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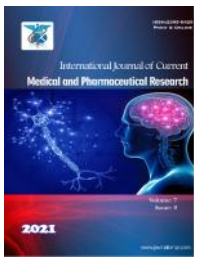

Research Article

# SICKLE CELL DISEASE PATIENTS ATTENDING THE EMERGENCY DEPARTMENT OF AL JAFFAR GENERAL HOSPITAL OF SAUDI ARABIA WITH TYPICAL COMPLICATIONS: A CHART REVIEW OF THE LAST THREE MONTHS

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**ABSTRACT**

**Background:** Sickle cell disease (SCD), an autosomal recessive disorder resulting in abnormal hemoglobin S production is one of the commonest genetic disorders in Saudi Arabia and the worldwide. The clinical implications of SCD are diverse and any organ system may be affected which results in high morbidity and mortality. The acute clinical manifestations of SCD can occur in vaso occlusive, hematologic and infectious crises. Patients with sickle cell disease are frequently visiting emergency room of the hospital with acute symptoms such as acute pain crisis and shortness of breath. This is the reason that the emergency rooms of the hospital are frequently receiving SCD patients with serious complications which decreases quality of life and morbidity among the affected people. The present study was done to review the patients with sickle cell disease and attending the emergency room of AlJaffar general hospital which is situated in the eastern part of Al Ahsa with a catchment area of around 20 PHCs.

**Material and Methods:** This was a retrospective descriptive chart review study. The medical records of all the patients with SCD related problem attending the Emergency room of Al Jaffar hospital during the last 3 months were reviewed in this study. Study variables consisted of patients characteristics including age, sex, main symptoms for which the patient attended the ER. Any diagnosed sickle cell disease with complain of severe body pain localized or generalized attending the emergency room of the hospital were considered as suffering from VOC. The data were entered and analyzed by the SPSS version 21. Frequencies via descriptive studies were used for categorical variables, whereas means and standard deviation were obtained for continuous variables. Chi-square statistics were used to assess associations between variables followed by multivariable analysis. Data were calculated with theirrespective95% CI. A Pvalue less than 0.05 was considered statistically significant.

**Result:** The files of a total of one hundred and forty eight patients (N=148) of SCD who attended the ER of AlJaffar Hospital during the last 3 months with an average of 1.64 patients per day were studied. Almost fifty nine percent (N=87) of the patients were male. The mean age of the participants was 28.13 ±12.32 Std. Devyears. More than fifty five percent of the patients (N=82) attended due to severe body pain followed by twenty three percent (N=34) of those patients who attended due to leg pain. Seventeen percent (11.49%) of the patients attended with the complaint of SOB and chest pain while seven (4.73%), two (1.35%) and six (4.06%) patients were having complains with shoulder pain, hip joint pain and back pain respectively.

More than eighty eight percent of the participants presented with vasculo occlusive complication (VOC) of sickle cell disease while minority of the patients (11.49%) with more severe complication of Acute Chest complication. The majority of them (74.07%) had clinical and radiographic findings consistent with AVN of the hip joint while 11.11% and 7.4% each had acute vascular necrosis in knee joint, vertebrae and shoulder joint respectively. As far as the treatment in ER is concerned majority of the patients (62.8%, N=87) were treated With IV Paracetamol + Fentanyl + Tramadol followed by 31.8% of the patients who were treated with systemic NSAID. Only 5.4% (N=14) of the patients were treated with Morphine. The likelihood of VOC was significantly more among females (Adj. OR: 2.1; 95% CI 1.02- 4.7)and ACS was significantly less among the female (Adj. OR: 0.72, 95% CI 0.30-1.2). The likelihood of acute vascular necrosis of hip joint was more among male (Adj. OR 1.80, 95% CI 0.45-4.0) while the likelihood of acute necrosis of vertebrae and shoulder was more among the females (Adj. OR .2.20, 95% CI 0.85-4.50).

**Conclusion:** Patients with an acute painful episode related to sickle cell disease frequently visited the emergency room of Al jaffar hospital.VOC was the most common cause of the painful episodes. Short term treatment with IV Paracetamol + Fentanyl + Tramadol had been very effective in the present study and patients were discharged in 48 hours of time on oral NSAID. However less dependency on morphinre has been reported in the present study



## INTRODUCTION

Sickle cell disease (SCD), an autosomal recessive disorder resulting in abnormal hemoglobin S production is one of the commonest genetic disorders in Saudi Arabia and the worldwide. Data from a national community based study in Saudi Arabia has found a prevalence of 24 per 10000 in children and adolescent.[1] According to a data released by Ministry of Health Saudi Arabia on June 19, 2015, the number of people living with this inherited condition is in the Kingdom 145,750.[2]

The genetic alteration in SCD causes an unstable RBC with a shortened survival which when deoxygenated becomes sickle shaped. Once the cell is sickled, the RBC becomes rigid, its membrane proteins change and there is an increased expression of adhesion molecules. The sticky erythrocyte adheres to the endothelium of the blood vessels triggering an inflammatory process, activating coagulation and causing

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hypoxia, ischemia and local infarction. The clinical implications of SCD are diverse and any organ system may be affected which results in high morbidity and mortality.

The implications of this condition affect the quality of life of the patients in various ways. The patients have difficulties at study, work and at home which results in low esteem. The acute clinical manifestations of SCD can occur in vaso occlusive, hematologic and infectious crises which are the main reasons of mortality and morbidity. Acute chest syndrome is one of the most serious vaso occlusive complications, the frequency of which reaches to 50% and recurring in up to 80% of those affected. It accounts for 25% of deaths in SCD patients.[3] Other systems affected by microcirculatory occlusion are bone, brain, kidneys, and spleen. According to a multicenter study in USA the researchers have found the life expectancy among the patients with sickle cell disease to be 42 years for men and 48 years for women. [4]The three other types of haematological crises of SCD are known to be aplastic, acute sequestration and hyper-haemolytic crises. They are responsible for severe anaemia and are common among the children with SCD.[5]

Patients with sickle cell disease are frequently visiting emergency room of the hospital with acute symptoms such as acute pain crisis and shortness of breath .The acute pain crisis is often referred as vaso-occlusive (VOC) .The patients with VOC often present with severe pain in different parts of the body which is severe and often with sudden onset. While the frequency and severity of complications vary widely, it is likely that all persons with SCD will seek care in the emergency room at some point in time. Various studies around the world have shown the frequent visit of the SCD patients in the emergency room. A Sickle Cell Data Collection (SCDC) program study has found that people with SCD living in California go to the Emergency department on an average of 3 times a year during their late teens and continue this pattern into their late 50's. [6] Similarly a Tennessee study reported that African Americans with SCD go to the ED two to six times more than African Americans without SCD. [7]

A study conducted with Florida Medicaid program data across all patients showed that during the 5-year study period, SCD patients incurred an average of 3.7 inpatient hospitalizations and 24.1 hospital days. Other studies have found that SCD patients are associated with acute SCD pain episodes are the most commonly observed cause of inpatient admission in SCD patients. [8]In another similar USA study on the visit of SCD patients in the emergency rooms have found that most patients were admitted for acute pain in various parts of the body for which eighty seven percent received morphine and hydromorphone.[9]

Sickle cell disease (SCD is highly prevalent in the Eastern province of Saudi Arabia, followed by the southwestern provinces. According to one study (2007) the researchers have found a prevalence rate of sickle cell trait to be 16.89% and sickle cell disease to be 1.20% in Al Ahsa district of eastern province. This is the reason that the emergency rooms of the hospital in these areas are frequently receiving SCD patients with serious complications which decreases quality of life and morbidity among the affected people. [10,11]The present study was done to review the patients with sickle cell disease and attending the emergency room of Al Jaffar general hospital which is situated in the eastern part of Al Ahsa with a catchment area of around 20 PHCs.

## MATERIAL AND METHODS

This was a retrospective descriptive chart review study. The medical records of all the patients with SCD related problem attending the Emergency room of Al Jaffar hospital during the last 3 months were reviewed in this study. Study variables consisted of patients characteristics including age, sex, main symptoms for which the patient attended the ER, Diagnosisof the symptoms (such as Vaso occlusive crisis (VOC),H emolytic Crisis (HC), Shortness of Breath, Past medical history, Abdominal ultrasound finding, drug history, management plan , outcome of the treatment and duration and rate of inpatient stay at the hospital. Any diagnosed sickle cell disease with complain of severe body pain localized or generalized attending the emergency room of the hospital were considered as suffering from VOC. The data were retrieved from the health files of the patients and entered and analyzed by the SPSS version 21. Frequencies via descriptive studies were used for categorical variables, whereas means and standard deviation were obtained for continuous variables. Chi-square statistics were used to assess associations between variables followed by multivariable analysis. Data were calculated with theirrespective95% CI. A Pvalue less than 0.05 was considered statistically significant. Permission from the authority of Al Jaffar General hospital was taken before starting the study. Consent from the study population was also taken.

## RESULT

The files of a total of one hundred and forty eight patients (N=148) of SCD who attended the ER of AlJaffar Hospital during the last 3 months were selected for this study with an average of 1.64 patients per day. Almost fifty nine percent (N=87) of the patients were male. The mean age of the participants was 28.13 years with a range of 15-47 years. Majority of the patients (56.76%) were discharged within 1-2 days of time while 43.24% of the patients were admitted for 3-5 days before discharge. The details of the clinical and demographic characteristics are shown in table 1.

**Table 1** Showing clinical and demographic characteristics of the patients

| Variables | Number | Percentage |
|---|---|---|
| Age | | |
| Mean age 28.19±12.32 Std.Dev. | | |
| Sex | | |
| Male | 87 | 58.78 |
| Female | 61 | 41.22 |
| Patients complain for attending the ER | | |
| Severe body Pain | 82 | 55.40 |
| Leg pain | 34 | 22.97 |
| Shortness of breath and chest pain | 17 | 11.49 |
| Shoulder pain | 7 | 4.73 |
| Hip joint pain | 2 | 1.35 |
| Back ache | 6 | 4.06 |
| Other associated condition | | |
| No associated disease | 134 | 90.54 |
| Hypertension | 4 | 2.70 |
| Bronchial Asthma | 4 | 2.70 |
| Renal disease | 2 | 1.36 |
| Deep venous thrombosis | 4 | 2.70 |
| Previous admissionfor the same problem | | |
| Once | 34 | 22.97 |
| Twice | 44 | 29.73 |
| Thrice and more | 70 | 47.30 |
| Duration of Stay in the hospital | | |

| | | |
|---|---|---|
| 1-2 days | 84 | 56.76 |
| 3-5 days | 64 | 43.24 |

More than eighty eight percent of the participants presented with vasculo occlusive complication (VOC) of sickle cell disease while minority of the patients (11.49%) with more severe complication of Acute Chest complication. The majority of them (74.07%) had clinical and radiographic findings consistent with AVN of the hip joint while 11.11% and 7.4% each had acute vascular necrosis in knee joint, vertebrae and shoulder joint respectively. On ultrasound finding,more than thirty one percent (N=46) of the patients had the feature of auto splenectomy followed by 29.05% (N=43) of the patients who had splenomegaly. Fifteen patients (10.13%) and eleven patients (7.44%) had undergone surgical splenectomy and cholecystectomy respectively. While more than eleven percent (.48%, N=17) and 5.1% (N=8) had splenomegaly with cholecystectomy and splenomegaly with gall stones respectively. As far as the treatment in ER is concerned majority of the patients (62.8%, N=87) were treated With IV Paracetamol + Fentanyl + Tramadol followed by 31.8% of the patients who were treated with systemic NSAID. Only 5.4% (N=14) of the patients were treated with Morphine. Almost seventy nine percent (N=127) of the patients improved with the treatment and discharged 11.5 % (N=17) referred to higher center. The details of the clinical characteristics and management is shown in the table 2.

**Table 2** Showing the clinical characteristic, treatment and outcome of treatment of the patients

| Variables | Number | Percentage |
|---|---|---|
| Diagnosis at presentation | | |
| VOC | 131 | 88.51 |
| CS | 17 | 11.49 |
| Acute vascular necrosis | | |
| Present (N=27) | 27 | 18.24 |
| Hip joint | 20 | 74.07 |
| Knee joint | 3 | 11.11 |
| Vertebrae | 2 | 7.41 |
| Shoulder | 2 | 7.41 |
| Absent | 121 | 81.76 |
| Ultrasonography findings | | |
| Normal | 8 | 5.41 |
| Splenomegaly | 43 | 29.05 |
| Auto spleenectomy | 46 | 31.08 |
| Surgical spleenectomy | 15 | 10.13 |
| Cholecystectomy | 11 | 7.44 |
| Splenomegaly + Cholecystectomy | 17 | 11.48 |
| Splenomegaly +Gall stones | 8 | 5.41 |
| Management | | |
| IV Paracetamol + Fentanyl + Tramadol | 87 | 62.8 |
| NSAID | 47 | 31.8 |
| Morphine | 14 | 5.4 |
| Outcome of the treatment | | |
| Discharged | 127 | 78.5 |
| Referred to higher center | 17 | 11.5 |

VOC was significantly more among females than that of males (91.80% vs. 86.20%, p= 0.023) and ACS was significantly less prevalent among the male (8.20% vs. 13.80%).Acute vascular necrosis of the hip joint (19.54% vs. 9.83%,p = 0.021) and knee joint (3.44% vs. 00 % , p= 0.021) was significantly more among the male than the females while acute necrosis of vertebrae and shoulder was significantly more among the females than the male (3.27%vs. 0.00 ,p=0.021). Female patients who were discharged within 48 hours were significantly more than that of male (65% vs. 35%, P=0.0032). Similarly the number of males was significantly higher among whom who were discharged after 3 and 5 days of admission (60% vs. 40%, p= 0.0032).

The likelihood of VOC was significantly more among females than that of males (Adj. OR: 2.1; 95% CI 1.02- 4.7) and ACS was significantly less among the male than females (Adj. OR: 0.72, 95% CI 0.30-1.2). The likelihood of acute vascular necrosis of hip joint was more among male than the female (Adj. OR 1.80, 95% CI 0.45-4.0) while the likelihood of acute necrosis of vertebrae and shoulder was more among the females than the male (Adj. OR .2.20, 95% CI 0.85-4.50).

The details of the significance of the sickle cell disease attendance in the emergency room among the genders are shown in table 3.

**Table 3** showing significance of the sickle cell disease attendance in the emergency room among the genders

| | Gender | | | |
|---|---|---|---|---|
| | **Male (n=87)** | **Female (n=61)** | **Adj.OR** | **P value** |
| Diagnosis | | | | |
| VOC | 75(86.20) | 56(91.80) | 2.1; 95% CI 1.02- 4.7 | |
| ACS | 12(13.80) | 5(8.20) | 0.72, 95% CI 0.30-1.2 | 0.023 |
| Acute vascular necrosis | 17(19.54) | 6(9.83) | 1.80, 95% CI 0.45-4.0 | |
| Hip joint | 3(3.44) | 0(0.00) | | |
| Knee joint | 0(0.00) | 2(3.27) | 2.20, 95% CI 0.85-4.50 | 0.021 |
| Vertebrae | 0(0.00) | 2 (3.27) | | |
| Shoulder | | | | |
| Duration of Stay in the hospital | | | | |
| 1-2 days | 35 (40.22) | 49(80.33) | | 0.0032 |
| 3-5 days | 53 (59.78) | 11(19.67) | | |

## DISCUSSION

The present study was the chart review study to estimate the complications with which the Sickle cell disease patients have attended the emergency room of Al jaffar hospital, AL Ahsa, Saudi Arabia during the last three months. The vast majority of patients attending the ER visit in our study were VOC (88.51%) while the rest were diagnosed as suffering from ACS. in a similar study in USA, approximately 85.0% of SCD-related ER visits had VOC as the primary reason for admission.[8] However in another study conducted in other region of Saudi Arabia, Ahmad Ali Hazzazi *et al* (2020) has reported that vast majority of sickle disease patients had VOC (91.2%), and more than half of them had ACS 58.2% as a complication .[12]In contrast, a study conducted in southern province (Holy Mecca) of Saudi Arabia, the patients reporting to emergency with VOC complication was 55.9%.[13]In one Riyadh study also, Veno-occlusive disease was seen in 84% of patients and was the most common complication.[14] 76% of the VOC cases were uncomplicated episodes in our study. Most of the VOC episodes (70.3%) were uncomplicated episodes in the USA study. In a Nigerian study 10.3% of the SCD suffering patients attending the emergency room were suffering from Acute vascular necrosis.[15]Morey A. Blinder, *et al* has found 48% of the patients with sickle cell disease suffering from AVN. Of them almost 60% were had clinical and radiological findings consistent with AVN of hip joint while the rest 40% had findings consistent with AVN of shoulder. More than seventy four percent of the patients with SCD in our study also had AVN in hip joint followed by knee joint (11.11%) while shoulder joints and vertebra were involved in 7.4% cases each.[16]

Seventy seven percent of the patients in our study had two and more than 2 visits to ER over the last three months of time. Frequent ER visits by Sickle cell disease patients with acute

complications have been reported by many studies. In one study Tanabe P *et al* (2010) has found that 52% of patients had between one and three emergency department visits. Over the 10 months of time while 21% had four to nine visits and 27% had between 10 and 67 visits.[17]In a Georgian study the high user of Sickle cell disease patients had 14 times visit to the Emergency room during the 1 year of time while moderate users visited twice and low user had one time visit to the ER.[18]In a large Cooperative Study of Sickle Cell Disease in which >3000 patients were recruited , Kidwell K *et al* showed that the majority of SCD patients (80%) experienced 0–3 major pain crises/year. Only a small minority (~5%) experienced ≥6 VOEs/ year.[19]

Painful crisis due to VOC was significantly more among the females than the males in our study (91.80% Vs. 86.20%, p= 0.023) and ACS was significantly less prevalent among the male (8.20% vs. 13.80%). In contrast, Giulia Ceglie, *et al* has found a comparatively higher prevalence of painful crisis due to VOC among males than the females in the Italian population.[20]Unlike other study where females experienced longer mean inpatient stay for treatment, our study has shown just reverse.[21] Female patients who were discharged within 48 was significantly more than that of male (65% vs. 35%, P=0.0032). Similarly the number of males was significantly higher among whom who were discharged after 3 and 5 days of admission (60% vs. 40%, p= 0.0032).

Acute Chest complication was significantly higher among the males than the females in our study (13.80 Vs. 8.20, p= 0.023). The estimated prevalence of acute chest syndrome and pneumonia was only among 6.46% of the female in a systematic review and meta-analysis done by SivarajiniInparaj *et al*.[22]

Repeated attack of VOC results in shrinkage of spleen and auto spleenectomy. More than 31 percent of the cases in the present study were detected with the sign of autosplenectomy. A higher percentage of autosplenectomy has been observed among the patient with SCD in a Nigerian study.[23]However a significantly higher number of patients had splenomegaly (29.05%) as compared to Nigerian study (4.05%) in our study. A systematic review study has found the prevalence of splenomegaly among the sickle cell disease adult patients attending the hospital to be between 15% to 67%.The highest rate of splenomegaly was found among the Africans (54%to 88%) who had HbS-β-thal.[24]

Almost one fourth of the patients in our study were suffering from different ailments of liver and gall bladder stones. In a similar Indian study, Ambika Prasad Mohanty *et al* have found that as high as 59% of Sickle cell disease patients had hepatobiliary involvement. The most common ultrasound finding in this study was hepatomegaly, hepato-splenomegaly, cholelithiasis, and gall bladder sludge. [25]In the present study eighteen percent of the patients had already undergone cholecystectomy while 5.4% of the patients were having cholelithiasis. In one Nigerian study also cholelithiasis and biliary sludge were the most common hepatobiliary ultrasound findings in patients with sickle cell anemia. Thirty percent of the patients were affected by cholelithiasis and 6% by biliary sludge in this study. [26]

Majority of the patients (62.8%) were successfully relieved of their pain by IV Paracetamol + Fentanyl + Tramadol followed by 31.8% of the patients who were treated with systemic NSAID. Only 5.4% (N=14) of the patients were treated with Morphine. However other study has shown high percentage of the patients (87%) with painful episode receiving morphine and hydromorphone. [9] Similarly, TanabeP, *et al* reported in their study that a significant number of patients with sickle disease attending the emergency room with pain received analgesic doses of morphine sulfate (42%) and hydromorphone (46%). While minority of the patients received meperidine (4%) and ibuprofen or ketorolac (7%).[17] The present study showed less dependency on morphine and majority of the patients (70%) improved with the short term treatment other than morphine and only 1.5 % referred to higher center. Short term treatment with IV ketorolac 30-60 mg or IV morphine 2-5 mg half hourly till the pain is relieved has been very effective in controlling the pain and discharging the patients with on oral analgesic. One study has shown that 80% of SCD patients with acute pain were relieved with this short term protocol and were discharged from the Emergency room within 72 hours.[27] Similarly short term treatment with IV Paracetamol + Fentanyl + Tramadol had been very effective in the present study and patients were discharged in 48 hours of time on oral NSAID.

## CONCLUSION

Patients with an acute painful episode related to sickle cell disease frequently visited the emergency room of Al jaffar hospital.VOC was the most common cause of the painful episodes. Short term treatment with IV Paracetamol + Fentanyl + Tramadol had been very effective in the present study and patients were discharged in 48 hours of time on oral NSAID. However less dependency on morphinre has been reported in the present study

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