African Journal of Urology

REVIEW

Open Access

Predictors of priapism incidence and recurrence in sickle cell disease patients

Agustin J. Nanda De Niro[1*], Gede Wirya Kusuma Duarsa[1], I Wayan Yudiana[1], Nyoman Gede Prayudi[1], Pande Made Wisnu Tirtayasa[1], Kadek Budi Santosa[1] and Yudhistira Pradnyan Kloping[2]

Abstract

Background Sickle cell disease (SCD) is a prevalent genetic blood disorder with a high global incidence rate. Individuals with SCD experience lifelong complications; one such recurrent complication is priapism. Given the unfavorable prognosis and the limited knowledge of patients regarding priapism, healthcare professionals need to identify factors that can aid in diagnosing priapism in SCD patients.

Main body of the abstract A comprehensive literature search was conducted using four databases, namely MEDLINE, The Cochrane Library, ScienceDirect, and Google Scholar, following the PRISMA guidelines. The quality and risk of bias assessment were performed using the ROBINS-I tool (Risk Of Bias in Non-Randomized Studies of Interventions) according to guidelines by the Cochrane Collaboration. The literature search yielded a total of 4434 studies, out of which six studies met the eligibility criteria.

Short conclusions The findings from the selected studies revealed that advancing age and a higher frequency of priapism episodes were significant predictors of priapism occurrence in SCD patients. These findings underscore the importance of early recognition and management of priapism in this patient population.

Keywords Priapism, Sickle cell disease, Predictors

1 Background

Sickle cell disease (SCD) is an inherited genetic disorder of red blood cells that causes abnormal hemoglobin formation, called hemoglobin S (HbS) [1]. Although the actual SCD cases are underreported, SCD is the genetic blood disease with the highest number of cases globally. The high incidence of SCD is worrying because it has been associated with high complication rates in many countries [2, 3].

The main characteristics of SCD are the presence of lifelong chronic hemolytic anemia and intermittent vaso-occlusion which can lead to complications such as tissue ischemia [4]. For male SCD patients, one of the most potential complications is priapism [5].

Priapism is defined as a prolonged erection that is painful, persistent, and unwanted [6]. There are two classifications of priapism: ischemic or low flow and non-ischemic or high flow. Ischemic priapism is the predominant form found in SCD patients. Persistent pain or burning is the clinical manifestation of Priapism. In terms of duration, priapism is divided into two types. The first type is major priapism, where erection lasts ≥ 4 h. Another type is minor priapism, where resolution occurs < 4 h [7, 8]. Scholars found a strong association between priapism and decreased mental health in SCD patients [9, 10].

Prevention of priapism is key to avoid prolonged complications. However, patient's knowledge and awareness of priapism incidence are still limited. For example, a survey of SCD patients showed that only 7% of the study subjects were aware of priapism and its potential to arise

*Correspondence:
Agustin J. Nanda De Niro
deniro_nanda@yahoo.co.id
[1] Urology Surgery Department, Prof. dr. I.G.N.G Ngoerah General Hospital, Jalan Diponegoro, Dauh Puri Kelod, Denpasar, Bali 80113, Indonesia
[2] Airlangga University, Jalan Mayjen Prof. Dr. Moestopo No.47, Surabaya, East Java 60132, Indonesia

[6]. Therefore, the current research conducted a systematic review to search and evaluate the incidence of priapism in SCD patients, hoping that various predictors of priapism can be identified to become the guidelines for preventing the incidence and recurrence of priapism in SCD patients.

2 Main text

2.1 Study design

This systematic review was prepared using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. These guidelines helped the authors to analyze factors that can be predictors of priapism incidence in SCD patients.

2.2 Search strategy

The authors conducted literature research that was published in widely used electronic databases, including MEDLINE, the Cochrane Library, Science Direct, and Google Scholar. Studies included in this literature review were those written in Indonesian or English languages. The selection of journals that emerged from the literature research was made independently by the authors. Any differences of opinion were resolved by brainstorming and discussion between the authors.

To guide the authors, several keywords were used, such as priapism, anemia, predictors of priapism and anemia, anemia and predictors, priapism and anemia, and predictors. These keywords were searched in appropriate combinations. They were also used in series and through truncation.

2.3 Selection criteria

2.3.1 Inclusion and exclusion criteria

In this study, the authors used three inclusion criteria: (1) observational and interventional studies, (2) having SCD patients who experienced priapism, and (3) assessed predictors of priapism as study outcomes. Meanwhile, the exclusion criteria included: (1) inaccessible studies and (2) non-research articles.

2.4 Extraction and data analysis

The authors independently reviewed the content of each literature and extracted data from the following variables: (1) author names, (2) year of publication, (3) study characteristics including study design, sampling method, and study location, (4) characteristics of study subjects including sample size and participant characteristics, and (5) study results including a description of priapism such frequency, duration, and type, laboratory parameters analyzed, frequency and duration of priapism, and age of participants.

After extracting the data, separate analyses of laboratory findings with similar effect sizes were conducted to evaluate their combined effect. The effect size analysis for categorical variables was performed using Odds Ratio (OR), while Standardized Mean Difference (SMD) was used for numerical or continuous variables. Utilizing Cohen's (d) value, SMD was designed to differentiate between two groups on a continuous dependent variable and could be calculated from means, standard deviations, *t* tests, and one-way ANOVA.

To assess heterogeneity among studies, this research used I^2. The fixed-effect model was employed when $I^2 < 50\%$, while the random-effect model was used when $I^2 > 50\%$. A coefficient estimate (β) was used as the effect size for meta-analysis (ES). Results were considered statistically significant when $p < 0.05$ (2-tailed). A forest plot was utilized to report the analysis results, and publication bias was assessed using a Funnel plot. All data were analyzed using JASP and STATA version 15 software for Mac OS.

2.5 Quality assessments and risk of bias

The quality assessments and risk of bias of each piece of literature were conducted using the risk of bias tool according to guidelines by the Cochrane Collaboration. These guidelines evaluate the accuracy of the literature using seven domains: bias due to confounding, bias in the selection of participants, bias in the classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in the measurement of outcomes, and bias in the selection of the reported result. The scoring of each domain is separated according to the risk of bias and its application. The risk of each study was assessed and categorized as "low," "moderate," "serious," "critical," and "no information." The risk of bias assessment was evaluated by the authors collaboratively through discussion.

2.6 Study results

The initial literature research obtained 4434 studies in four databases. The research then reviewed the title and abstract and yielded 68 relevant studies. After excluding seven studies due to access barriers and eight duplicate studies, 53 studies were included in the whole-text screening process. A total of 47 studies were eventually excluded for the following reasons. Eight studies were excluded because they had different target participants, and 28 studies were ineligible because of outcome differences. The other 11 studies were omitted because the study design did not match our systematic literature review leaving the final six studies to proceed to the data

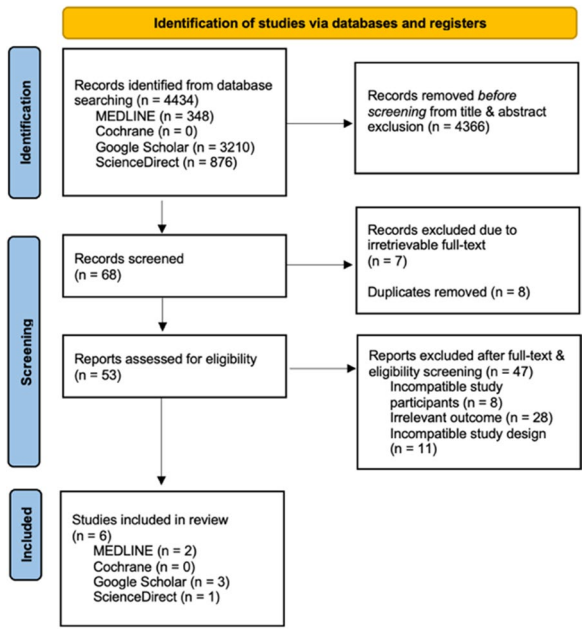

Fig. 1 Literature research chart based on PRISMA 2020

analysis stage. The process of the literature research is summarized in Fig. 1.

2.7 Bias risk assessment

The quality of each study was comprehensively evaluated using the ROBINS-I tool (Risk Of Bias in Non-Randomized Studies—of Interventions). This tool was used according to guidelines by the Cochrane Collaboration. Most studies had sufficient information and met the criteria to be classified as "Low risk." (Figs. 2 and 3)

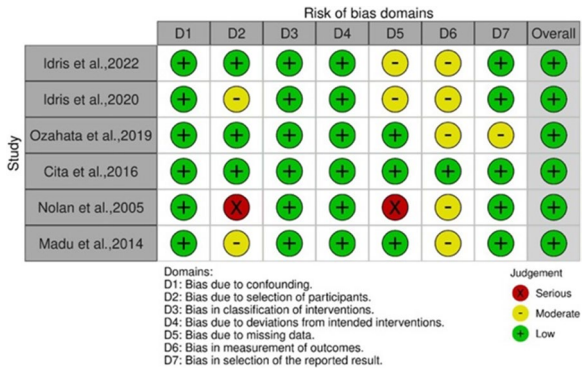

Fig. 2 Risk of bias summary: review author's assessment of each risk of bias for each included study

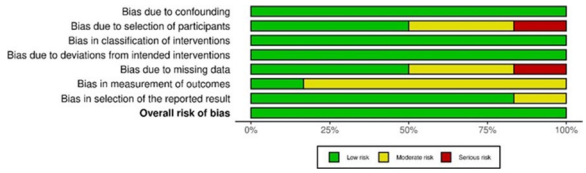

Fig. 3 Risk of bias chart: review author's assessment of each risk of bias item, presented as a percentage of all included studies

2.8 Population

The six studies included in this literature review were conducted in Nigeria, Brazil, France, and the USA. The studies involved a total of 3321 subjects experiencing SCD, including 781 who had a history of priapism. The age range of the participants was 0–77 years, with the majority of the study subjects belonging to adulthood.

2.9 Intervention

The 196 participants of this study received treatment interventions during the study period. The treatment intervention was divided into daily medication and surgical intervention. The medications included stilbesterol, analgesics, hydroxyurea, hydroxycarbamide, finasteride, intrapenile etilefrine injection, transfusion, penile aspiration, and surgical shunt.

2.10 Comparison

A qualitative and quantitative comparison of risk factors was performed in SCD patients with and without priapism. Age and several laboratory indicators, including hemoglobin, reticulocyte count, leukocyte count, and platelet count, were quantitatively analyzed across studies. On the other hand, the analysis of priapism episodes was conducted qualitatively due to variations in categorical definitions between studies.

2.11 Research results age

A pooled analysis was conducted on three out of six studies with sufficient data to compare the age of patients with priapism and non-priapism. The literature has discussed how older age increases the risk of priapism in SCD patients. This risk is usually associated with unfavorable vascular changes and increased morbidity, such as hypertension and diabetes mellitus. However, several studies still yielded varied results.

The effect size of age in this meta-analysis was calculated using standardized mean difference (SMD). Using a random-effect model ($I2 = 58\%$), the forest plot displayed three studies evaluating the effect of age on priapism occurrence in SCD patients (Fig. 4). The results showed a significant association between increasing age

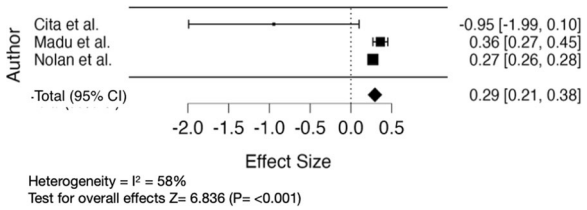

Fig. 4 Forrest plot of age effect on priapism

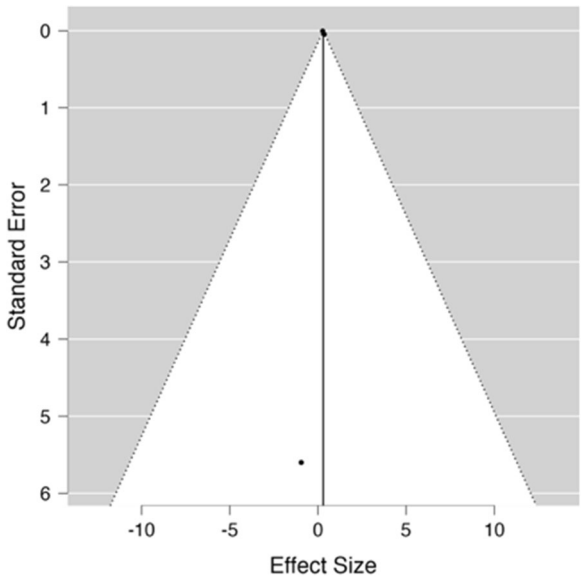

Fig. 5 Funnel plot of age effect on priapism

and priapism occurrence in SCD patients (standardized mean difference [SMD]: 0.29; 95% Confidence Interval [CI]: 0.21–0.38, $p < 0.001$). Further, the included funnel plot indicated a potential significant publication bias with Kendall's τ value of 0.056. (Fig. 5)

3 Laboratory indicators

Various laboratory parameters were analyzed and compared between patients with and without priapism, including the degree of difference from the normal range. One study revealed a significant association between hemoglobin levels and the incidence of priapism. Additionally, two other studies demonstrated significant differences in reticulocyte, LDH, and leukocyte levels between patients with priapism and those without. However, only a few laboratory indicators had sufficient data for pooled analysis in this study. These included hemoglobin (3 studies), reticulocyte count, leukocyte count, and platelet count (4 studies). The effect size analysis for these four laboratory indicators was conducted using SMD due to the continuous nature of the data. The forest plot, utilizing a random-effect model ($I^2 = 99\%$), displayed the results of each pooled analysis for the four different indicators (Fig. 6). The results revealed no significant association between the laboratory indicators and the occurrence of priapism in patients with sickle cell disease ($p > 0.05$). Furthermore, the included funnel plot indicated a potential significant publication bias with Kendall's τ values of 5.01 (Hb), 5.45 (reticulocyte), 0.85 (leucocyte), and 0.59 (platelet). (Fig. 7).

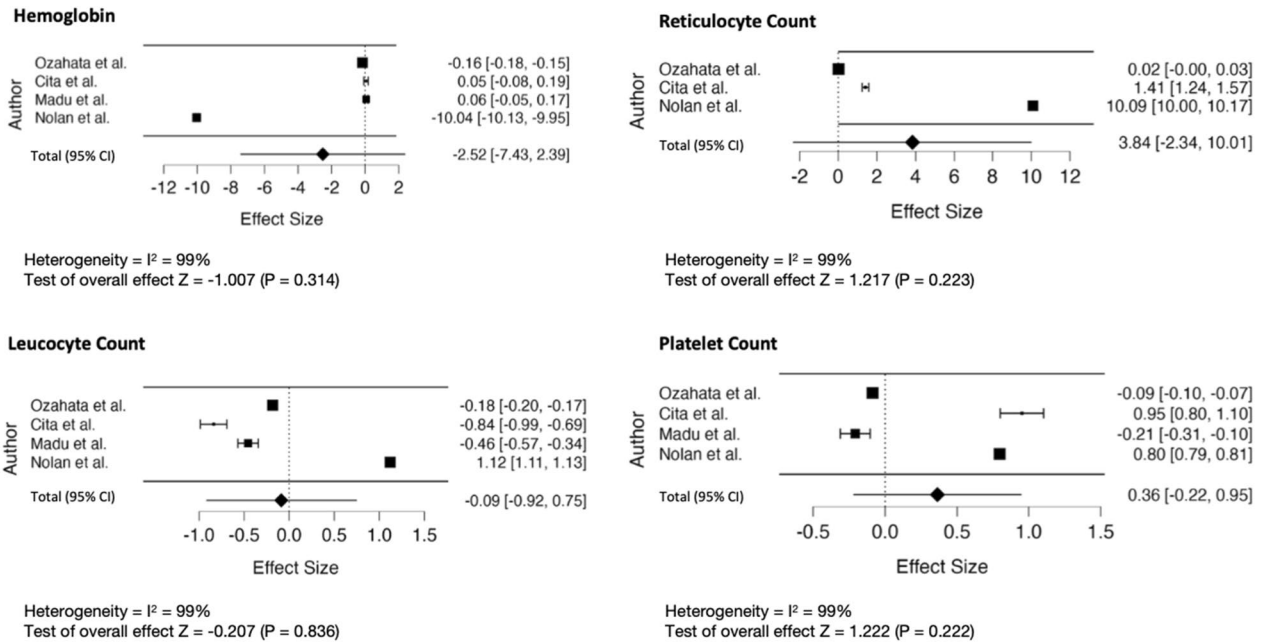

Fig. 6 Forrest plot of several laboratory indicators in predicting priapism

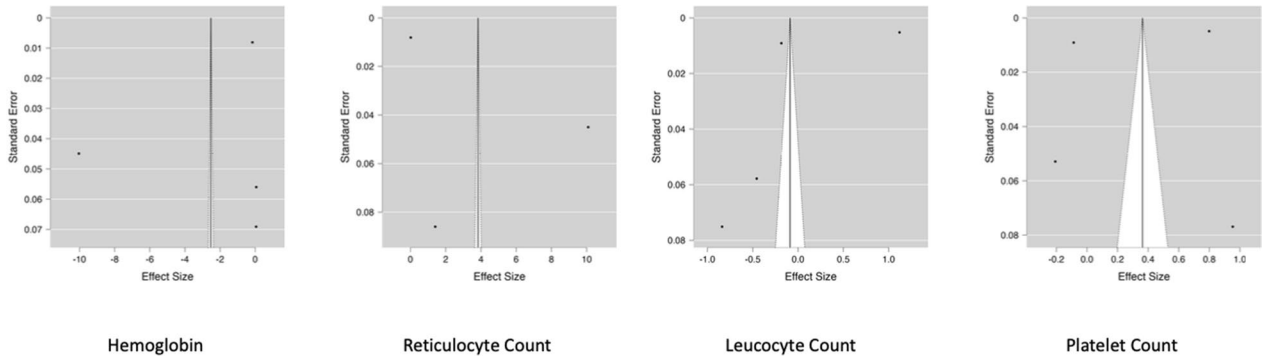

Fig. 7 Funnel plot of several laboratory indicators in predicting priapism

4 Frequency of priapism

The frequency of priapism cannot be assessed through pooled analysis due to the varying categories used in each study. However, the majority of studies (4/6) reported that the frequency of priapism was a predictor of future priapism recurrence.

4.1 Predictors of priapism incidence and recurrence in sickle cell disease patients

Advances in medical research and studies have improved the survival rate of SCD patients. As a result, the wide spectrum of morbidity from SCD has become apparent, leading to a shift in the focus of studies from reducing mortality from SCD to reducing morbidity and complications of SCD such as priapism. In other words, improvement of the life quality of these patients is the goal of the majority of current studies [9, 11, 12].

Priapism is common in patients with SCD. The risk of developing priapism increases with age in men with SCD. Several studies have reported the incidence of priapism to be around 30% to 40% in men with SCD, and the cumulative incidence reaches 60% by age 40 [9, 13, 14]. Specifically, this study found that increased age was associated with a higher risk of developing priapism. This association may be attributed to age-related changes in vascular function and an increased prevalence of comorbidities such as hypertension and diabetes mellitus. Moreover, the recurrent nature of priapism significantly impacts the quality of life for individuals with SCD. Despite the burden of priapism, many patients do not seek treatment. One study found that 50% of priapism patients in their study did not take any action to address their condition [14, 15]. Similarly, in this study, only 5.9% of priapism patients received treatment. Several factors contribute to this trend, including limited awareness and understanding of priapism, embarrassment experienced by patients, and the intermittent nature of the condition. These factors often make patients hesitate to seek medical assistance [8, 16].

While there is no pooled analysis evidence, most studies showed that men who experience at least three episodes of priapism are at a higher risk of recurrence [9, 10, 15, 17]. Therefore, this study recommends these individuals seek medical consultation every three months to monitor their condition closely. Each episode of priapism within these three months significantly amplifies the risk of developing severe priapism. Managing priapism involves using subjective approaches, including vaso-reactive agents, antidepressants, and α-blockers. However, careful consideration should be given to discontinuing these therapies [9].

In terms of laboratory indicators, apart from those reported in the pooled analysis, it is difficult to draw definitive conclusions because each study examines variables of interest with various biases and confounding considerations. With the limited literature in this study, conclusions about differences in laboratory risk indicators are difficult to express unequivocally.

4.2 Education challenges and strategies

One of the notable yet unrecognized difficulties often faced by SCD patients with priapism is mental health challenges. The high rate of depression, anxiety, and suicidality have been associated with poor medical compliance and low quality of life. Patients tend to disregard their symptoms and dismiss medical help because of embarrassment. Unfortunately, some patients who presented with depression or suicidal ideation were prescribed treatment with medication that could worsen priapism symptoms. Hence, pharmacists should also discuss the risk of priapism with patients receiving drugs about the possible side effects. Such cases indicate the importance of a multidisciplinary approach in priapism management [18, 19].

Collaborative efforts must be pursued when patients come and seek treatment. The authors recommend that all SCD patients with the first episode of priapism should consult a psychiatrist, as this condition can lead to anxiety or depression.

As priapism is related to permanent dysfunction, preventive efforts, especially education from interprofessional team members to patients, are crucial. When patients are discharged from the hospital, the in-charged medical staff should educate the patients regarding the importance of seeking medical help as soon as priapism symptoms develop. The characteristics of priapism must be well documented by clinicians, and follow-up by a urologist must be encouraged. Comprehensive strategies are recommended to encompass urologists, hematologists, and psychiatrists in patients with mental health complaints.

5 Conclusions

Priapism is a common complication observed in men with SCD. It is a recurring condition that can intermittently manifest throughout the lifelong course of SCD. Given the significant impact and poor prognosis associated with priapism, it is crucial to identify factors that can predict its incidence and recurrence. This study indicates that advancing age and a higher frequency of priapism episodes predict priapism occurrence in SCD patients. Unfortunately, there is a lack of awareness among the public, particularly individuals with SCD, regarding the signs and symptoms of priapism. As a result, this condition is underrecognized among healthcare professionals. The authors recommend the development of educational programs within the interprofessional medical team so that SCD patients can identify or predict the signs of priapism and seek medical help before complications develop. In addition, collaborative cooperation must be pursued between urologists, hematologists, and psychiatrists to provide comprehensive treatment for priapism in SCD patients. Through the implementation of these efforts, we believe the number of priapism relapses and the consequent complications in SCD patients can be reduced significantly.

Appendix 1

No	Author, year	Location of study	study Design	Number of Participants	Characteristics of participants	Research objectives	Intervention
1	Idris et al., 2022 [10]	Nigeria	Prospective	71 subjects with SCD	Men with SCD aged between 18–40 years who had experience ≥ 3 episode of priapism in the past 12 months Seven (9.6%) of the subjects were married	Proving the hypothesis that estimation of incidence of priapism through clinical history of priapism is lower than pain diaries of priapism, as well as evaluating predictors of major priapism	Stilbesterol (24%), Analgesic (24%), Hydroxyurea (12%), Penile aspiration (2.7%), Surgical Shunt (1.4%)
2	Idris et al., 2020 [9]	Nigeria	Cross-sectional	500 SCD patients, with 163 patients (32.6%) experiencing priapism	Men with an age range of 18–40 years old. A total of 43 (8.6%) subjects with SCD were married	Evaluate the characteristics and types of Priapism to prove the hypothesis that sexual dysfunction is more common in SCD patients	84 subjects undergoing treatment

No	Author, year	Location of study	study Design	Number of Participants	Characteristics of participants	Research objectives	Intervention
3	Ozahata et al., 2019 [15]	Brazil	Case–control	1.314 subjects with 188 subjects having Priapism	Patients with sickle cell anemia between 0 and 77 years old	Characterize the clinical and genetic factors associated with Priapism in sickle cell anemia patients	Transfusion (28.5%) Cavernous aspiration (17.5%) Finasteride (13%) Analgesic (13%) Hidroxyurea (1.5%)
4	Cita et al., 2016 [17]	France	Prospective	58 subjects with SCD, 28 subjects with priapism and 30 subjects without priapism	Patient with a history of Priapism	Investigate the association of Priapism in SCD patients with hemolytic and bleeding parameters	Hydroxycarbamide in 22 patients Surgery in 3 patients Intrapenis ethylephrine injection in 4 patients Transfusion in 2 patients
5	Nolan et al., 2005 [12]	United States of America	Case–control	1.252 subjects with SCD, 273 subjects with priapism and 979 subjects without priapism	273 patients with a history of Priapism	Analyzed the clinical and hematological characteristics of SCD patients with Priapism	N/A
6	Madu et al., 2014 [18]	Nigeria	Retrospective	126 subjects with SCD, 28 subjects with priapism and 95 subjects without priapism	126 subjects with an age range of 13–55 years who have experienced Priapism	Evaluate the association of Priapism incidence with clinical and laboratory parameters in homozygous SCD	N/A

Appendix 2

No.	Author, Year	Study design	Predictors of priapism incidence				
			Age	Lab Parameters	Frequency of Priapism	Duration of Priapism	Type of Priapism
1	Idris et al., 2022 [10]	Prospective Cohort over 12 months	Median age 24.0 years (IQR 21.5–28.5)	Median total Hemoglobin 8 g/dL (6.9–9.6) LDH 540 U/L (379–729) Thrombocytes 297.000/microliter Leukocytes 13.3×10^9/L (9.6–17.6)Bilirubin 79.0 mg/dL(46.5–125.5) AST 46 IU/L (34.5–59)	80% of men experience at least 1 instance of Priapism	Average 120 min with IQR 25.-180 min	Major Priapism ($n=18$) Minor Priapism ($n=264$)
2	Idris et al., 2020 [9]	*Cross-sectional*	Mean age 23.6 years	N/A	Every day ($n=13$) Every other day ($n=14$) Every week ($n=31$) Every month (51) Rarely ($n=54$)	N/A	Major Priapism in 43 subjects (26.4%) *Stuttering* in 120 subjects (73.6%)
3	Ozahata et al., 2019 [15]	Case–control	0–9 years old = 6%	Average from Priapism Patients	1 episode ($n=21$)	1 h for 10 people (16%)	Recurrent Priapism ($n=8$)
			10–17 years old = 8%	Hemoglobin 9.04 g/dL (4.86–15.7)	2 episodes ($n=11$)	2 h for 6 people (9.5%)	Major Priapism ($n=8$)
			18–29 years old = 24%	Reticulocytes10.36% (0.8–26.2)	3 episodes ($n=3$)	3 h for 11 people (17.5%)	Minor Priapism(n = 27)
			30–41 years old = 27%	Thrombocytes 396.000 per microliter	5 episodes ($n=11$)	4 h for 2 people (3%)	

No.	Author, Year	Study design	Predictors of priapism incidence				
			Age	Lab Parameters	Frequency of Priapism	Duration of Priapism	Type of Priapism
			42 + years old = 17%	Bilirubin 1.75 mg/dL	6 episodes ($n=11$)	6 h for 6 people (9.5%)	
				Leukocytes 10.6×10^9/L			
				Average from Non-Priapism Patients			
				Hemoglobin 8.82 g/dL			
				Reticulocytes 10.15%			
				Thrombocytes 397.000 per microliter			
				Bilirubin 1.76 mg/dL			
				Leukocyte 11.2×10^9/L			
4	Cita et al., 2016 [17]	Prospective for 1 year 10 months	Median age 39 years (IQR 26–46)	Median from Priapism Patients	Multiple episodes ($n=23$)	N/A	Major Priapism ($n=3$)
				Hemoglobin 8.6 g/dL (7.6–9.4)	< 1 episode per year ($n=10$)		
				Reticulocytes 8.2% (6.2–10.5)*	1 episode per year: ($n=3$)		
				LDH 442 IU/L (381–618)*	1 episode per month ($n=5$)		
				Hemolytic Index 0.52 ± 1.7*	1 episode per week ($n=4$)		
				Leukocytes 9×10^9/L (6.5–9.6)	Every day ($n=1$)		
				AST 34 IU/L (31–42)			
				Thrombocytes 331.000 per microliter			
				Median from Non-Priapism Patients			
				Hemoglobin 8.5 g/dL (7.5–9.6)			
				Reticulocytes 6.2% (4.2–9.0)*			
				LDH 348 IU/L (292–493)*			
				Hemolytic Index -0.50 ± 1.2*			
				Leukocytes 7.9×10^9/L (5.1–9.1)			
				AST 28 IU/L (23–34)			
				Thrombocytes 277.000 per microliter			
5	Nolan et al., 2005 [12]	Case–control	Mean age 26.2 ± 12.28 SD	Average from Priapism Patients	N/A	N/A	N/A
				Hemoglobin 8.64 ± 0.13 g/dL*			
				Bilirubin 3.52 ± 0.13 mg/dL*			
				LDH 526.19 ± 13.08 g/dL*			
				Reticulocytes 11.67 ± 0.35*			
				Thrombocytes 425.660 ± 7.61 per microliter *			

No.	Author, Year	Study design	Predictors of priapism incidence				
			Age	Lab Parameters	Frequency of Priapism	Duration of Priapism	Type of Priapism
				Leukocytes $11.62 \pm 0.20 \times 10^9$/L*			
				AST 50.34 ± 1.44 units/L*			
				MCV 89.82 ± 0.48 μm^3*			
				Average from Non-Priapism Patients			
				Hemoglobin 9.51 ± 0.07 g/dL*			
				Bilirubin 2.92 ± 0.07 mg/dL*			
				LDH 459.23 ± 6.92 g/dL*			
				Reticulocytes 9.37 ± 0.18*			
				Thrombocytes 358.160 ± 4.04 per microliter *			
				Leukocytes $10.18 \pm 0.10 \times 10^9$/L*			
				AST 45.78 ± 0.76 units/L*			
				MCV 87.18 ± 0.25 μm^3*			
6	Madu et al., 2014 [18]	Retrospective	Mean age 26.8 ± 15.4 SD with a median of 26	Average from Priapism Patients	N/A	N/A	N/A
				Hemoglobin 7.9 g/dL			
				Thrombocytes 323.000 per microliter			
				Leukocytes 10.5×10^9/L*			
				Average from Non-Priapism Patients			
				Hemoglobin 7.6 g/dL			
				Thrombocytes 354.000 per microliter			
				Leukocytes 13.9×10^9/L*			

*Indicates laboratory parameters that have a p value < 0.05 between SCD patients with Priapism and the control group.

Abbreviations

SCD	Sickle cell disease
HbS	Hemoglobin S
LDH	Lactate dehydrogenase
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
OR	Odds ratio
SMD	Standardized mean difference
ES	Effect size
ROBINS-I:	Risk of bias in non-randomized studies of interventions

Acknowledgements
Not applicable.

Author contributions
This work was carried out in collaborations among all authors. Authors AJND and GWKD design the study and performed the data collection. Authors AJND, IWY, NGP, and PMWT manage the data analysis and intepretation of the study. Authors AJND, IWY, NGP, PMWT, KBS and YPK wrote the article's first draft. Authors AJND and YPK made a critical revision. All authors read and approved the final manuscript.

Funding
Not applicable.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Received: 30 March 2023 Accepted: 27 August 2023
Published online: 14 September 2023

References

1. Alrayyes S, Baghdan D, Haddad RY (2018) Sickle cell disease; an overview of the disease and its systemic effects. Dis Mon 64(6):283–289. https://doi.org/10.1016/j.disamonth.2017.12.003
2. Lubeck D, Agodoa I, Bhakta N (2019) Estimated life expectancy and income of patients with sickle cell disease compared with those without sickle cell disease. JAMA Netw Open 2(11):e1915374. https://doi.org/10.1001/jamanetworkopen.2019.15374
3. Grossi G (2018) New estimate for the risk of child mortality due to sickle cell anemia in Africa. https://www.hcplive.com/view/new-estimate-risk-child-mortality-sickle-cell-anemia-in-africa. Accessed Mar 24 2023
4. Weatherall DJ (2013) Sickle cell anemia-in brenner's encyclopedia of genetics: 2nd edn. 6:429–431. Elsevier, Oxford. https://doi.org/10.1016/b978-0-12-374984-0.01421-2
5. Akil H, Gordon J, Hen R (2017) Treatment resistant depression: a multi-scale, systems biology approach. Neurosci Biobehav Rev 84:1–56. https://doi.org/10.1016/j.neubiorev.2017.08.019
6. Tanabe P, Spratling R, Smith D (2019) Understanding the complications of sickle cell disease. Am J Nurs 119(6):26–35. https://doi.org/10.1097/01.naj.0000559779.40570.2c
7. Alvaia MA, da Silva Maia HAA, de Medeiros NA (2022) Prevalence of priapism in individuals with sickle cell disease and implications on male sexual function. Einstein 18:1–6. https://doi.org/10.31744/einstein_journal/2020AO5070
8. Whyte N, Blidgen BM, Asnani M (2021) Priapism in sickle cell disease: an evaluation of the knowledge of an at risk population in Jamaica. Sex Med 9:1–6. https://doi.org/10.1016/j.esxm.2021.100339
9. Idris IM, Abba A, Galadanci JA (2020) Men with sickle cell disease experience greater sexual dysfunction when compared with men without sickle cell disease. Blood Adv 4(14):3277–3283. https://doi.org/10.1182/bloodadvances.202000206
10. Idris IM, Abba A, Galadanci JA (2022) Incidence and predictors of priapism events in sickle cell anemia: a diary-based analysis. Blood Adv 6(20):5676–5683. https://doi.org/10.1182/bloodadvances.202200728
11. Hou L, Jing Y, Trock B (2022) PD47-12 predicting major ischemic priapism: a novel dynamic nomogram based on recurrent ischemic priapism risk factors. J Urol 207(5S):798. https://doi.org/10.1097/JU.0000000000002615.12
12. Nolan VG, Wyszynski DF, Farrer LA (2005) Hemolysis-associated priapism in sickle cell disease. Blood 106(9):3264–3267. https://doi.org/10.1182/blood-2005-04-1594
13. Alkindi S, Almufargi SS, Pathare A (2019) Clinical and laboratory parameters, risk factors predisposing to the development of priapism in sickle cell patients. Exp Biol Med. https://doi.org/10.1177/1535370219892846
14. Alkindi S, Almufargi S, Pathare A (2018) Risk factors predisposing development of priapism in sickle cell disease patients. Blood 132(Supplement 1):4917. https://doi.org/10.1182/blood-2018-99-118475
15. Figueiredo CVB, Santiago RP, da Guarda CC (2021) Priapism in sickle cell disease: associations between NOS3 and EDN1 genetic polymorphisms and laboratory biomarkers. PLoS ONE 16(2):1–15. https://doi.org/10.1371/journal.pone.0246067
16. Ozahata MC, Page GP, Guo Y (2019) Clinical and genetic predictors of priapism in sickle cell disease: results from the recipient epidemiology and donor evaluation Study III Brazil cohort study. J Sex Med 16:1–12. https://doi.org/10.1016/j.jsxm.2019.09.012
17. Kato GJ, McGowan V, Machado RF (2006) Lactate dehydrogenase as a biomarker of hemolysis-associated nitric oxide resistance, priapism, leg ulceration, pulmonary hypertension, and death in patients with sickle cell disease. Blood 107(6):2279–2285. https://doi.org/10.1182/blood-2005-06-2373
18. Cita KZ, Brureau L, Lemonne N (2016) Men with sickle cell anemia and priapism exhibit increased hemolytic rate, decreased red blood cell deformability and increased red blood cell aggregate strength. PLoS ONE 11(5):1–10. https://doi.org/10.1371/journal.pone.0154866
19. Madu AJ, Ubesie A, Ocheni S (2014) Priapism in homozygous sickle cell patients: important clinical and laboratory associations. Med Princ Pract 23:259–263. https://doi.org/10.1159/000360608
20. Idris IM, Burnett AL, DeBaun MR (2022) Epidemiology and treatment of priapism in sickle cell disease. Hematology 2022(1):450–458

Publisher's Note