1	<u>Case Study</u>	
2 3	Case Report: Successful Management of Opioid Abuse and Addiction in a	
-	Known SCD Dationt at the University of Colohon Teaching Hegnited	
4	Known SCD Patient at the University of Calabar Teaching Hospital,	
5	Calabar, Nigeria	
6		
7	ABSTRACT	
8 9 10	<b>BACKGROUND:</b> Opioids are group of potent analgesic with mixed receptor activities. Pain related symptom accounts for the main reason for substance dependence among sickle cell disease (SCD) patients.	
11 12 13	<b>AIMS:</b> The report aims to elucidate the adverse effects of opioid and it's complication (abuse, dependency and addiction) and provide management strategy for health practitioners to curtail the dependency of SCD patients to opioid use.	
14 15 16 17 18 19 20 21 22	<b>PRESENTATION OF CASE:</b> The patient was a 27 years old lady that was diagnosed with sickle cell disease at the age of two. She presented with a two years history of oral self-medication of DF118 and Tramadol. She became dependent on the opioid on the account of sickle cell bone pain crises affecting both her upper and lower limbs with a pain score of 9/10. Other anagelsic like Diclofenac and Pentazocin couldn't ameliorate her excruciating pain but administration of 60mg of oral DF118 provided her with quick relieve. The sedative effect of Tramadol and DF118 allows her sleep comfortably and hence the beginning of her dependency. On review, patient's system was essentially intact and she was further referred for psychiatrist evaluation and possible rehabilitation.	
23 24 25 26 27 28	<b>DISCUSSION:</b> Recurrent bone pain crisis represent the most common reason patient with SCD seek acute medical care. Due to the quick analgesic relief and euphoric effect derive from both medication, patients feign pain after genuine pain had subsided in other to continue getting the prescription. The immediate pain assessment and frequent reassessment at 15min, 30min, 1hour then 2hours with appropriate application of medication until pain relief is very important to prevent drug abuse.	
29 30 31	<b>CONCLUSION:</b> Less addictive analgesic should be <b>considered</b> first after observing the nature of the pain before moving to stronger analgesic that have high potential for abuse and when stronger analgesic is to be used it should be for a short duration.	
32	Keywords: Opioid Abuse, Sickle Cell Disease, Dependency, Addiction, UCTH	

# 35 INTRODUCTION

Sickle cell disease (SCD) is a heterogeneous group of disorder, with a highly variable clinical
spectrum. It is an autosomal recessive structural haemoglobin disorder.<sup>1</sup> The most prevalent
form is sickle cell anaemia(HbSS), which is due to inheritance of the sickle cell gene in a
homozygous state. Other forms of SCD include the compound heterozygous forms in which
the sickle beta globin gene is co-inherited with another abnormal haemoglobin gene such as
HbC in HbSC, βthalassaemia in HbSβ thalassaemia among others.<sup>1, 2</sup>

SCD is the most common genetic disorder in Sub-Sahara Africa. Nigeria is bearing a high disease burden with an estimated 1 - 2% of its population affected by the disease. An estimated 20 - 30% of her populace carry the sickle cell gene with a normal haemoglobin gene (carrier state). The disease burden differ slightly from one geographical region to another. Nwogoh et al<sup>3</sup> reported the prevalence rate of SCD to be 2.4% and a 23% carrier state in Benin City. Inyama et al<sup>4</sup> reported a prevalence of 3.7% in a multi-centre study in Nigeria.

The pathophysiology of Sickle cell anaemia is the substitution in the sixth position amino 49 acid of β globin gene or also the substitution of GAG for GTG at chromosome 11.<sup>5</sup> This 50 substitution results in the broad clinical spectrum of the disease that extend beyond the red 51 cell, as a result of the tactoid formation which is due to the effect of the substitution of the 52 glutamic acid which is hydrophilic with a less polar hydrophobic, neutral amino acid valine. 53 During hypoxic condition, this abnormal valine amino acid causes intraerythrocytic 54 hydrophobic interaction of affected haemoglobin tetramers, thereafter causing their 55 precipitation and finally polymer formation, leading to the loss of potassium and water 56 resulting in cellular dehydration which also worsens the whole process<sup>5</sup>. Other contributing 57 factor include Nitric oxides depletion, endothelia activation with increase expression of 58

Comment [PT1]: due to

Comment [PT3]: promotes further precipitation and red cell rigidity. Comment [PT4]: factors Comment [PT5]: oxide adhesion molecule, inflammation and activation of coagulation system all play a vital role in

60 the pathophysiology of this disease.<sup>5</sup> Despite understanding the molecular basis for this

disease the mechanism of vaso-occlussive crisis remain so vast that it cannot be completely

avoided thereby predisposing many of this patient to recurrent recalcitrant and unbearable
bone pain crisis.

Opioid are group of potent analgesic with mixed receptor activities. Opioid is said to be absorbed from the gastrointestinal tract and metabolized in the liver, gastrointestinal tract and kidney. There are four types of opioid receptors (Mu, Kappa, Delta, Nociceptor-OR) with a major analgesic effect and a subtype nociceptor-OR which is termed the MOP.<sup>6</sup> Most opioid tend to cause a reduction in consciousness and euphoria predisposing them to abuse.<sup>6</sup>

69 Recurrent bone pain crisis represent the most common reason patient with SCD seek acute 70 medical care. In a study among sickle cell anaemia patient that are substance dependent, pain related symptom accounted for about 88% of all symptom.<sup>7</sup> Opioid analgesic are the 71 mainstay of therapy for bone pain crisis in SCD, thus before adulthood most SCD patients 72 must have had intermittent exposure to opioids. Opioids are potent analgesic associated with 73 decrease hospitalization.<sup>8</sup>The management of bone pain crisis has been an issue of debate 74 75 among physician. Some physician advocate minimal use of these drug for fear of addiction, while others believe that inadequate analgesia predisposes patients to pseudoaddiction.<sup>9</sup> 76 77 There have been several report in substance abuse by SCD patients with a prevalence of less than 10% worldwide,<sup>10</sup> but varies from one region to another in Nigeria. Ahmed et al<sup>11</sup> 78 reported a prevalence of 17.8% of opiate dependence among patient with SCD in Maiduguri, 79 North East Nigeria with a male preponderance. Similarly, in a study by Mabayoje et al<sup>10</sup> an 80 incident of less than 10% was reported in the South West. Furthermore, Iheanachoet al<sup>12</sup> also 81 82 reported a less than 18.2% with male preponderance. From the various studies, it could be said that the incidence varies with geographical location with a more prevalence of male sex 83

Comment [PT6]: delete

Comment [PT7]: add

Comment [PT8]: patients

Comment [PT9]: delete

# 84 CASE REPORT

Miss EO is a 27 years old Nigerian Female graduate with sickle cell anaemia. That was 85 diagnosed when she was 2 years old using Haemoglobin electrophoresis. She presented on 86 the 4<sup>th</sup> of January 2017 with a 2 years history of self-medication of DF118 and a self-87 medication of Tramadol. She said she got addicted to these drugs about 2 years ago while she 88 was admitted at government hospital in Calabar on account of sickle cell bone pain crisis 89 affecting her upper and lower limb which was so severe with a pain score of 9/10(based on 90 numerical pain rating scale) and lasted for about 48hours despite administration of several 91 analgesic such as Diclofenac and Pentazocin. Pain began to subside on administration of oral 92 DF118 at 60mg to alternate with Tramadol 100mg which was given for a week. Patient said 93 while she was on admission she enjoyed the feelings of the quick relief of the pain and 94 sedative effect that allows her to sleep comfortably following the administration of DF118 95 96 and Tramadol. Patient on account of this improvement sought to know the name of the 97 medication that could give such a wonderful relief and also because of fear of reoccurrence of the pain. She also noticed that both medication become drug of choice each time she has 98 severe bone pain and present to the same health centre. She said on account of the 99 psychological burden of the disease on her parents, who were worried of the repeated bone 100 pain crisis with frequent hospital visits and was also discovered that both medication give 101 their daughter relief and reduce their hospital visit, therefore decided to purchase a card of 102 each medication weekly for her. Administering 30mg of DF118 twice daily initially but after 103 5 months increased the dosage to 60mg twice daily for a year because the initial dosage could 104 not control the pain and she was very uncomfortable. She started with the new dose in the 105 absence of pain because she was enjoying the euphoric effect. Patient revealed she was 106 107 purchasing the drug on her own and even exaggerates her pain to get the drug prescription 108 from her physician and at most time she gets it without prescription from a private pharmacy

Comment [PT10]: It

Comment [PT11]: delete

109 whose identity she does not want to disclose. Patient said she spends about \300 (approximately \$1) to purchase a card, which she finances with her pocket money, selling her 110 belonging, borrowing and buying on credit. Patient said after a year of self-medication of oral 111 112 DF118 at 60mg twice daily she discovered she was not getting the relief she used to get. Patient said she got depressed and decided to change to another potent oral opioid (Tramadol) 113 114 not the injectable because she reacts to the injectable, with nausea and continuous vomiting. She said she started with 50mg of Tramadol twice daily, got relief and also enjoyed the 115 euphoric effect and later increased the dose to 100mg then 200mg twice daily which she took 116 every day for 1year even in the absence of pain. She gets the drug from a pharmacy and each 117 card costs between №1700 - №2000 (approximately \$7). She also gets prescription from a 118 doctor who she refuse to mention the name or address. She also claims that anytime she tries 119 to stop the medication she is being thrown into withdrawal symptoms which include lack of 120 sleep, restlessness, sweating, dizziness, blurred vision, headache, joint pain and abdominal 121 cramping, depression, agitation and craving for the drugs. Thus, these made her to seek help. 122 123 On examination, a young lady, pale, anicteric, conscious, alert and coherent, well oriented in

person, time and place, well groomed with good motor function with intact both long and short term memory, sense of judgement was mildly impaired. A review of her system were essentially intact, patient was referred to the psychiatric for further evaluation and possible detoxification and rehabilitation.

128 The following were the full blood count; PCV was 27%, Hb 9g/dl, WBC 11.2 x 10<sup>9</sup>/L,

129 Neutrophiles 68%, Lymphocyte 32%, and Platelet 452 x  $10^{9}$ /L

130

131

132

Comment [PT12]: whose name she refused
 Comment [PT13]: develops
 Comment [PT14]: delete
 Comment [PT15]: systems
 Comment [PT16]: psychiatric team

### DISCUSSION 133

This is a case study of a SCA patient who is dependent and addicted to tramadol and DF118. 134

BPC is the most commonest presentation among SCD,<sup>14</sup> which our index patients suffers [Comment [PT17]: common 135 about 10-12 episodes annually necessitating her to seek treatment from an health practitioner 136 137 who prescribed Tramadol and DF118. It was also noticed that the patient was on these 138 prescribed drug (DF118 & Tramadol) for too long with prescription note not properly controlled, which made her to have access to this prescription note. Due to the quick 139 analgesic relief and euphoric effect derived from both medications, patient has to feign pain 140 after genuine pain had subsided, in order to continue getting the prescription<sup>14</sup>. Based on this 141 142 it is pertinent to say patient is addicted to both drug and the primary aim of both drugs is now 143 being abused. Lack of proper orientation and counselling of the parents of the patient also 144 contributed to the abuse of the above medications. At this juncture clinical expertise and 145 judgement of the physician is highly needed to distinguish genuine pain from feigned pain in patient with SCD with DF118 & Tramadol abuse. There is paucity of information on DF118 146 and Tramadol abuse among sickle cell disease patient. Alao et al<sup>13</sup> reported the case of a 38 147 year old female sickle cell anaemia patient, though the drug of choice in this instance was 148 149 cocaine.

The immediate pain assessment and frequent reassessment at 15min, 30min, 1hour then 150 2 hours with appropriate application of medication until pain relief, are very important to 151 prevent drug abuse.<sup>15,16</sup> Therefore the less addictive analgesic should be administered first 152 after considering the nature of the pain before moving to stronger analgesic that have high 153 potential for abuse and when stronger analgesic is to be used it should be for a short 154 duration.15,16 155

## Comment [PT18]: a

The psychiatrist made an impression of opoid abuse and addiction in a known SCD patient.
Patient was initially managed on outpatient basis because patient had full insight of her
problem and also has the desire to stop but does not wish to be admitted.

On mental state examination, patient was calm with good hygiene, cooperative and appears motivated and emotionally stable. Her perception was normal, thoughts well collected with normal cognition.

On physical examination, the patient was a young slim tall lady, afebrile, anicteric, acyanose 162 with long limbs. Patient was gradually tapered off tramadol with a 50mg weekly reduction 163 for about 6weeks until she suddenly developed an episode of bone pain crisis. She was then 164 165 admitted for five weeks where she was treated with NSAID (Arthrotec) 75mg which was alternated with paracetamol 1000mg. Patient was also given diazepam 10mg and was 166 167 carefully observed all through the period of admission with total avoidance of opoid and was 168 discharged and placed on a routine medication of folic acid, paludrine and was given 2 weekly clinic appointment to ensure proper follow up. The patient was also counselled to 169

170 adopt pain tolerance.

# 171 CONCLUSION

172 It is suggested that regular orientation of health worker on the use of opioid particular DF118 173 and Tramadol among opoid naive SCD, a careful objective assessment of sickle cell patient 174 presenting with painful episodes should be carried out by an experienced health caregiver 175 with each case taken on its own merit. A non-opioid analgesic should be commenced first and if an opioid should be used, it should be used for a short duration. Prescription note of opioid 176 177 analgesic should be properly controlled; there should be a drug unit established and also 178 legislation against sales of this controlled drug.Opioid addictive patient should be taught how to tolerate pains and referred to a psychiatrist for detoxification and rehabilitation. 179

Comment [PT19]: opiod. She

# 180 **REFERENCES**

- 181 1 Ashley-koch A, yang Q, onley RS. Sickle haemoglobin alleles and sickle cell disease Am
- 182 J Epidemol 2000; 151(9) 839-45.
- 183 2 Davies SC, Oni L. Management of sickle disease. Br. Med. J .1997; 315: 655-660.
- 184 3 Nwogoh B, Adewoyin AS, Iheanacho OE, and Bazuaye GN. Prevalence of haemoglobin
  185 variant in Benin City, Nigeria. Annals of Biomedical Science. 2012; 11(2):60-64.
- Inyama M et al stroke prevalence among sickle cell disease patients in Nigeria a muticentre study. Africa Health. 2014; 14(2): 446-452.
- 188 5 Fronticelli C, Gold R.(1976) conformational relevance of the beta6glu replaced val
- mutation in the beta subunit and in the Beta(1-55) and Beta(1-30) peptides of haemoglobin

190 S.J Biol Chem251:4968.

- 191 6 Daya P, Desmeules J, Collart L. Pharmacology of tramadol Drug 1997; 53 suppl 2:18-24
- 192 7 Elander J, Lusher J, Bevan D, Telfer P (2003). Pain management and symptoms of
  193 substance dependence among patients with sickle cell disease. SocSci Med. 57(9), 1683-

194 1696

- Makanjuola A B, Olatunji P O(2009). Pentazocine abuse in sickle cell anaemia patients: A
  report of two case vignettes. African J Drug & Alcohol Studies. 8(2):59-64
- 9 Kotila T, Management of acute painful crisis in sickle cell disease clinical and laboratory
  haematology 2005 27(4)221
- 199 10 -223
- 11 Mabayoje V O, Adeyemo M A, Akinola N O. Case Review; Drug Addiction in sickle cell
  disease, A possible ongoing challenge in management of pain? Journal of global
  bioscience 2015,4(4):2021-2025

- 203 12 Ahmed S G, Ibrahim U A, The prevalence of therapeutic opiate dependence among patient
- with sickle cell disease in Maiduguri, North East Nigeria. Nigerian journal of pharmacy,
  2001,32:56-59
- 206 13 Iheanacho O E, Ezenwenyi I P, Enosolease M. G. Pentazocine abuse in sickle cell disease
- patient seen at a tertiary hospital in Nigeria: A chronic menace International journal of
  tropical disease & health 2015,9(1):1-8
- 14 Alao AO1, Westmoreland N, Jindal S (2003) Drug addiction in sickle cell disease: case
  report. Int J Psychiatry Med. ;33(1):97-101.
- 211 15 Okpala I, Add T. management of pain in sickle cell disorder. J Rsoc med.2002
  212 sep;95(9):456-458
- 213 16 D. C. Rees, A. D. Olujohungbe, N. E. Parker, A. D. Stephens, P. Telfer, and J. Wright,
- "Guidelines for the management of the acute painful crisis in sickle cell disease," British
  Journal of Haematology, vol. 120, no. 5, pp. 744–752, 2003.
- 216 17 Ibidapo M O, Akinyanju O O. Acute illness in Nigeria children with SCA annals of
- 217 Tropical paediatrics 1987, 7:181-186