



CODEN [USA]: IAJ PBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.2551670>Available online at: <http://www.iajps.com>

Research Article

**AWARENESS TOWARDS OPIOIDS SIDE EFFECTS AMONG SICKLE
CELL DISEASE PATIENTS IN AL AHSA, SAUDI ARABIA****Ibrahim Yousef Aldarwish¹, Somaia Abdelmohsen Shehab-Eldeen¹, Sayed Ibrahim Ali¹,
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Mohammed Abdultife Alkhalfan¹, Ahmed Khalid Almulhim¹, Omar Abdulaziz Alanzi¹,
Abdullah Fareed Almulhim¹**¹College of Medicine, King Faisal University, Al-Ahsa, Saudi Arabia**Abstract:**

Background: One of the most important treatment modalities for SCD patients is opioid drugs. These drugs have been the mainstay of treatment for patients with sickle cell disease especially when they are having vaso-occlusive sickle cell crisis. However, opioids are known to have a pleasurable effect on the patients in which may cause many patients of SCD continue to demand those medications. As a result, if the patient takes unnecessary doses of opioids on a regular basis, that may lead to undesirable side effects like opioid dependence or addiction.

Material and Methods: This is a cross-sectional study conducted in AlAhsa, which focuses on perception of Saudi patients with sickle cell disease towards opioid drugs using self-administrated questionnaires from February 2018 to July 2018. The data were analyzed using Statistical Packages for Social Sciences [SPSS] version 21. All categorical variables presented in this study had been summarized by using numbers and percentages. The analyses measure the association between socio-demographic and other related variables in the survey by using chi-square test. Regression analysis had been conducted as well where Odds ratio and 95% CI were also being reported for the risk factor of the dependent variables versus socio demographic characteristics of the SCD patients.

Results: A total of 309 SCD patients were involved in this study. Of the 309 patients, 175 [56.6%] of them were females and 134 [43.4%] were males. Age range was from 10 – 60 years old. The prevalence of perception of SCD patients toward opioid drugs revealed, 218 [70.6%] with good perception and 91 [29.4%] with poor perception. Binary logistics regression revealed that sickle cell group is likely to have significant effect on good perception [odds ratio 0.084, p-0.002] where carriers were likely to have 92% decline to be in good perception compared SCD patient. Family history of sickle cell anemia also shows significant influence [odds ratio 0.462, p-0.015] where negative group were having 54% decreases to be in the good perception compared to positive group.

Conclusion: The prevalence of good perception toward opioid drug utilization in this study was relatively high as opposed to poor perception. However, perception of patients about the symptoms of drug dependency was deemed moderate which was necessary to address given the different diseases attributed to the continuous usage of opioid medications.

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Please cite this article in press Ibrahim Yousef Aldarwish et al., *Awareness Towards Opioids Side Effects Among Sickle Cell Disease Patients In Al Ahsa, Saudi Arabia.*, Indo Am. J. P. Sci, 2019; 06[01].

INTRODUCTION:

Sickle cell disease [SCD] is one of the most prevalent blood disorders in the kingdom of Saudi Arabia specially the eastern province. It is estimated that for every 10,000 children and adolescents in the eastern province, there are 145 cases of sickle cell disease. The chronicity of this disorder makes it an important cause of morbidity and mortality. Even so, the majority of these patients require multiple treatment modalities to treat their condition [1].

Vaso-occlusive crisis [VOC] is one of the most common devastating complication of sickle cell disease [SCD]. It is described as acute painful episodes caused by sickled RBCs that adhere to the vascular endothelium producing microcirculation occlusions that would lead to tissue ischemia and subsequent damage of the tissues [2]. These painful episodes are very important factor for visiting emergency department [ED] and hospitalizations among SCD patients. It has been shown that 5.2% of patients with SCD had 3–10 episodes of severe painful crisis every year. The highest mortality rate in patients with SCD is during painful crisis episodes [3].

VOC is managed mainly by supportive measures including bed rest, hydration, oxygen, and analgesia. The use of analgesia during the VOC should follow a three-step ladder recommended by the WHO for the management of cancer-related pain, even though sickle cell pain is managed mainly using opioid analgesics, especially in the adult population [2]. So, one of the most important treatment modalities for SCD patients is opioid drugs. These drugs have been the mainstay of treatment for patients with sickle cell disease especially when they are having vaso-occlusive sickle cell crisis. However, opioids are known to have a pleasurable effect on the patients in which may cause many patients of SCD continue to demand those medications. As a result, if the patient takes unnecessary doses of opioids on a regular basis, that may lead to undesirable side effects like opioid dependence or addiction [4].

Furthermore, it is well known among clinicians who are treating SCD patients that they are always demanding opioids management without the need of it; this may be attributed to their lack of knowledge of the harms of taking opioids drugs [5].

Better knowledge and awareness towards the proper use of opioid drugs in SCD patients will eventually lead to a better attitude and behavior towards opioid drugs among sickle cell patients. Nonetheless, to the best of our knowledge, there is no research have been published which documents the awareness, attitude and behavior of sickle cell patients towards opioid drugs in Al Ahsa.

MATERIAL AND METHODS:

This is a cross-sectional study conducted in Al Ahsa, which focuses on perception of Saudi patients with sickle cell disease towards opioid drugs using self-administrated questionnaires from February 2018 to July 2018. The data were analyzed using Statistical Packages for Social Sciences [SPSS] version 21. Both descriptive and inferential statistics had been conducted. A p-value cut off point of 0.05 at 95% CI used to determine statistical significance. All categorical variables presented in this study had been summarized by using numbers and percentages. The analyses measure the association between socio-demographic and other related variables in the survey by using chi-square test. Regression analysis had been conducted as well where Odds ratio and 95% CI were also being reported for the risk factor of the dependent variables versus socio demographic characteristics of the SCD patients.

On assessment of perception of SCD patients toward opioid drugs which was comprised of 11 questions presented at table 2, a categorical question had been asked where “yes” or “no” were the answer options. The most appropriate answer had been coded as 1 and the wrong answer had been coded as 0. Score range from 0 to 11 were obtained to which 0 – 5 had been classified as poor perception and 6 – 11 had been classified as good perception.

Table 1: Demographic data of participants

Study Variables	N [%] [n=309]
Gender	
• Male	134 [43.4%]
• Female	175 [56.6%]
Age group in years	
• ≤30 years old	256 [82.8%]
• >30 years old	53 [17.2%]
Marital Status	
• Non married	154 [49.8%]
• Married	155 [50.2%]
Educational level	
• High school or below	128 [41.4%]
• University or higher	181 [58.6%]
Sickle cell group	
• Patient	298 [96.4%]
• Carrier	11 [03.6%]
Family history of sickle cell anemia	
• Yes	259 [83.8%]
• No	50 [16.2%]
Age at diagnosis†	
• Since birth	41 [14.9%]
• Since 5 years old or less	80 [29.1%]
• Since 6 – 10 years old	86 [31.3%]
• Since above 10 years old	68 [24.7%]
How many times you suffered from sickle cell crisis per year? †	
• Once	69 [28.3%]
• Twice	46 [18.9%]
• Three times	37 [15.2%]
• More than three times	92 [37.7%]
Usual hospitalization period	
• 2 days or less	176 [57.0%]
• 3 days – 1 week	98 [31.7%]
• More than a week – 2 weeks	24 [07.8%]
• More than 2 weeks	11 [03.6%]
Level of perception	
• Good	218 [70.6%]
• Poor	91 [29.4%]

†Excluded missing cases.

RESULTS:

A total of 309 SCD patients were involved in this study. Of the 309 patients, 175 [56.6%] of them were

females and 134 [43.4%] were males. Age range was from 10 – 60 years old, of whom 256 [82.8%] were in the group of 30 years old or less and 53 [17.2%]

were in the group of more than 30 years old. Slightly more patients were married [50.2%] while 49.8% were non-married. 58.6% of the patients were having university degree or higher whereas 41.4% who were having high school or below. Nearly all participants were sickle cell patients [96.4%] with 3.6% were sickle cell carrier. There were 83.8% with family history of sickle cell anemia. Among these numbers 14.9% of them had been diagnosed with the disease since birth, 29.1% had been diagnosed since 5 years old or less, 31.3% had been diagnosed since 6 – 10 years old and 24.7% were diagnosed since more than 10 years old. Majority of them suffered sickle cell crisis more than three times per year with 37.7%, 15.2% encountered three times per year, 18.9%

encountered twice and 28.3% encountered once a year. There were 57% with 2 days or less hospitalization period during sickle cell crisis, 31.7% with 3 days to 1 week, 7.8% with more than a week to 2 weeks and 3.6% with more than 2 weeks hospitalization due to sickle cell crisis. The prevalence of perception of SCD patients toward opioid drugs revealed, 218 [70.6%] with good perception and 91 [29.4%] with poor perception [Table 1].

The perception of SCD patients toward opioid drugs has been elaborated at table 2 where the most appropriate answer had been indicated per each question.

Table 2: Perception of SCD patients toward Opioid drugs ^[n=309]

Statement	Positive Answer [%]
Q1. Have you ever heard of opioid drugs?	247 [79.9%]
Q2. Have you ever been prescribed any opioid drugs?	188 [60.8%]
Q3. Do you know that taking multiple doses of these drugs can lead to addiction?	203 [65.7%]
Q4. Is any of these drugs [opioid drugs] was prescribed to you, have you ever encounter any side effects? †	223 [72.2%]
Q5. Do you know that drug dependence/addiction can cause the following symptoms: Dry mouth, Drowsiness, Nausea, Constipation, Abdominal cramping, depressed respiration, Skin rashes, Depression, Headaches and Bad dreams?	124 [40.1%]
Q6. Do you know that opioid drug withdrawal can cause the following symptoms: Low energy, Irritability, Anxiety, Agitation, Insomnia, abdominal cramping, Nausea, Vomiting and Diarrhea?	116 [37.5%]
Q7. Do you know that these medications can cause respiratory depression	112 [36.2%]
Q8. Do you know that opioid drugs can cause addiction?	240 [77.7%]
Q9. Do you always go to the hospital and ask for opioid drugs if you are having sickle cell crisis †	263 [85.1%]
Q10. Does it always require hospitalization?	124 [40.1%]
Q11. Have you ever had to go to multiple hospitals in case if you haven't been given your medication [opioid drugs]? †	263 [85.1%]

† Signifies negative answer.

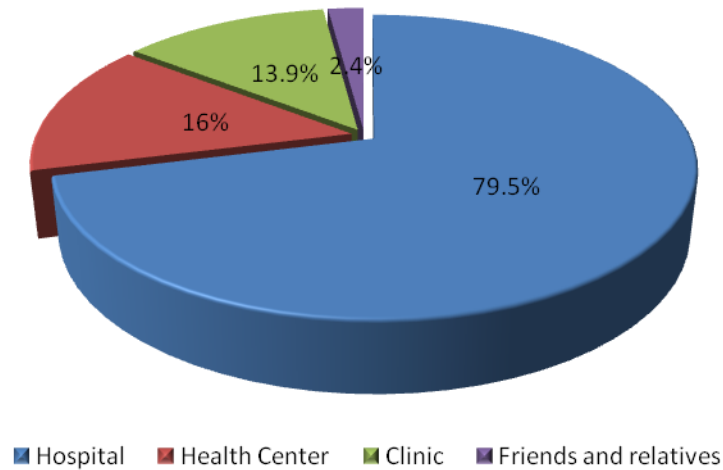
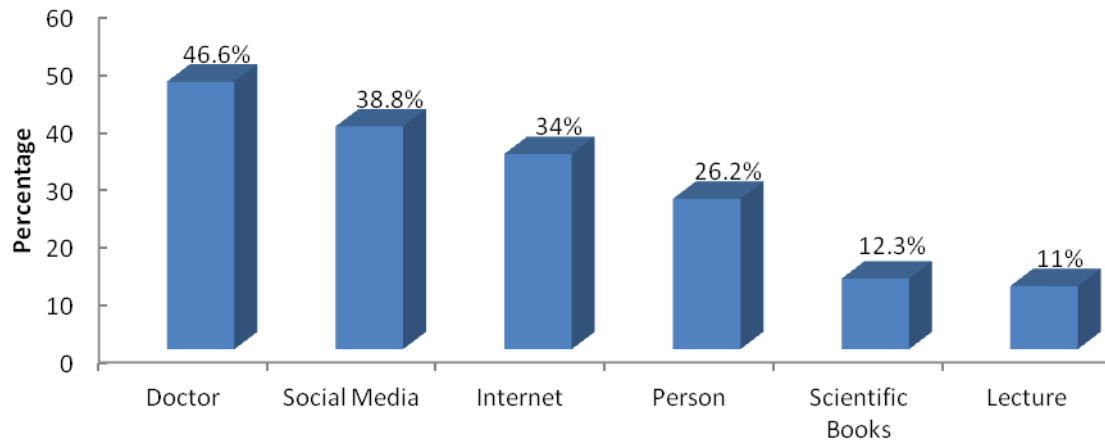
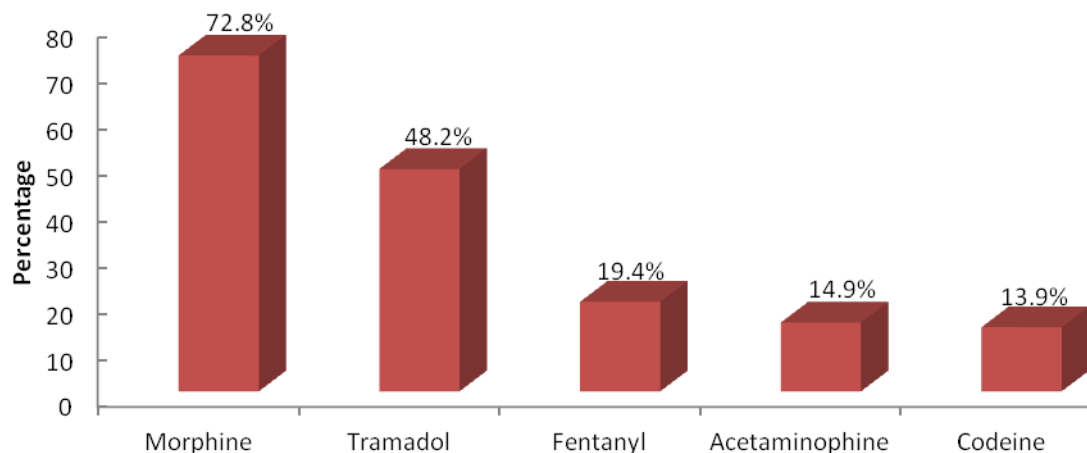
Figure 1: Institution that prescribed opioid drugs

Figure 1 presented the institution of entity that prescribed opioid drugs. Based of patients rating, majority of them agreed about hospital [79.5%], followed by health center [16%], next was clinic [13.9%] and friends and relative with 2.4%.

Figure 2: Sources of information

Doctor was the primary source of information regarding opioid drugs [46.6%], followed by social media [38.8%], next was internet [34%], a person [26.2%], scientific books [12.3%] and lecture [11%] [**Figure 2**].

Figure 3: Knowledge of different type of opioid medications

The most common opioid drugs was morphine, followed by tramadol [48.2%], next was fentanyl [19.4%], acetaminophen [14.9%] and codeine [13.9%] [Figure 3].

Table 3: Relationship between socio demographic characteristics and patients' perception toward opioid drugs [n=309]

Factor	Level of Perception		P-value §
	Good N [%] [n=318]	Poor N [%] [n=91]	
Gender			
• Male	89 [40.8%]	45 [49.5%]	0.163
• Female	129 [59.2%]	46 [50.5%]	
Age group in years			
• ≤30 years old	179 [82.1%]	77 [84.6%]	0.594
• >30 years old	39 [17.9%]	14 [15.4%]	
Marital Status			
• Non married	108 [49.5%]	46 [50.5%]	0.872
• Married	110 [50.5%]	45 [49.5%]	
Educational level			
• High school or less	84 [38.5%]	44 [48.4%]	0.110
• University or higher	134 [61.5%]	47 [51.6%]	
Sickle cell group			
• Patient	216 [99.1%]	82 [90.1%]	<0.001 **
• Carrier	02 [0.9%]	09 [09.9%]	
Family history of sickle cell anemia			
• Yes	190 [87.2%]	69 [75.8%]	0.014 **
• No	28 [12.8%]	22 [24.2%]	

§ P-value has been calculated using chi square test. ** Significant at p≤0.05 level.

We used chi square test at **table 3** to validate the relationship between the levels of perception among the socio demographic characteristics of SCD patients with p-values which indicates whether the relationship is statistically significant where $p \leq 0.05$ has been used as the significant level for all statistical tests. Based on the results, there was significant difference found on sickle cell group [$p < 0.001$] where patients were far off distant compared to carrier group of patients. We also found significant association on family history of sickle cell anemia [$p = 0.014$] where positive is far off higher compared to negative group. However, there was no significant relationship found on the following socio demographic characteristics such as; gender, age group in years, marital status and educational level.

Table 4: Regression analysis to predict good perception toward opioid drugs among the socio demographic characteristics of patients ^[n=309]

Factor	Odds Ratio	95% CI	P-value
Gender			
• Female vs Male	1.418	0.867 – 2.319	0.164
Age group in years			
• >30 years old vs ≤30 years old	1.198	0.615 – 2.334	0.595
Marital Status			
• Married vs Non married	1.041	0.638 – 1.698	0.872
Educational level			
• University or higher vs High school or less	1.493	0.912 – 2.446	0.111
Sickle cell group			
• Carrier vs Patient	0.084	0.018 – 0.399	0.002 **
Family history of sickle cell anemia			
• No vs Yes	0.462	0.248 – 0.861	0.015 **

CI – Confidence Interval. ** Significant at $p \leq 0.05$ level.

A binary logistics regression analysis was conducted at **table 4** to ascertain the effect of good perception among the socio demographic characteristics of SCD patients. Logistics regression analysis included in the model such as gender, age group in years, marital status, educational level, sickle cell group and family history of sickle cell anemia. Analysis revealed that sickle cell group is likely to have significant effect on good perception [odds ratio 0.084, $p = 0.002$] where carriers were likely to have 92% decline to be in good perception compared SCD patient. Family history of sickle cell anemia also shows significant influence [odds ratio 0.462, $p = 0.015$] where negative group were having 54% decreases to be in the good perception compared to positive group. Other socio demographic variables we included in the model show no direct influence in the good perception toward opioid drugs.

DISCUSSION:

A significant rise in the misuse of opioid prescription pain relievers and opioid overdose deaths has been put into notice. Many people with majority of them were in the early age misusing prescription opioids

get addicted to these drugs, and the consequences are sometimes fatal. [7] This has been further validated by Pack-Mebien and colleagues, [8] the study was about “nurses’ attitudes and practices in sickle cell pain management.” They reported that among the nurses they surveyed, 63% of them believe that drug addiction frequently develops in the treatment of sickle cell pain episodes. The overall perception of SCD patients toward opioid drugs in this study was relatively high 218 [70.6%] while poor perception was accounted to 91 [29.4%]. This study was the first paper in the Saudi Arabia to discuss the perception of SCD patients toward opioid drugs utilization.

Further findings of this study show 80% of the patients were aware of opioid drug with 60.8% received prescriptions of opioid medication. While many of them believe opioid drugs can cause addiction, still less than a half of the patients were having lack of knowledge regarding the symptoms it may cause due to their dependency of the drugs. Some of the symptoms they might encounter are the following; dry mouth, drowsiness, nausea, constipation, abdominal cramping, depressed

respiratory, skin rashes, depression, headaches and even bad dreams. In United States, an article published by Goesling et al which was about “discrepancies between perceived benefit of opioid and self-reported patients’ outcome.” [9] They reported that among 150 patients with chronic pain, 56% of them were currently in opioid use. This study finding was in congruent to what we reported above. Although the latter paper was focused on the chronic pain management of patient nonetheless, these signifies that opioid drugs are the most effective medication for pain relief.

The most common sources of information regarding opioid drugs in this study were doctor, followed by social media and internet while the most common opioid medication were morphine, tramadol and fentanyl. Morphine was the most commonly used opioid drugs to treat chronic pain as indicated in the paper published by Morley-Forster and associates. [9] They reported that 48% of the physicians preferred morphine followed by codeine while the article of Han et al, accounted acetaminophen and morphine to treat short acting and long acting SCD adult patient. [10] Our study also in comparable to the previous mentioned articles where we also exhibited similar findings about the utilization of morphine for the treatment of chronic pain during sickle cell episodes. In the likelihood effect of good perception among the demographic data of SCD patients, binary logistics regression revealed that sickle cell group is likely to have significant effect on good perception where carriers were likely to have 92% decline to be in good perception compared SCD patient. Family history of sickle cell anemia also shows significant influence where negative group were having 54% decreases to be in the good perception compared to positive group. We further observed that this is the first paper in Saudi Arabia to presents the likelihood ratio about the certain effect of opioid drugs in the perception of SCD patients. Although we found limited significant value in our results most especially in correlating to the socio demographic data, still we viewed the outcome of this study to be substantial enough as it may open the door for further research in the same subject. As this is the first paper to tackle this subject here in Saudi Arabia, further research in the same field is highly recommended to further validate the findings of this research.

CONCLUSION:

The prevalence of good perception toward opioid drug utilization in this study was relatively high compared to poor perception. However, perception of patients about the symptoms of drug dependency was deemed moderate which was necessary to address

given the different diseases attributed to the continuous usage of opioid medications. Concerning this, continuous education to the patients are essential. Medical practitioner should ensure that patients is properly oriented regarding the danger of opioid drugs in their physical and mental helath condition.

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