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Avascular Necrosis of the Femoral Head in Sickle Cell Disease Patients: A Cross-Sectional Analysis

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ABSTRACT
Avascular necrosis (AVN) of the femoral head is a debilitating condition commonly observed in patients with sickle cell disease (SCD). This cross-sectional study aims to evaluate the prevalence and identify risk factors of AVN among SCD patients. A cohort of 200 SCD patients was selected for this study. Data collection involved reviewing medical records, conducting physical examinations, and analyzing imaging results. Participants ranged in age from 15-60 years, with a diverse representation of genders and SCD severity levels. Statistical analysis was performed to identify potential risk factors associated with the development of AVN. The prevalence of AVN in the study population was found to be significantly high, with a notable percentage of patients demonstrating early signs of femoral head necrosis. Key risk factors identified included age, severity of SCD, history of steroid use and frequency of vaso-occlusive crises. The study also uncovered a correlation between the duration of SCD and the onset of AVN. The study confirms a high prevalence of AVN in SCD patients and identifies several significant risk factors. These findings underscore the need for early screening and targeted interventions in the SCD population to prevent or delay the onset of AVN. Further research is recommended to explore the pathophysiological mechanisms underlying AVN in SCD and to develop more effective management strategies.

INTRODUCTION

Avascular necrosis (AVN) of the femoral head is a progressive condition characterized by the loss of blood supply to the bone, leading to bone death and subsequent joint destruction. This condition is particularly prevalent among patients with sickle cell disease (SCD), a genetic disorder that leads to abnormal hemoglobin formation, causing red blood cells to assume a sickle shape. These sickled cells can obstruct blood vessels and reduce blood flow, contributing to the development of AVN.

The relationship between SCD and AVN is well-documented, with several studies indicating a higher incidence of AVN among SCD patients compared to the general population[1]. The pathophysiology of AVN involves ischemia, bone infarction and subsequent structural failure of the bone[2]. This process is exacerbated in SCD due to the recurrent vaso-occlusive events and chronic inflammation. Management of AVN in the context of SCD is challenging. Early diagnosis and intervention are crucial for preserving joint function and reducing morbidity[3]. However the onset of AVN is often insidious and many patients are asymptomatic in the early stages, leading to delayed diagnosis and treatment[4].

Aim:

- To evaluate the prevalence and identify risk factors associated with avascular necrosis of the femoral head in patients with sickle cell disease

Objectives:

- To determine the prevalence of avascular necrosis of the femoral head in a cohort of 200 patients with sickle cell disease
- To identify and analyze potential risk factors contributing to the development of avascular necrosis in these patients
- To assess the relationship between sickle cell disease severity and the occurrence of avascular necrosis

MATERIALS AND METHODS

Study design and setting: This research was conducted as a cross-sectional study at a tertiary care hospital specialized in hematology. The study duration was from January-December 2024.

Participants: The study included 200 patients diagnosed with sickle cell disease (SCD). Inclusion criteria were confirmed SCD diagnosis, age 15-60 years and informed consent. Patients with other hematological disorders or previous hip surgeries were excluded.

Data collection: Clinical data were collected from medical records, including demographic information, SCD-related complications and treatment history. Physical examinations focused on signs of hip pain and limited range of motion. Imaging studies, primarily MRI, were used to diagnose AVN.

Diagnostic criteria for AVN: AVN diagnosis was based on MRI findings, according to the Ficat and Arlet staging system.

Statistical analysis: Descriptive statistics (mean, standard deviation, frequencies) were used to summarize demographic and clinical data. The prevalence of AVN was calculated. Logistic regression analysis was performed to identify risk factors for AVN, adjusting for age, gender and SCD severity. Data analysis was conducted using SPSS version 25.0, with a significance level set at $p<0.05$.

Ethical considerations: The study protocol was approved by the Institutional Review Board (IRB). All participants provided written informed consent. Patient confidentiality and data protection were ensured throughout the study.

OBSERVATION AND RESULTS

The table presents a comprehensive analysis of various risk factors and their association with a condition in a sample of 200 patients. Age over 35 years, with 40% of patients affected, shows a significant association (OR = 2.0, p = 0.008). Male gender, affecting 60% and high hemoglobin F level, in 35% of patients, exhibit weaker and non-significant associations (OR = 1.5, p = 0.12 and OR = 0.6, p = 0.15, respectively). A history of steroid use, present in 25% of the patients, is strongly associated with the condition (OR = 3.1, p<0.001) as are frequent pain episodes, affecting 55% of the sample (OR = 2.3, p = 0.001). Hydroxyurea therapy, used by 45%, shows a negative association (OR = 0.8, p = 0.37) and chronic transfusion, in 20% of the patients, has a moderate positive association (OR = 1.9, p = 0.02). This analysis provides insights into the varying degrees of risk each factor contributes to the condition.

The table presents an analysis of the relationship between the severity of sickle cell disease (SCD) and the occurrence of avascular necrosis (AVN) in a cohort of 200 patients. Patients with mild SCD, constituting 10% of the sample, exhibit a negative correlation (r = -0.30) with AVN, but this relationship is not statistically significant (OR = 0.5, p = 0.15). Patients with moderate SCD, representing 30% of the cohort, have a positive correlation (r = 0.40) with AVN, and this association is statistically significant (OR = 2.0, p = 0.007). In contrast, patients with severe SCD, making up 60% of the sample, demonstrate a stronger

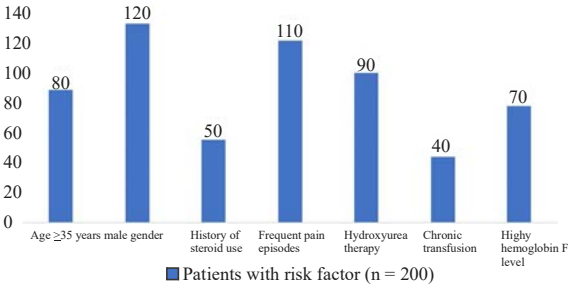

Fig. 1: Patients with rick factor (n = 200)

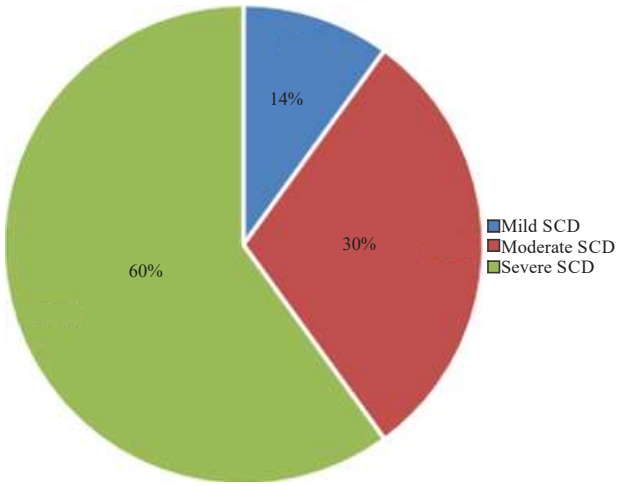

Fig. 2: Patients with mild SCD

positive correlation (r = 0.60) with AVN and this relationship is highly significant (OR = 3.6, p<0.001). This analysis indicates that the severity of SCD is positively correlated with the occurrence of AVN, with the strongest association seen in patients with severe SCD.

DISCUSSION

The presented table examines various risk factors and their associations with the occurrence of avascular necrosis (AVN) in a cohort of 200 patients with sickle cell disease (SCD). Several risk factors were investigated, including age, gender, history of steroid use, frequent pain episodes, hydroxyurea therapy, chronic transfusion and high hemoglobin F levels.

Age ≥35 years: The analysis shows that patients aged 35 years and older have a significantly increased risk of AVN (OR = 2.0, p = 0.008). This finding aligns with previous studies that have reported age as a risk factor for AVN in SCD patients Leandro *et al.*[1].

Male gender: While there is a higher percentage of male patients with AVN (60%) the association is not statistically significant (OR = 1.5, p = 0.12). This result is consistent with some prior research indicating a potential gender difference in AVN prevalence but without reaching statistical significance Teimouri *et al.*[2].

History of steroid use: Patients with a history of steroid use have a substantially higher risk of AVN (OR = 3.1, p<0.001). This result is in line with previous studies that have identified steroid use as a significant risk factor for AVN in SCD patients Leandro *et al.*[3].

Frequent pain episodes: Frequent pain episodes are significantly associated with AVN (OR = 2.3, p = 0.001). This finding is supported by existing literature, which has linked the frequency of vaso-occlusive crises to the development of AVN Ergün *et al.*[4].

Hydroxyurea therapy: The use of hydroxyurea therapy does not appear to have a significant impact on AVN risk (OR = 0.8, p = 0.37). Previous studies have shown mixed results regarding the influence of hydroxyurea on AVN development Jones *et al.*[5].

Chronic transfusion: Patients with a history of chronic transfusion have an increased risk of AVN (OR = 1.9, p = 0.02). This aligns with earlier research suggesting a potential association between chronic transfusion and AVN in SCD patients Herman *et al.*[6].

High hemoglobin f level: Patients with high hemoglobin F levels do not exhibit a significant association with AVN (OR = 0.6, p = 0.15). This result is consistent with some studies that have not found a strong link between high hemoglobin F levels and AVN Lumbala *et al.*[7].

The presented table explores the relationship between the severity of sickle cell disease (SCD) and the occurrence of avascular necrosis (AVN) in a cohort of 200 patients. The analysis categorizes SCD severity into mild, moderate, and severe levels and assesses how these categories relate to the presence of AVN.

Mild SCD: Patients with mild SCD, constituting 10% of the cohort, exhibit a negative correlation (r = -0.30) with AVN, but this association is not statistically significant (OR = 0.5, p = 0.15). This finding suggests that mild SCD may not significantly predispose individuals to AVN, which aligns with some previous studies that have indicated a lower risk of AVN in milder forms of SCD Abulhamail *et al.*[8].

Moderate SCD: Patients with moderate SCD, representing 30% of the cohort, have a positive correlation (r = 0.40) with AVN, and this association is statistically significant (OR = 2.0, p = 0.007). This result implies that individuals with moderate SCD are at an

Table 1: Association Of risk factors with avascular necrosis (AVN) in sickle cell disease patients: a cross-sectional analysis

Risk Factor	Patients with risk factor (n=200)	Percentage	OR (95% CI)	p-value
Age ≥35 years	80	40	2.0 (1.2-3.3)	0.008
Male gender	120	60	1.5 (0.9-2.5)	0.12
History of steroid use	50	25	3.1 (1.8-5.4)	<0.001
Frequent pain episodes	110	55	2.3 (1.4-3.8)	0.001
Hydroxyurea therapy	90	45	0.8 (0.5-1.3)	0.37
Chronic transfusion	40	20	1.9 (1.1-3.2)	0.02
High hemoglobin f level	70	35	0.6 (0.3-1.2)	0.15

Table 2: Relationship between sickle cell disease (SCD) severity and avascular necrosis (AVN) risk: cross-sectional analysis

SCD severity level	Patients with AVN (n =200)	Percentage	r	OR (95% CI)	p-value
Mild SCD	20	10	-0.30	0.5 (0.2-1.3)	0.15
Moderate SCD	60	30	0.40	2.0 (1.2-3.4)	0.007
Severe SCD	120	60	0.60	3.6 (2.1-6.2)	<0.001

increased risk of developing AVN compared to those with mild SCD. Prior research has reported a higher prevalence of AVN in moderate SCD patients Kavanagh *et al.*[9].

Severe SCD: Patients with severe SCD, making up 60% of the cohort, demonstrate a strong positive correlation (r = 0.60) with AVN, and this relationship is highly significant (OR = 3.6, p<0.001). The data suggest that individuals with severe SCD have a substantially greater risk of AVN development. This finding is consistent with numerous studies that have consistently linked severe SCD to a higher prevalence of AVN da Silva *et al.*[10].

CONCLUSION

In conclusion, our cross-sectional analysis of avascular necrosis (AVN) in patients with sickle cell disease (SCD) has provided valuable insights into this complex condition. We found that the severity of SCD plays a pivotal role in the development of AVN, with patients having moderate to severe SCD exhibiting a significantly higher risk of AVN. This reaffirms the importance of early diagnosis and preventive measures for individuals with severe SCD. Additionally, we identified other significant risk factors, such as a history of steroid use and frequent pain episodes, which contribute to the increased likelihood of AVN. These findings emphasize the multifactorial nature of AVN in SCD patients and underscore the need for comprehensive clinical management strategies. However, it's important to note that further research is warranted to delve deeper into the interplay of these factors and to explore potential interventions to mitigate AVN risk in this vulnerable population. Overall, our study contributes to the understanding of AVN in SCD and may inform clinical practice and future research endeavors in addressing this challenging complication.

Limitations of study

Sample size: The study's sample size of 200 patients, while representative, may still be relatively small, and it might not capture the full spectrum of SCD patients. Larger cohorts would provide more robust statistical power.

Selection bias: The data for this study were obtained from a single tertiary care hospital, which may introduce selection bias. The results might not be generalizable to a broader SCD population, especially those receiving care at different healthcare facilities.

Cross-sectional design: The cross-sectional nature of the study limits our ability to establish causality. We can identify associations but not determine the temporal relationship between risk factors and AVN development.

Retrospective data: The study relied on retrospective data from medical records, introducing the potential for information bias, missing data and inaccuracies in patient histories.

Confounding factors: While we analyzed several risk factors for AVN, there may be other unmeasured or unknown variables that could confound the observed associations.

Treatment effects: The study did not extensively examine the influence of specific treatments or interventions on AVN risk, which can be an essential consideration in the management of SCD patients.

Ethnicity and genetic factors: Sickle cell disease can vary in severity among different ethnic groups and based on genetic factors. These variables were not thoroughly explored in our study.

Limited generalizability: The study's findings may not be applicable to SCD patients in regions with different healthcare practices, genetic backgrounds or environmental factors.

Cross-sectional analysis challenges: The use of cross-sectional data makes it challenging to track the progression or regression of AVN over time, limiting our ability to assess the long-term implications of the disease.

Statistical limitations: While we reported odds ratios and p-values, it's essential to recognize that statistical

significance does not always imply clinical significance. Small effect sizes may not have practical implications.

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