables		(n=30)
MRI findings	Myositis	5 (16.67%)
	Synovitis and effusion	10 (33.33%)
	AVN hip	4 (13.33%)
	Bone infarction	3 (10%)
	Adhesive capsulitis	5 (16.67%)
	Septic arthritis	3 (10%)
Joint affection	Shoulder	8 (26.67%)
	Sacroiliac	2 (6.67%)
	Hip	4 (13.33%)
	Knee	11 (36.67%)
	Ankle	2 (6.67%)
	Wrist	2 (6.67%)
	Elbow	1 (3.33%)

Data are presented as frequency (%). MRI: Magnetic resonance imaging. AVN: Avascular necrosis.

Table 5. Characterization of musculoskeletal pathologies at different MRI pulse sequences

Variables		(n=30)
T1 signal	Low	30/30 (100%)
T2 signal	Low	5/30 (16.67%)
	High	21/30 (70%)
STIR/PD fat saturation	High	30/30 (100%)
DWI	Restricted	3/3 (10%)
	Free diffusion	0/0 (0%)
ADC	Low	3/3 (100%)
	High	0/0 (0%)
T1 post contrast	Positive enhancement	3/3 (100%)
	No enhancement	0/3 (0%)

Data are presented as frequency (%). DWI: Diffusion weighted imaging, ADC: Apparent diffusion coefficient

Cases

Case No.1:22-year-old male patient, had mild COVID symptoms, didn't receive corticosteroids, presented by arthlagia within 9 days of illness, laboratory findings: mild leukopenia and non-elevated D-dimer. MRI right elbow joint showing marked amount of synovial effusion filling the elbow joint recesses with synovial thickening together with diffuse regional soft tissue edema suggesting synovitis. As shown in (**Fig.1**).

Case No.2: 29-year-old female patient, had moderate COVID symptoms post-delivery, received corticosteroids, presented by limitation of movement after 21 days of illness, laboratory findings: moderate leukopenia and elevated D-dimer . MRI both hip joints showing geographic areas of abnormal signal intensity seen at both femoral heads involving mainly the superio-antero-medial portion of the femoral head, being fairly-demarcated from the adjacent normal bone marrow by a thin rim of low T1 and T2 WI signal intensity with intervening marrow edema together

subchondral fissuring and cortical irregularities, the femoral head/neck marrow edema is more pronounced at the right side which showed additional acetabular focal areas of bone marrow edema and focal subchondral collapse. As shown in (**Fig.2**).

Fig.1.MRI right elbow joint: A: Sagittal T2WI, B: Sagittal T1WI, C: Coronal STIR, D: Axial T2WI, showing marked amount of synovial effusion filling the elbow joint recesses with synovial thickening together with diffuse regional soft tissue edema suggesting synovitis. Final diagnosis: elbow joint effusion and synovitis.

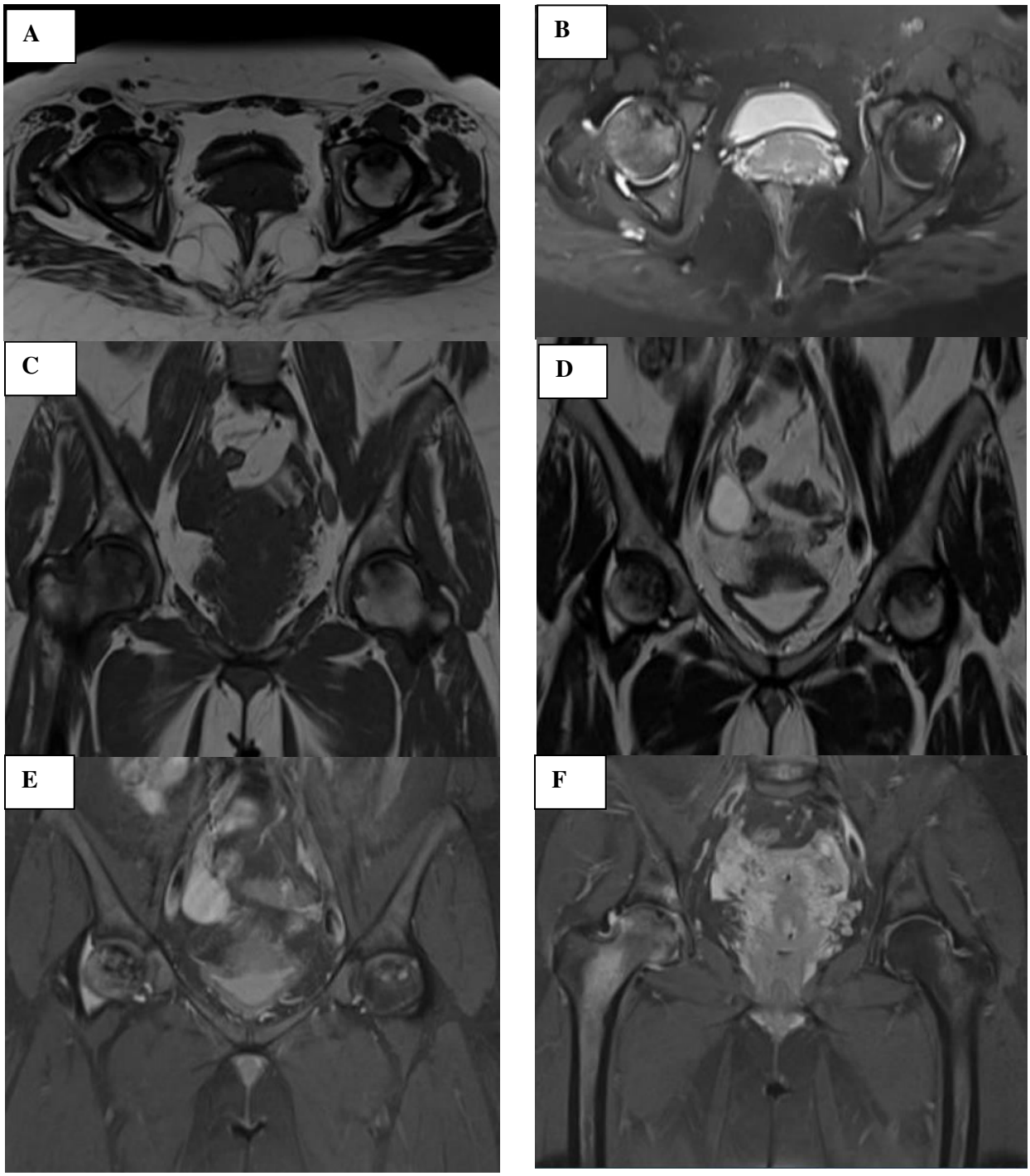

Fig2. MRI both hip joints. A: axial T1WI sequence, B: axial T2WI sequence, C: coronal T1WI sequence, D: coronal T2WI sequence, E&F coronal PD FAT SAT sequences, showing geographic areas of abnormal signal intensity seen at both femoral heads involving mainly the superio-antero-medial portion of the femoral head, being fairly-demarcated from the adjacent normal bone marrow by a thin rim of low T1 and T2 WI signal intensity with intervening marrow edema together subchondral fissuring and cortical irregularities, the femoral head/neck marrow edema is more pronounced at the right side which showed additional acetabular focal areas of bone marrow edema and focal subchondral collapse Final diagnosis: bilateral femoral head avascular necrosis

Case No.3: 36-year-old female patient, had moderate COVID symptoms, post-delivery, received corticosteroids, presented by limitation of movement after 14 days of illness, laboratory findings; severe leukopenia. MRI sacroiliac joint showing moderate right sided sacro-iliac joint effusion with articular surface enhancement, articular erosion, subarticular patchy areas of bone marrow edema more evident at its iliac side with swollen edematous overlying iliacus muscle showed a well-defined intramuscular marginally enhanced fluid collection (22 x 20 x 38 mm in its greatest dimensions) and displaying low T1WI, high T2WI, high STIR with restricted diffusion with marginal enhancement after Gd-DTPA administration. The soft tissue edema and enhancement are also seen extended to the underlying glutei yet no collection could be detected. As shown in (**Fig.3**).

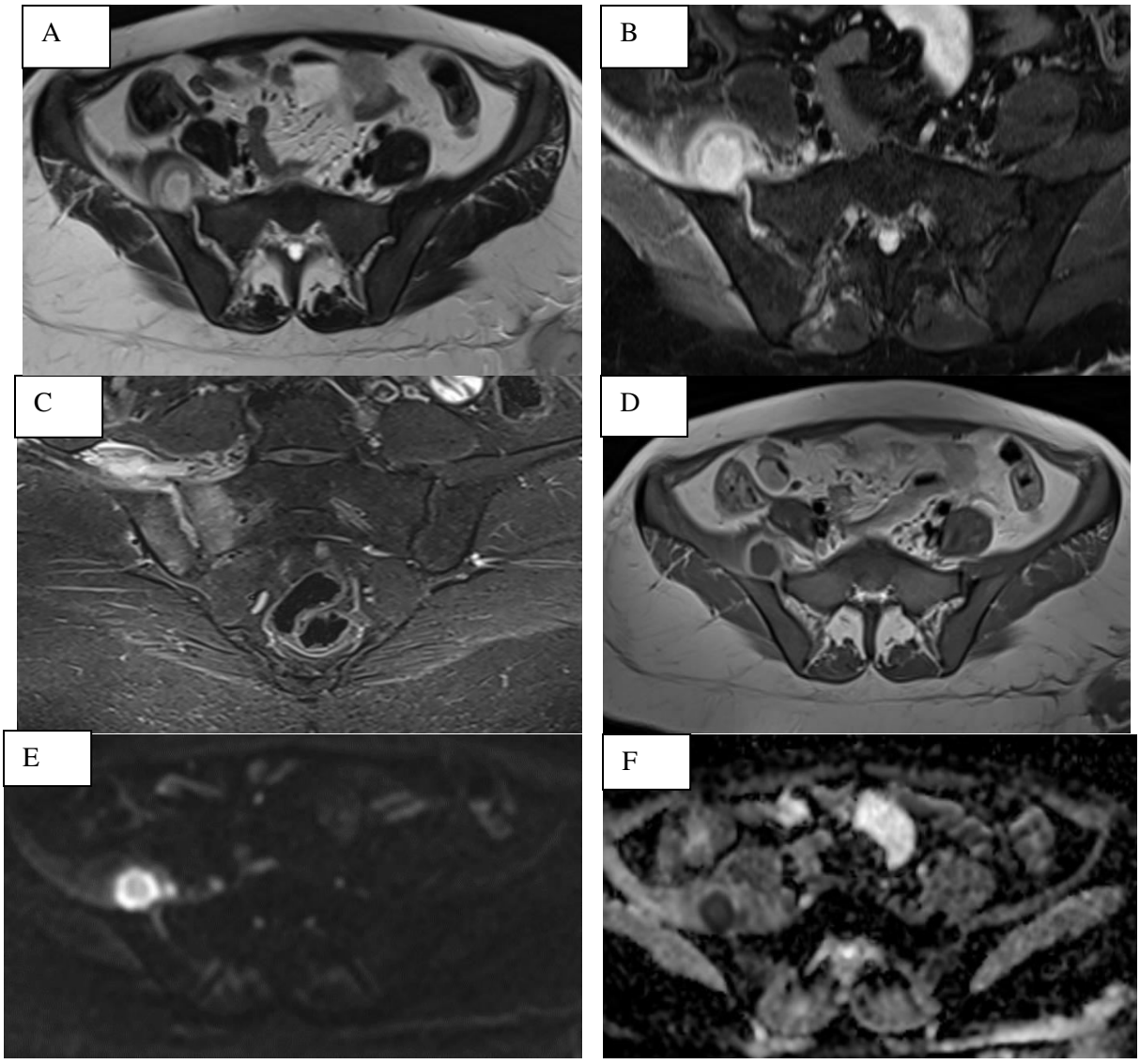

Fig.3.MRI sacroiliac joint: A: axial T2WI, B: axial T2 FAT SAT sequence, C: coronal STIR, D: axial T1 post-contrast, E: axial diffusion weighted image (DWI), F: axial ADC, showing

moderate right sided sacro-iliac joint effusion with articular surface enhancement, articular erosion, subarticular patchy areas of bone marrow edema more evident at its iliac side with swollen edematous overlying iliacus muscle showed a well-defined intramuscular marginally enhanced fluid collection (22 x 20 x 38 mm in its greatest dimensions) and displaying low T1WI, high T2WI, high STIR with restricted diffusion with marginal enhancement after Gd-DTPA administration. The soft tissue edema and enhancement are also seen extended to the underlying glutei yet no collection could be detected. Final diagnosis: right sacroiliac joint septic arthritis with overlying ipsilateral iliacus muscle abscess formation and inflammatory changes of the regional muscles

Case No.4:36-year-old female patient, had moderate COVID symptoms, received corticosteroids, presented by arthralgia after 18 days of illness, laboratory findings: moderate leukopenia and elevated D-dimer MRI right knee joint showing large femoral and tibial metaphyseal irregular shaped serpiginous abnormal signal intensity lines with intervening bone marrow edema, smaller areas of similar signal intensity at superior patellar, eliciting serpiginous peripheral low signal with central signal that of bone marrow on T1WI (D), showing double line sign (hyper-intense line parallel to inner surface of hypo-intense line within the marrow) on T2 STIR and PD sequences (A, B, C). As shown in (**Fig.4**).

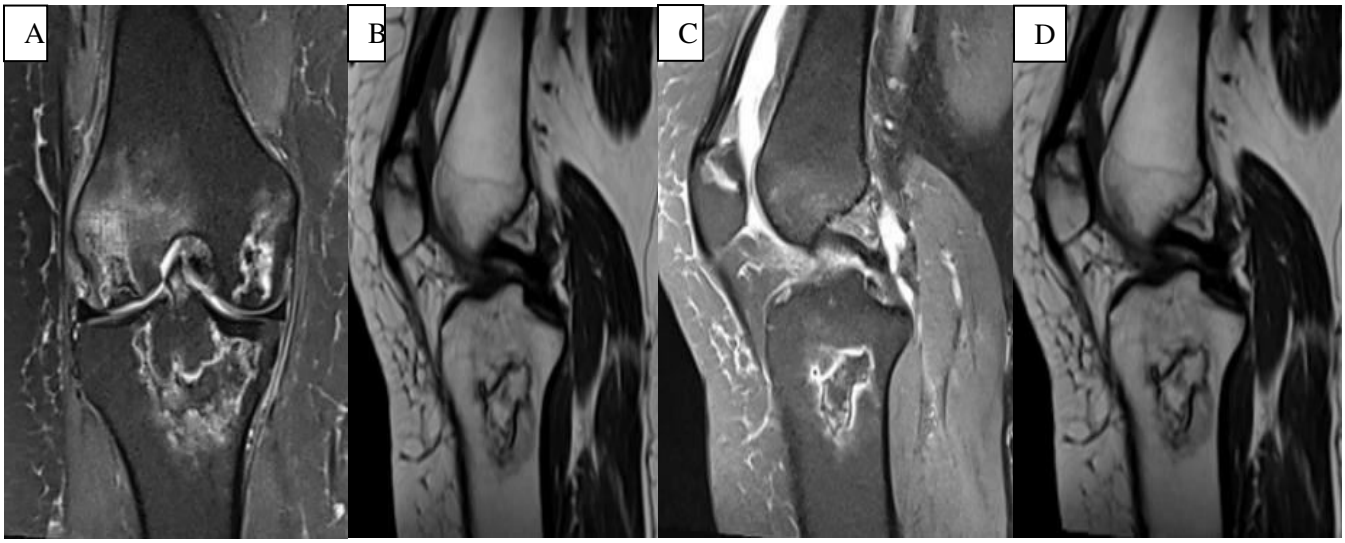

Fig.4. MRI right knee joint: A: coronal PD FAT SAT sequence, B: Sagittal PD, C: Sagittal T2WI sequence, D: Sagittal T1WI, showing large femoral and tibial metaphyseal irregular shaped serpiginous abnormal signal intensity lines with intervening bone marrow edema, smaller areas of similar signal intensity at superior patellar, eliciting serpiginous peripheral low signal with central signal that of bone marrow on T1WI (D), showing double line sign (hyper-intense line parallel to inner surface of hypo-intense line within the marrow) on T2WI and PD sequences (A, B, C). Final diagnosis: Multifocal bone infarcts.

Discussion

Musculoskeletal (MSK) manifestations frequently emerge as among the initial symptoms of COVID-19, yet their documentation has been comparatively limited, potentially leading to under recognition. This phenomenon may stem from several factors. **(Tuzun et al., 2021).**

In the current study, 30 patients with clinical manifestation of musculoskeletal manifestation of COVID-19. In our study the mean age was 50.1(± 12.04) years which is relatively lower than study done by **Priti et al. (2023)** that reported the mean age was 61 years.

In the present study the musculoskeletal complications were common in female which found in 19 (63.33%) patients than in male that found in 11 (36.67%) patients and this in agreement with **Priti et al. (2023)** that reported the majority of cases were female than in male.

In our study we found that majority of cases received steroids as line of treatments which were found in 17 cases (56.67%), this higher than **Sulewski et al. (2021)** that found that only 4 cases out of 10 cases received steroids therapy .

The major cases of the current study were moderate in severity accounted about 14 cases (46.67%) followed by mild cases that found in 11 (36.67%) then sever cases seen in 5 cases (16.67%) , this in agreement with **Sulewski et al. (2021)** that reported that most cases were moderate followed by mild then sever .

Regarding the symptoms of our study most common symptoms was muscles pain seen in 11 cases followed by arthralgia seen in 9 cases then limitation of movements that found in 7 cases and this is in agreement with **Disser et al. (2020)** .

Most cases in our study developed musculoskeletal complication about 14 days after infection that seen in 18 patients (60%) of cases and this near to **Sulewski et al. (2021)** that reported the musculoskeletal complication begins to occurred 7 to 22 days from infection onset (mean 14 days) .

Regarding laboratory findings in our study, leukopenia was mild in 14 (46.67%) patients, moderate in 8 (26.67%) patients and severe in 3 (10%) patients. D.dimer was elevated in 11 (36.67%) patients, however, study done by **Batur et al. (2021)** stated that white blood cells level was low in 3.8%, high in 18.8% and within normal range in 77.5% of the total enrolled patients in the study and also D-dimer was high in 40% of enrolled patients and within normal in 60% .

Regarding MRI findings of the different musculoskeletal pathogenesis , in our study we found that adhesive capsulitis was found in 5 (16.67%) patients which showed increased T2 & PD fat sat signal intensities of inferior glenohumeral ligament, thickened coracohumral ligament, thickened both anterior joint capsule and axillary pouch and abnormal soft tissue thickening of the rotator interval, these finding in acceptance with **Daste et al (2023)** who found same finding in their studies that include 39 patients with shoulder affection in cases with ICU admitted Covid 19 patients.

We reported MRI findings of synovitis and effusion of much joints affection as sign of reactive inflammatory arthritis seen in 9 cases (30%) and this in acceptance with **Migliorini et al. (2023)**

MRI findings of myositis was

detected in 5 cases (16.67%) in the form of high T2 and STAIR signal intensities seen at the affected muscles and this in acceptance with **Sheraz et al. (2021)** that found signs of MRI myositis in their studied cases.

AVN hip was found in 4 (13.33%) patients with MRI signs in the form of low signal at T1 with high T2 signal line seen between the normal marrow and affected necrotic bonny segment with high STAIR signal in this accepted with **Priti et al. (2023)** whom their study involving 10 patients with MRI findings of Avascular necrosis of the femoral head

In our study we detect bone infarction was found in 3 (10%) patients mainly seen after receiving steroids drugs in the form of serpiginous peripheral area of low signal in T1, ill-defined nonspecific area of high signal with hyperintense inner ring of granulation tissue and hypointense outer ring of sclerosis with high signal in STAIR sequence and these in acceptance with **Sulewski et al. (2021)** who found same findings in 10 cases with suspected bone infractions at different joint .

Septic arthritis was found in 3 (10%) patients with MRI signs in the form of low T1 signal intensity of subchondral bone, thin rim of high T2signal of subchnodral edema with adjacent enhancement of nearby soft tissue component with diffusion restriction could be noted and this relatively accepted with **Ardakani et al (2021),** who found relatively similar finding of septic arthritis in 5 cases with COVID19 infection .

In our study most common joint affection was knee joint seen in 11 cases followed by shoulder joint that seen in 8 cases then hip joint in 4 cases then wrist, sacroiliac and ankle joints that seen in 2 cases for each of them and only one case with elbow joint affection and this accepted with **Kocyigit et al. (2021)** who in agreement with our study that found that knee joint is most common joint affected while elbow joint is a least one to be affected.)

Our study had several limitations; first, the small number of the patients included in the study, second, the study structure and the lack of a control study to compare results with, third is the short time limit, and finally, time taken for proper disinfection, sterilization of the MRI unit.

Conclusion

Magnetic resonance (MR) imaging, either with or without contrast can help in the diagnosis and characterization of the musculoskeletal pathologies associated with COVID-19.

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Conflict of Interest: Nil

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