International Journal of Research in Medical Sciences
Jaishetwar GS et al. Int J Res Med Sci. 2023 Feb;11(2):600-605
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20230171

Original Research Article

A cross-sectional study on pain management during vaso-occlusive crisis in sickle cell disease

Ganesh S. Jaishetwar[1], Fouqia Mahnaz Khanam[2]*

[1]Department of Hematology and Bone Marrow Transplant, Yashoda Hospital, Somajiguda, Hyderabad, Telangana, India
[2]Doctor of Pharmacy, Shadan College of Pharmacy, Hyderabad, Telangana, India

Received: 27 November 2022
Revised: 29 December 2022
Accepted: 12 January 2023

***Correspondence:**
Dr. Fouqia Mahnaz Khanam,
E-mail: fouqiakhanam@gmail.com

ABSTRACT

Background: Sickle cell disease is an inherited hematological disorder characterized by hard and sticky red blood cells that appears like a C-shaped "sickle" in contrast to the healthy, round red blood cells which tend to stick and clog the blood vessels during blood flow leading to pain or vaso-occlusive crisis.
Methods: A cross-sectional study was conducted at Yashoda hospital in Hyderabad, India. Data regarding the management of acute pain during VOC in SCD patients was gathered from the hematology department on a daily basis during the duration of the study**.** The data was recorded in an online questionnaire form and a subsequent DUE was conducted.
Results: Among all the patients that were enrolled in the study, acute pain as VOC was presented in 72%, whereas 28% did not experience pain. Pain was manifested as acute chest syndrome, generalized body pain, headache. Crizanlizumab, a monoclonal antibody was administered to patients who were ≥16 years to decrease the frequency of VOC. Upon DUE, per prescription distribution of crizanlizumab was 11.2%, while 88.8% constituted of anti-metabolites, antibiotics, analgesics, opiate antagonist, etc. Frequency of use of crizanlizumab among SCD patients was 69.23%
Conclusions: Management of VOC cannot be described as one size fits all. Interindividual variability must be considered at all times during planning and implementing a treatment regimen. Assessment of pain on pain scale to ensure targeted treatment at maximum effective concentration followed by titration of dose to reduce the occurrence of tolerance, withdrawal, dependence and addiction should be basis of management.

Keywords: Sickle cell disease, Pain management, Vaso-occlusive crisis, Drug utilization evaluation, Crizanlizumab

INTRODUCTION

Sickle cell disease (SCD) is a hematological disorder which is inherited and characterized by hard and sticky red blood cells that appears like a C-shaped "sickle" in contrast to the healthy, round red blood cells. Sickle cells have a short life-span ultimately resulting in a shortage of red blood cells within the body and these cells also tend to stick and clog the blood vessels during blood flow leading to pain or vaso-occlusive crisis.[1] SCD is termed as a single gene disorder which can cause chronic anaemia, acute chest syndrome, organ infraction, stroke, chronic organ damage and a significant reduction in life expectancy.[2]

Types of SCD

Following are the most common types of SCD; HbSS: patients with this form of SCD inherit two sickle cell genes "S", one from each parent. This is commonly called as sickle cell anemia and this is usually categorized as the

most severe form of the disease. HbSC: patients with this form of SCD inherit a sickle cell gene "S" from one parent and from the other parent a gene for abnormal hemoglobin "C". This is usually categorized as a milder form of SCD.

HbS beta thalassemia

Patients with this form of SCD inherit one sickle cell gene "S" from one parent and one gene for beta thalassemia, another type of anemia, from the other parent. There are classified into two types: "0" and "+". Those with HbS beta 0-thalassemia have a severe form of SCD and those with HbS beta +-thalassemia are said to have a milder form of SCD. There also are a few rare types of SCD: HbSD, HbSE, and HbSO: patients with these forms of SCD inherit one sickle cell gene "S" and one gene from an abnormal type of hemoglobin "D", "E", or "O". HbAS: patients with Sickle Cell Trait inherit one sickle cell gene "S" from one parent and one normal gene "A" from the other parent. People with SCT usually do not have any signs or manifestations of the disease and lead a normal life, but it is possible that they can pass the trait on to their children.[3]

Cause of SCD

SCD is a genetic condition and it is caused when a patient inherits one or more faulty genes from their biological parents. If a patient inherits a faulty gene from just one parent, then they will have sickle cell trait (SCT) but not sickle cell disease. If a patient inherits a faulty gene from each parent, then they will have sickle cell disease (SCD).[4]

Pathophysiology

When exposed to a deoxygenated environment, red blood cells (RBCs) with HbS or HbS in conjunction with other defective alleles go through polymerization and become hard. Due to their increased density and propensity for hemolysis, stiff RBCs can have an adverse effect on endothelial vessel wall integrity and blood flow. The rigid RBCs cause hemolysis, tissue ischaemia, infarction, and vaso-occlusion. Nitric oxide consumption, haemolysis-linked nitric oxide dysregulation, and endothelial dysfunction are all side effects of hemolysis that contribute to problems such leg ulcers, stroke, pulmonary hypertension, and priapism. Sickle RBCs (sRBC) have a half-life of just 10 to 20 days, compared to normal RBCs, which have a half-life of about 120 days. Intravascular hemolysis causes free haemoglobin to accumulate in the serum during acute sickling, while RBCs gain Na^+, Ca^{2+}, and lose K^+ in proportion. The calcium pump becomes dysfunctional as the concentration of Ca^{2+} rises. Although calcium is dependent on ATPase, it is not known how calcium contributes to the stiffness of membranes related to cytoskeletal membrane contacts. Additionally, hypoxia prevents the synthesis of nitric oxide, which leads to sickle cells adhering to the arterial endothelium. Extracellular matrix production rises as a result of erythrocyte lysis which causes a rise in extracellular haemoglobin that further increases the affinity and binding of the haemoglobin to nitric oxide or nitric oxide precursors, decreasing the levels of the nitric oxide precursor and promoting vasoconstriction.[5]

Manifestations

Yellowing of the skin or eye whites as a result of a significant number of red cells undergoing hemolysis. Anemia-related tiredness or fatigue. Dactylitis, a painful swelling of the hands and feet.[6]

Evaluation

The majority of sickle cell disease patients are identified through newborn or prenatal screening. Hemoglobin electrophoresis, which measures the different forms of haemoglobin and finds different hemoglobinopathies, is the basis for the diagnosis. Complete blood count (CBC) with differential, reticulocyte count, full metabolic panel, LDH level, bilirubin level, determination of blood type, and crossmatch for potential transfusion therapy make up the typical lab examination for patients with symptoms. If an infectious process is suspected, appropriate cultures should be collected, including blood cultures.[7]

Complications

Complications of sickle cell disease include acute chest syndrome, acute pain crisis, chronic pain, delayed growth and puberty, eye problems, gallstones, heart problems, infections, joint problems, kidney problems, leg ulcers, liver problems, problems during pregnancy, priapism, severe anemia, aplastic crisis, splenic sequestration crisis, stroke or silent brain injury.[8]

Management

The goal of sickle cell disease management is to reduce or eliminate pain episodes, symptoms, and consequences. Blood transfusions and medicines are possible forms of treatment. A stem cell transplant may be able to provide cure for the condition in certain children and teenagers.

Medications

Hydroxyurea (Hydrea): Daily hydroxyurea usage lowers the frequency of pain crises and may lessen the requirement for hospital stays and blood transfusions. It is contraindicated in pregnancy. Oral L-glutamine powder (Endari): This medication has been given FDA approval to treat sickle cell anaemia. It helps to lessen the overall frequency of pain crises. Crizanlizumab (Adakveo): This medication, administered intravenously, can assist in lowering the frequency of pain crises in both adults and children older than 16. Neonasal symptoms, joint discomfort, back pain, and fever are possible side effects. Voxelotor (Oxbryta): This medication is used to treat adults and children over the age of 12 who have sickle cell disease. This medication, when taken orally, can increase blood flow throughout the body and reduce the risk of

anaemia. Headache, nausea, diarrhoea, exhaustion, rash, and fever are some of potential side effects. Pain-relieving medications: Narcotics and analgesics are prescribed to help relieve pain during sickle cell pain crises.[9]

Types of pain in sickle cell disease

Acute pain: acute painful episodes should be treated as a medical emergency in sickle cell disease patients because it often results from a vaso-occlusive crisis (VOC). VOC develops when sickle-shaped red blood cells obstruct tiny blood arteries, preventing normal blood flow. This results in discomfort and tissue damage.

Chronic pain: pain that lasts for three to six months or more is considered chronic. In sickle cell illness, chronic pain may be a continuation of recurring painful episodes, while the exact cause is unknown. Neuropathic pain, which is brought on by damaged nerves, is frequently linked to chronic pain. It's frequently described as tingling, burning, numbing, or lancinating (sharp), and it can even be compared to a pins-and-needles sensation. Neuropathic pain is caused by the occlusion of blood vessels that supply nerves ultimately resulting in nerve cell damage or by persistent chronic pain.

Pain management guidelines

Acute pain management: Pain caused by VOC is managed using analgesic therapy as a first line of treatment. The treatment is started within 30 minutes of arrival at the hospital. The dose and type of painkiller differs with respect to interindividual variability. When pain is categorized between mild to moderate, NSAIDs are prescribed. Diclofenac and Ibuprofen are commonly used in SCD patients. Moderate-to-severe pain usually is managed with opioids. For moderate pain, a weaker opioid such as codeine is given whereas for severe pain, a stronger opioid such as morphine or equivalent opioid such as levorphanol, methadone, oxymorphone, or fentanyl may be used. Since sickle cell disease patients usually have difficult access to veins, subcutaneous injection rather than intravenous treatment is advised. The patient is to be reevaluated every 15 to 30 minutes and if necessary, more opioids should be given to manage the pain. A continuous infusion is advised to prevent repeated injections and may enable the patient to more effectively manage their pain (sometimes referred to as patient-controlled analgesia) (PCA). When necessary, the patient can add single regulated dosages of the painkiller to a PCA pump's background infusion rate. Non-pharmacologic approaches include local heat application, massage, and positioning might provide additional pain relief.

Chronic pain: The type of pain and its cause should be identified for chronic pain management. The patient's response mostly determines the therapy option. The type and dosage of opioids employed should be determined by pain alleviation, side effects, and functional outcomes. Pharmacological pain management may be supplemented with massage and muscle relaxation therapy. Chronic pain should be evaluated at least once a year, and medication should be modified as necessary.[10]

CDC prescription guidelines

In accordance with CDC prescription guidelines based on the overdose risk when opioids are prescribed for pain: it is advised to use caution when prescribing opioids at any dosage, monitor patients who receive dose increases of more than 50 MME per day, reduce or stop opioid therapy if the benefits do not outweigh the risks, avoid or carefully plan doses of more than 90 MME per day.[11]

Objectives

Objectives of current study were; to determine the percentage of sickle-cell disease patients experiencing pain manifested in the form of vaso-occlusive crisis. To study the management of pain with analgesics, monoclonal antibody, anti-metabolites, antibiotics, opiate antagonist during vaso-occlusive crisis in sickle cell disease patients. To analyze the drug distribution based upon prescription patterns and frequency of use in patients with sickle cell disease. To assess vaso-occlusive pain on a pain scale before the initiation and after the completion of the treatment. To promote rational use of drugs in pain management and alternate therapies which are non-addictive like ketamine or lidocaine, warm compressors and acupuncture to improve the quality of life of sickle cell disease patients.

METHODS

Study design, location and duration

A cross-sectional study was conducted at Yashoda Hospital in Hyderabad, India. Data regarding the management of acute pain during vaso-occlusive crisis with analgesics, NSAIDs, opioids in sickle cell disease patients was gathered from the hemato-oncology department of the hospital on a daily basis during the duration of the study. The study duration was 6 months i.e., from the beginning of April 2022 to the end of September 2022.

Sampling technique

A sample size of 25 were admitted in the study based on the technique of random sampling method whereby an inclusion and exclusion criterion were set and patients in alignment with that criteria were chosen at random.

Inclusion criteria

Inclusion criteria for current study were; patients affected with sickle cell disease that are willing to participate in the study, Patients with any grade of pain during vaso-occlusive crisis are taken into consideration, Patients of any age group and gender are included in the study and

Patients who are on opioids for the management of vaso-occlusive crisis during hospitalization are considered.

Exclusion criteria

Exclusion criteria for current study were; Patients who are not willing to participate in the study, Patients of sickle cell disease who did not experience pain manifested as vaso-occlusive crisis, Patients who are pregnant and the pain management therapy that is undertaken during a C-Section are not considered.

Study procedure

The patients in alignment with the inclusion criteria were asked for consent to be included in the study conducted in the hospital. The data from the sickle cell disease patients was recorded in an online questionnaire form and a subsequent drug utilization evaluation was conducted. The data was then tabulated and classified according to the distribution based upon the prescribing patterns of the class of drugs and distribution based upon the frequency of use of the drug. Tabulated data was analyzed and distribution percentage was calculated. Pie charts and bar diagrams were used for demonstration. Furthermore, results were interpreted and subsequent conclusions were drawn.

RESULTS

Distribution based upon the demographic details of the study participants

The demographic data of all the sickle cell disease patients that were enrolled in the study was analyzed and the prevalence of males to females was found in the ratio of 18:7 as illustrated in (Table 1). Furthermore, age distribution i.e., ≤18 years and >18 years was in the ratio of 2:3 as shown in (Table 2).

Table 1: Distribution based upon the gender of the study participants.

Gender	% distribution
Males	72
Females	28

Table 2: Distribution based upon the age of the study participants.

Age (years)	% distribution
≤18	40
>18	60

Out of all the sickle cell disease patients that were enrolled in the study, acute pain as vaso-occlusive crisis was presented in 72% of patients, whereas the rest 28% did not experience pain**.** Pain was manifested in the form of acute chest syndrome, generalized body pain, headache, backache and pain in both or either limbs and its percentage distribution is given in (Table 3). Pain was assessed on a pain scale ranging from 0-10 before the initiation and after the completion of treatment. The five degrees with its respective range on the pain scale are no pain (0), mild pain (1-3), moderate pain (4-6), severe pain (7-9) and very severe pain (10). According to the American Pain Society guidelines, the objectives of pain assessment should constitute evaluation of patient's pain status and associated experiences throughout time, provision of a foundation for treatment decisions and determination of efficacy of pain management techniques.[12] Prescriptions of sickle cell disease patients were analyzed and it constituted of a total of eleven classes of drugs, out of which anti-metabolites class of drugs accounted for 16.06% of a prescription. Antibiotics, analgesics, supplements, alkalinizing agents, monoclonal antibody, fluids, opiate antagonists, tricyclic antidepressants, antioxidants, antifibrinolytic agents added up to the rest 83.94% of an average prescription of a sickle cell disease patient which is presented in (Table 4).

Table 3: Distribution based upon the clinical manifestations of the study participants.

Clinical Manifestation	% distribution
Generalized Body Pain	60
Acute Chest Syndrome	30
Headache	40
Backache	20
Pain in Limbs	20

Table 4: Distribution based upon the prescribing patterns of the class of drugs.

Class of drug	%
Anti-metabolite (hydroxyurea)	16.06
Antibiotics (penicillin G)	14.81
Analgesics (yramadol+APAP)	13.05
Vitamins and supplements (folic acid)	12.34
Alkalinizing agent (sodium bicarbonate)	12.34
Monoclonal antibody (crizanlizumab)	11.2
Fluids (IV hyperhydration)	9.8
Opiate antagonist (buprenorphine/ naloxone)	3.7
Tricyclic antidepressant (amitriptyline)	2.46
Antioxidant (glutathione)	2.46
Antifibrinolytic agent (tranexamic acid)	1.23
Total	100

Pharmacological approach for pain management

Patient is started with IV alkalinization with aggressive IV analgesic within 30 minutes of arrival at the hospital with complains of severe pain i.e., 7-10 on pain scale. The frequency of use of drugs in case of pain manifested as vaso-occlusive crisis in the sickle cell disease patients is given in (Table 5) along with its specific indications. Hydroxyurea was the only drug with an absolute frequency of use among sickle cell disease patients experiencing painful crisis.

Table 5: Distribution based upon the frequency of use of the drug in pain management.

Generic Name	Indication	Frequency of use %
Hydroxyurea	Decreases painful crisis	100
Tramadol+APAP	Moderate to severe pain during VOC	76.9
Crizanlizumab	Decreases VOC frequency	69.23
Glutathione	Antioxidant prevents acute complications	69.23
Diclofenac	Acute pain due to VOC	46.75
Vitamin B 6	Anti-sickling effect	15.38
Buprenorphine/naloxone	Acute chest syndrome/ Respiratory depression	15.38
Amitriptyline	Neuropathic pain reliever	7.67

Management of vaso-occlusive crisis with crizanlizumab (Adakveo manufactred by Novartis)

Crizanlizumab, a monoclonal antibody that inhibits adhesion of leukocyte with p selectin, is administered to sickle cell disease patients who were 16 years or older to decrease the frequency of vaso-occlusive crisis. Upon drug utilization evaluation, per prescription distribution percentage of crizanlizumab was found to be 11.2%, while the rest 88.8% constituted of anti-metabolites, antibiotics, analgesics, vitamins and supplements, fluids, opiate antagonist, tricyclic antidepressant, antioxidant, anti-fibrinolytic agents. Frequency of use of crizanlizumab among sickle cell disease patients was found to be 69.23%. Vitals, ECG and 2D Echo of patients experiencing vaso-occlusive crisis were taken upon hospitalization. Upon receiving reports within normal limits of all the investigations, crizanlizumab IV infusion for 30 minutes is started. Vitals were checked periodically before, during and after the administration of the drug. There were no reported premedications with acetaminophen or other analgesics given to patients on crizanlizumab. The first IV infusion of crizanlizumab was administered to the patients at week 0 followed by an IV infusion of crizanlizumab two weeks from the first administration. Subsequently, patients were administered crizanlizumab IV infusion once every four week after week 2. Reported adverse drug events which include arthralgia, hypersensitivity reaction, emesis and pyrexia were managed accordingly. Patients were discharged from the hospital following the treatment for vaso-occlusive crisis in haemodynamically stable and afebrile condition.

Frequency of vaso-occlusive crisis before and after the initiation of Crizanlizumab

The frequency of occurrence of vaso-occlusive crisis differed from patient to patient but the majority of patients experienced acute painful episodes periodically every 15-30 days before the initiation of treatment whereas the subsequent pain was mild and it was only seen once every 2 to 3 months after the initiation of treatment.

Pain experienced before and after the initiation of Crizanlizumab

Pain was assessed on a pain scale ranging from 0-10 before the initiation and after the completion of treatment. Pain experienced during vaso-occlusive crisis before the initiation of the treatment ranged in between 7-10 on the pain scale. Pain experienced after the completion of the treatment ranged in between 1-3 on the pain scale and it was categorized as mild.

Non-pharmacological approach for pain management

Drinking of 3-4 liters of water per day was recommended. Patients were advised to avoid dehydration, stress and extreme climatic conditions. Use of heating pads and massage were other techniques that were recommended to manage pain. IV hyperhydration or fluid replacement therapy was given to limit sickling during hypovolemia which was commonly seen in sickle cell disease patients. Leukocyte depleted RBC transfusion followed by Inj. Lasix 10 mg IV was administered to lower the risk of complications associated with sickle cell disease and to manage anemia. Laser Splenectomy has been performed to reduce the occurrence of acute splenic sequestration crisis.

DISCUSSION

Among all the sickle cell disease patients that were enrolled in the study, 72% of the patients experienced pain in the form of vaso-occlusive crisis whereas 28% did not experience any symptoms of pain. In a study done by Ballas SK et al, it confers that vaso-occlusive crisis is the primary morbidity associated with sickle cell disease leading to hospitalization in 95% of patients.[13] Hydroxyurea, an antimetabolite has the highest frequency of use in sickle cell disease patient as it reduces painful crisis significantly. This is comparable to a review done by Agrawal et al, suggesting that hydroxyurea is the only effective proven drug that decreases the rate of vaso-occlusive crisis by almost 50%.[14] Analgesics like tramadol and acetaminophen are used synergistically in the management of the disease. A study in American Academy of Pain Medicine by Niscola et al, reports that IV tramadol in combination with non-opioids like acetaminophen or NSAIDS is indicated during moderate to severe pain associated with vaso-occlusive crisis.[14] There is an increase use of monoclonal antibody, specifically crizanlizumab by sickle cell disease patients to decrease the frequency of vaso-occlusive crisis and the drug utilization evaluation conducted suggests that the majority of patients experienced acute painful episodes periodically every 15-30 days before the initiation of

treatment whereas the subsequent pain was mild and it was only seen once every 2 to 3 months upon the use of crizanlizumab. The results interpreted were similar to the study done by Stevens et al, which suggests crizanlizumab to be effective in the management of sickle cell disease by reducing the frequency of vaso-occlusive crisis with the only drawback of drug cost and administration.[14] Lastly, the cross-sectional study conducted assessed the pain before the initiation and after the completion of the treatment and it showed a significant decrease in pain i.e., 1-3 on the pain scale which is categorized as mild.

Limitations

The limitation to the study conducted is the concomitant use of drugs such as hydroxyurea, tramadol, diclofenac, crizanlizumab, glutathione for the management of pain during vaso-occlusive crisis, thereby leading to non-observance of individual effect of a particular drug. Furthermore, the assessment of pain after the completion of treatment is not specific to the action of an individual drug; however, it is based upon the efficacy of the entire treatment regimen.

CONCLUSION

Management of painful episodes during vaso-occlusive crisis cannot be described as one size fits all. Interindividual variability must be considered at all times during planning and implementing a treatment regimen. Assessment of pain on the pain scale provided by American Pain Society is essential to ensure targeted treatment at maximum effective concentration. Patients should be provided with information regarding pain and its best possible management as a part of the ongoing treatment. Patients presenting with acute pain during vaso-occlusive crisis should be treated immediately within an hour after seeking essential information regarding the efficacy and palliation of previously administered analgesics. Dose of the analgesics prescribed should be titrated in such a way so as to reduce the occurrence of tolerance, withdrawal, dependence and addiction. Patients should be made aware of various criteria under non-pharmacological management of the disease to prevent the frequency of sickle-cell pain crisis.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Sickle cell. Available at: https://www.cdc.gov/ncbddd/sicklecell/facts.html. Accessed on 20 November 2022.
2. Chakravorty S, Williams TN. Sickle cell disease: a neglected chronic disease of increasing global health importance. Global Child Health. 2015;100:48-53.
3. Johnson J. What to know about sickle cell disease. Available at: https://www.medicalnewstoday.com/articles/sickle-cell-beta-thalassemia. Accessed on 20 November 2022.
4. Baba PDI, Lewis LH, Neeraj K, Patel A, Ominu-Evbota K, Kofi A. Anie and Wale Atoyebi, Sickle Cell Disease Genetics, Pathophysiology, Clinical Presentation and Treatment. Int J Neonat Screen. 2019; 5(20):1-15.
5. Sickle cell disease. Available at: https://www.nhlbi.nih.gov/health-topics/sickle-cell-disease. Accessed on 20 November 2022.
6. Aziza Sedrak, Noah P. Kondamudi, Sickle Cell Disease. USA: Stat Pearls Publishing; 2022.
7. Sickle Cell Anemia: Diagnosis and Treatment. Available at: https://www.mayoclinic.org/diseases-conditions/sickle-cell-anemia/diagnosis-treatment/drc-20355882. Accessed on 20 November 2022.
8. Pain Management Guidelines for Sickle Cell Disease, Sickle Cell Disease News. Available at: https://sicklecellanemianews.com/pain-management-guidelines-for-sickle-cell-anemia/. Accessed on 20 November 2022.
9. Calculating total daily dose of opioids for safer dosage. Available at: https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a. Accessed on 20 November 2022.
10. Preboth M. Management of pain in sickle cell disease. Am Family Phys. 2000;61(5):1544-50.
11. Ballas SK, Lusardi M. Hospital readmission for adult acute sickle cell painful episodes: frequency, etiology, and prognostic significance. Am J Hematol. 2005; 79:17-25.
12. Agrawal RK, Patel RK, Shah V, Nainiwal L, Trivedi B. Indian J Hematol Blood Transfus. 2014;30(2):91-6.
13. Pasquale N, Sorrentino F, Scaramucci L, Fabritiis PD, Cianciulli P. Pain Syndromes in Sickle Cell Disease: An Update. Pain Med. 2009;10(3):470-80.
14. Stevens DL, Hix M, Gildon BL. Sickle cell disease. J Pharm Technol. 2021;37(4):209-15.

Cite this article as: Jaishetwar GS, Khanam FM. A cross-sectional study on pain management during vaso-occlusive crisis in sickle cell disease. Int J Res Med Sci 2023;11:600-5.