*Journal of Computer Science*

Original Research Paper

# Applying Neural Network-Based Approach to Sickle Cell Disease-Related Pain Classification

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*Article history*
Received: 19-06-2018
Revised: 08-01-2019
Accepted: 27-06-2019

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**Abstract:** Sickle Cell Disease (SCD), an inherited Red Blood Cell (RBC) disorder, is characterized by anaemia, end-organ damage, unpredictable episodes of pain and early mortality. SCD affects 25% of people living in Central and West Africa causing life threatening "silent" strokes and lifelong damage. Nigeria accounts for 50% of SCD births worldwide (estimated 150,000 of 300,000 babies born with Symptomatic Sickle Cell Anaemia (SSCA) yearly, an annual infant death of 100,000 (8% of her infant mortality)) and about 2.3% of her population suffers from SCD with 40 million (25%) being healthy carriers. The number of such babies born with SSCA yearly has been estimated as 400,000 by year 2050. Healthcare resources for SCD are inadequate and the numbers of SCD are increasing daily, thereby demanding more sufficient resources. Intermittent and recurrent acute pain episodes are associated with SCD as a result of vaso-occlusion. Pain management at the Emergency Department for vaso-occulsive crisis for patients with SCD has been obnoxious. Biopsychosocial assessment and multidisciplinary pain management may be required when treating patients with frequent, painful sickle cell crises. Early and aggressive SCD-related pain management becomes a priority to improve quality of life and prevent worsening morbidities. Computational Intelligence-based framework in promoting higher-quality care and consequent increased life-expectancy in SCD patients is expedient. Monte Carlo Simulation Technique of Random Number Generation was used to generate 515 datasets for enhanced fifteen attributes of SCD. The datasets' features of SCD were used to train the neural network according to the pain encountered in identifying and treating the patient as fast as possible. This paper provides back-propagation algorithm of Artificial Neural Network in optimizing SCD-related pain classification and treatment processes, to complementa multidisciplinary care team intervention thereby increasing the quality of life.

**Keywords:** Computational Intelligence, Healthcare, Artificial Neural Network, Sickle Cell Disease, Vaso-Occlusive Crisis

## Introduction

Siddique and Adeli (2013) stated that computational Intelligence (CI) promised to advance the healthcare sector and clinical practice of disease management in diagnosis, treatment, prevention, prescription and optimization of the fast delivery to patient with these diseases. Akinwonmi (2011) confirmed Artificial Neural Network (ANN)'s connection/strength could be determined by the activation function which could be either linear or non-linear. Further, ANN consists of three layers (the input layer, output layer and hidden layer which is between the previous two layers.ANN's learning capabilities (supervised, unsupervised and reinforcement) are techniques used in learning. By adjusting the weight, the neural network adapts itself to learn and optimise to produce the desired output. Liu *et al.* (2006) affirmed ANN has been used in healthcare sector by applying the classification methods as ANNs identify the dataset features in order to accurately

diagnose the nature of diseases, pains and sicknesses. According to Macintyre *et al*. (2010), Sickle Cell Disease (SCD), a systemic multiorgan disease that most commonly presents with painful vaso-occlusive crises, occurs either spontaneously or due to factors such as dehydration, infection, hypothermia and low oxygen tension. Jain and Gupta 2016); Xu *et al*., 2017) discovered that SCD, a hematological disorder, leads to blood vessel occlusion accompanied by painful episodes and even death. The three basic factors/blood components (RBC, MCH and Hb) that are affected in Symptomatic Sickle Cell Anaemia (SSCA) are: (1) Mean Corpuscular Haemoglobin (MCH), the average amount of haemoglobin found in red blood cells and measured in pictograms; (2) Red Blood Cells (RBCs), which carry oxygen. Normal RBC range in Males is 4.7 to 6.1 million cells per micro liter (cells/mcl) and in females is 4.2 to 5.4 million cells/mcl. People suffering from SSCA have RBC in the range 2.37-3.73 cells/mcl. RBCs of SCD patients have diverse shapes that reveal important biomechanical and bio-rheological characteristics, e.g., their density, fragility, adhesive properties, etc and (3) Hemoglobin (Hb or Hgb), the iron-containing oxygen-transport metalloprotein in the RBCs, is measured in g/dl. A short summary of the variation in the values of these factors is given in Table 1.

SCD becomes one of the most common severe life-threatening haematological and monogenic disorders affecting millions of people worldwide. Affected blood is less able to carry oxygen and flow smoothly, which causes a host of health problems and a shorter lifespan. Piel *et al*. (2013; Kristiansen, 2014) reported that SCD occurs in people of African, Arabic and Indian racial backgrounds while countries in Equatorial Africa bear the greatest burden. It was further stated that three-quarters of children who inherit SCD are born in sub-Saharan Africa, but most have no access to treatment and die before their fifth birthday. As shown in Table 2, worldwide, over 300,000 babies are born with SSCA yearly having sickle hemoglobin gene and this figure may increase to 400,000 by the year 2050.

**Table 1:** Normal andanaemicrange of RBC, MCH and Hb (Jain and Gupta, 2016)

| Blood components | Normal range | Anaemic range |
|---|---|---|
| RBC(cells/mcl) | 4.2-6.1 | 2.37-3.73 |
| MCH (pg) | 25.63-29.23 | 26.52-32.16 |
| Hb (g/dl) | 25.63-29.23 | 6.63-10.87 |

**Table 2:** Burden of sickle cell disease (Kristiansen, 2014)

| Country | Sickle cell births/year |
|---|---|
| Nigeria | 91,011 |
| Dem. Rep. Congo | 39,743 |
| Tanzania | 11,877 |
| Uganda | 10,877 |
| Angola | 9,017 |
| Cameroon | 7,172 |
| Zambia | 6,039 |
| Ghana | 5,815 |
| Guinea | 5,402 |
| Niger | 5,310 |
| Sub-Saharan Africa Total | 242,187 |
| Worldwide Total | 305,773 |

The usual disorder in an individual is SCD. Rees *et al*. (2010; Akinsete and Osu, 2017) have reported that 43 million people have sickle-cell traits and 4.4 million people have SCDs. Akinsete and Osu (2017) also estimated that 40 million Nigerians are carriers of this disease with over 150,000 infants born with SSCA. This situation translates to Nigeria having the highest record of SCD, where infant's death of this carrier is estimated to be 100,000 in Nigeria representing eight percent of her mortality rate.

Case *et al*. (2018) submitted that SCD's management would social and cultural sensitivity of the practitioner's expert and experience due to the patient's challenging condition. Pain is a major issue in the care of patients with SCD. Dampier *et al*. (2014) found out that mechanisms behind pain and the best way to treat it have not been well understood. Vaso-Occlusive Crises (VOC) constitute SCD's painful episodes. Acute and chronic pains are mostly associated with adult patients, while acute pain is common in infants and children to classify the pain based on recent findings. On their own part, Macintyre *et al*. (2010) recommended that biopsychosocial assessment and multidisciplinary pain management might be required when treating patients with frequent, painful sickle cell crises. Telfer *et al*. (2014) concluded that SCD's acute painful crisis management remained unsatisfactory despite advances in the understanding and management of acute pain in other clinical settings. In corroborating, Lanzkron and Carlton (2015) discovered that the lack of a strong evidence base to guide the management/treatment of SCD-associated acute pain episodes have made it difficult for patients to receive high quality care outside of specialty centers. According to Poku *et al*. (2018) and Ginter *et al*. (2018), most hospitals and healthcare practitioners are using the traditional manual approach for management of patients with SCD, which can be time consuming and stressful to both patients and practitioners. Lanig *et al*. (2018) affirmed the daily increase in SCD would require more sufficient resources, such as healthcare professionals and practitioners, which are said to be inadequate. These inadequate healthcare workforce resources for SCD also often lack the required clinical experience while those working in the rural areas often lack the knowledge for clinical practice. Devi *et al*. (2013; Reader *et al*., 2017) reported ANN has been applied to SCsD for diagnosis, prediction and classification but has not been applied for the management of pain in SCDs.

## *Treatment of Sickle Cell Disease*

### *Artificial Neural Network Optimization*

Jin *et al*. (2005) reported different researchers have compared various techniques such as Back-propagation, Simulated Annealing, ANN and Genetic Algorithm (GA) for optimizing processes in a network. While Simulated Annealing and GA have been proved to be global search techniques for optimization, Back-propagation algorithm is the mostly used for optimization techniques for training the neural network to find optimal solutions. While datasets are fed into the network through the input layer, the weight in the network is updated, by adjusting in an attempt to optimize the process and minimize the loss function, Sun *et al*. (2003) observed that best solutions are obtained in the area of the point which is more effective and consistent. In adjusting the weight, Agatonovic and Beresford (2000) had earlier stated that the interconnections of the nodes are strengthened while some are dropped (weakened) so that the neural network can output a better solution. Finally, the network training comes to halt when the best and optimal solution is obtained. Ibrić *et al.* (2012) opined that datasets' features could be classified into training and test datasets at a start of the training. Furthermore, the predictive uses test data while the training data is used to obtain optimal solution which changes the error, while the evaluation of the data is done by using both training and test data. The latter is done simultaneously. Table 3 shows the steps to follow in supervised training of network and usage.

**Table 3:** Optimization of the ANN in solid dosage form (Ibrić *et al*., 2012)

| Training of the network |
|---|
| Data is presented to the network |
| Network computes an output |
| Network output is compared to desired output |
| Network weights are modified to reduce error |
| Usage of the network |
| Present new, unseen data to the network |
| Network computes an output based on its training |

### *Pain in Sickle Cell Disease*

Macintyre *et al*. (2010) proposed that uncontrolled or unexpected pain would require a reassessment of the diagnosis and consideration of alternative causes for the pain (e.g., new surgical/medical diagnosis, neuropathic pain). Equally important is the fact that multiple outcome measures are required to adequately capture the complexity of the pain experience and how it may be modified by pain management interventions. Pain management in SCD is challenging due to both the frequent crisis being faced by the patient and the inability of the healthcare practitioner to quickly identify the pain as the RBC disorder constitutes the cause of the painful complication in SCD as ascertained by Case *et al*. (2017). Ballas (2005) had earlier classified pains in SCD as chronic pain, acute pain, neuropathic pain or mixed pain. These are unpredictable and can occur at any time. Chronic pain is the outcome of the frequent acute pain that has not been properly taken care of. The pain can be experienced between three months and more. Some of the symptoms are achy, frequent in nature and this happens in a pathophysiologic events. Acute pain can occur throughout the life of the SSCA patient. The pain can be so sudden leading to Vaso-Occlusion (VOC) crisis and can cause damage to the organ which can sometimes lead to death if not properly managed. Neuropathic pain occurs as a result of wound or dysfunction in the body and is associated with SCD which can be triggered by harmful or deadly things. Dampier *et al*. (2017) corroborated Ballas (2005)'s classification and expressed that SCD-related pain is associated with increased morbidity, mortality and high health care costs. Dampier *et al* (2017), in giving a common set of criteria for classifying chronic pain associated with SCD, concluded such classification would enhance SCD pain research efforts in epidemiology, pain mechanisms and clinical trials of pain management interventions and ultimately improve clinical assessment and management by adopting a Proforma for Pain Assessmentas given in Fig. 1 (Howard and Telfer, 2015).

Due to the challenges in identifying and treating the painful episodes of the SCD which occur from offspring and can continue throughout the lifespan of that patient, frequent pain of acute nature requires quality healthcare and attention by the practitioners. Macintyre *et al*. (2010; Case *et al*., 2017; Howard and Telfer, 2015) recommended that the Acute Painful Crisis (APC), an episode of pain, usually of abrupt onset, in severe cases would require hospital treatment with opioid analgesia. While parenteral corticosteroids appear to reduce the duration of analgesia requirements and length of hospital stay, without major side effects, during sickle cell crises, one of the most important complications of APC is Acute Chest Crisis (ACS). In their submissions, Macintyre *et al.* (2010), Howard and Telfer (2015) and Case *et al*. (2017) identified monitoring for development of ACS with regular assessment of respiratory rate, oxygen saturation and daily examination of the chest as an essential part of the management of APC. There is insufficient evidence to suggest that fluid replacement therapy reduces SCD- associated pain. Hydroxyurea is effective in decreasing the frequency of acute crises, life-threatening complications and transfusion requirements in SCD.

*The Sickling Phases*

Hemoglobin has a rope-like structure - the sickle - which is a trait in SSCA. Molecules of the hemoglobin are put together to form fibres and then aggregated into twisted pairs. US_NIH (2014) affirmed SSCA-hemoglobin consists of four sickling phases: HbS, $P^{+}$chain, deoxy+bs and polymer while each of the hemoglobin molecules is called heme group. Haemoglobin polymerisation leads to abnormal sickle-shaped erythrocytes' rigidity to disrupt blood flow in small vessels. Figure 2 shows the sickling phases (Howard and Telfer, 2015).

The most prevalent SCD genotypes associated with the most severe clinical manifestations include homozygous hemoglobin SS (HbSS) and the compound heterozygous conditions hemoglobin Sβ0-thalassemia (HbSβ0-thalassemia), hemoglobin Sβ+-thalassemia (HbS β +-thalassemia) and hemoglobin SC disease (HbSC). Vaso-occlusion (central to the pathophysiology SCD) leads to distal tissue ischaemia and inflammation, with symptoms defining the acute painful sickle-cell crisis. The importance of chronic anaemia, haemolysis and vasculopathy has been established. Nevertheless, repeated sickling and ongoing haemolyticanaemia, even when subclinical, lead to parenchymal injury and chronic organ damage, causing substantial morbidity and early mortality. Consequences of sickling include destruction to the membrane and cytoskeleton, removal in the RBC, red cell dehydration and impaired anti-oxidant mechanisms. Figure 3 shows the sickle cell crisis which causes obstruction of blood flow and pain.

| | |
|---|---|
| Patients name: | Hosp# |
| Sex M/F (circle) | DOB |

Pain and Analgesia Assessment

**Date/Time**

**Site of pain:** **Duration of pain:**

Description of pain:

Precipitant/Triggers:

| | |
|---|---|
| Sharp ☐ | Infection ☐ |
| Burning ☐ | Dehydration ☐ |
| Throbbing ☐ | Cold Weather ☐ |
| Shooting ☐ | Hot Weather ☐ |
| Aching ☐ | Stress ☐ |
| Stabbing ☐ | Physical activity ☐ |
| Sore ☐ | Other ☐ |
| Crushing ☐ | |
| Other ☐ | |

Analgesia taken in the last 8 hrs:.....

Patients with ANY of the below should be referred for medical review

- Chest Pain, Shortness of breath, Hypoxia (oxygen saturation <94%
- Fever/rigors (Temp>38°C). Hypertension (BP <90/60)
- Tachycardia>1100 (even after pain has settled following analgesia)
- Raised respiratory rate of >20(even after pain has settled following analgesia)
- New neurological symptoms, headache, confusion, numbness of limbs
- Abdominal pains
- Priapism (persistent erection)
- Pregnancy
- Visual loss or bleeding in the eye
- PAR>four
- Concerns from the nursing learn about the patients' clinical condition.

**Fig. 1:** Proforma for pain assessment (Howard and Telfer, 2015)

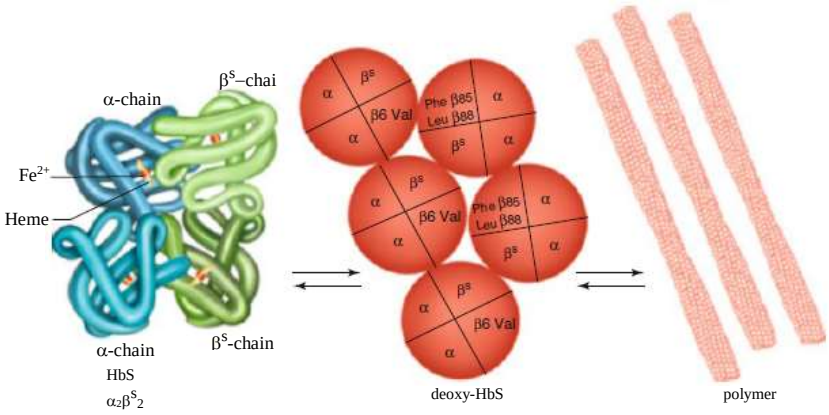


**Fig. 2:** Sickling Phases (Howard and Telfer, 2015)

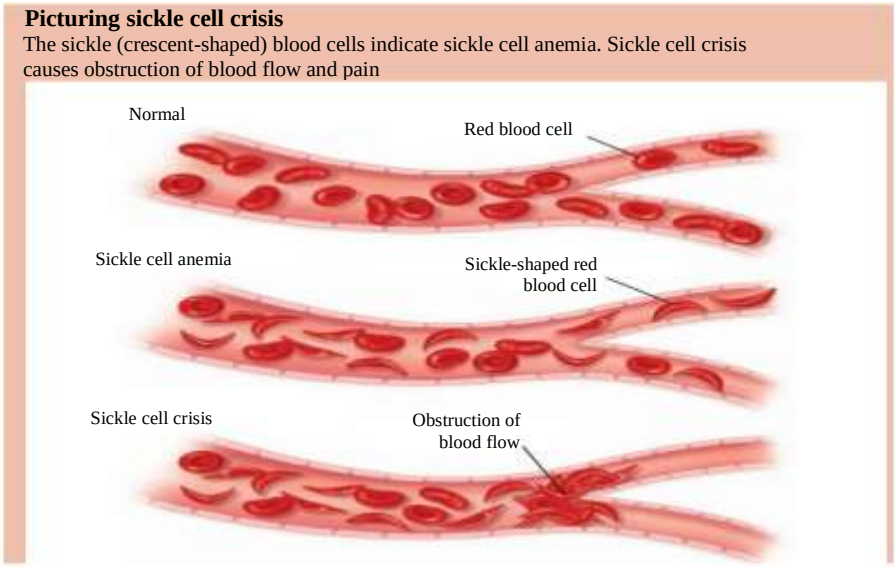


**Fig. 3:** Picturing sickle cell crisis (Creason, 2010)

Howard and Telfer (2015) certified opioid drugs are potentially toxic and inappropriate dosing could result in excess morbidity and mortality, particularly from respiratory suppression and excessive sedation. Consequently, Dampier *et al.* (2017) recommended frequent monitoring of vital observations including respiratory rate and sedation score be made mandatory, using Pain Assessment Scale of Fig. 4 (Howard and Telfer, 2015).

## *Vaso-Occlusive Crisis*

Lanzkron *et al.* (2010) reported SCD causes intermittent and recurrent acute pain episodes, referred to as 'Vaso-Occlusive Crises' (VOC), as a result of vaso-occlusion. Furthermore, most adults and infants experienced these painful episodes (being the most common with people having SSCA). VOC occurs when there is coagulation of the RBC and this can lead to severe injuries or damage to the organ of the body which is the most common in the complication. The SSCA's severe complication is responsible for Emergency Department (ED) and healthcare sector for SCD patient to receive quick treatment with high quality and outmost care to save life. Hereditary genetic disorder, also found in SCD, results in the predominant production of an abnormal/mutant hemoglobin called Hemoglobin S (Hb S) in RBCs. Persons carrying one normal hemoglobin gene and the S gene are known as having sickle trait (AS) and are usually healthy and haematologically normal. Sickle shaped red cells, formed when hemoglobin offloads oxygen to the tissues, are more rapidly removed from the circulation by the body (a process called hemolysis) leaving much less hemoglobin circulating (anaemia). Complication occurrences can lead to VOC. Every SCD patient experiences this VOC during his/her life span and if the person is not being taken care of during the time of the crisis, it might lead to death.

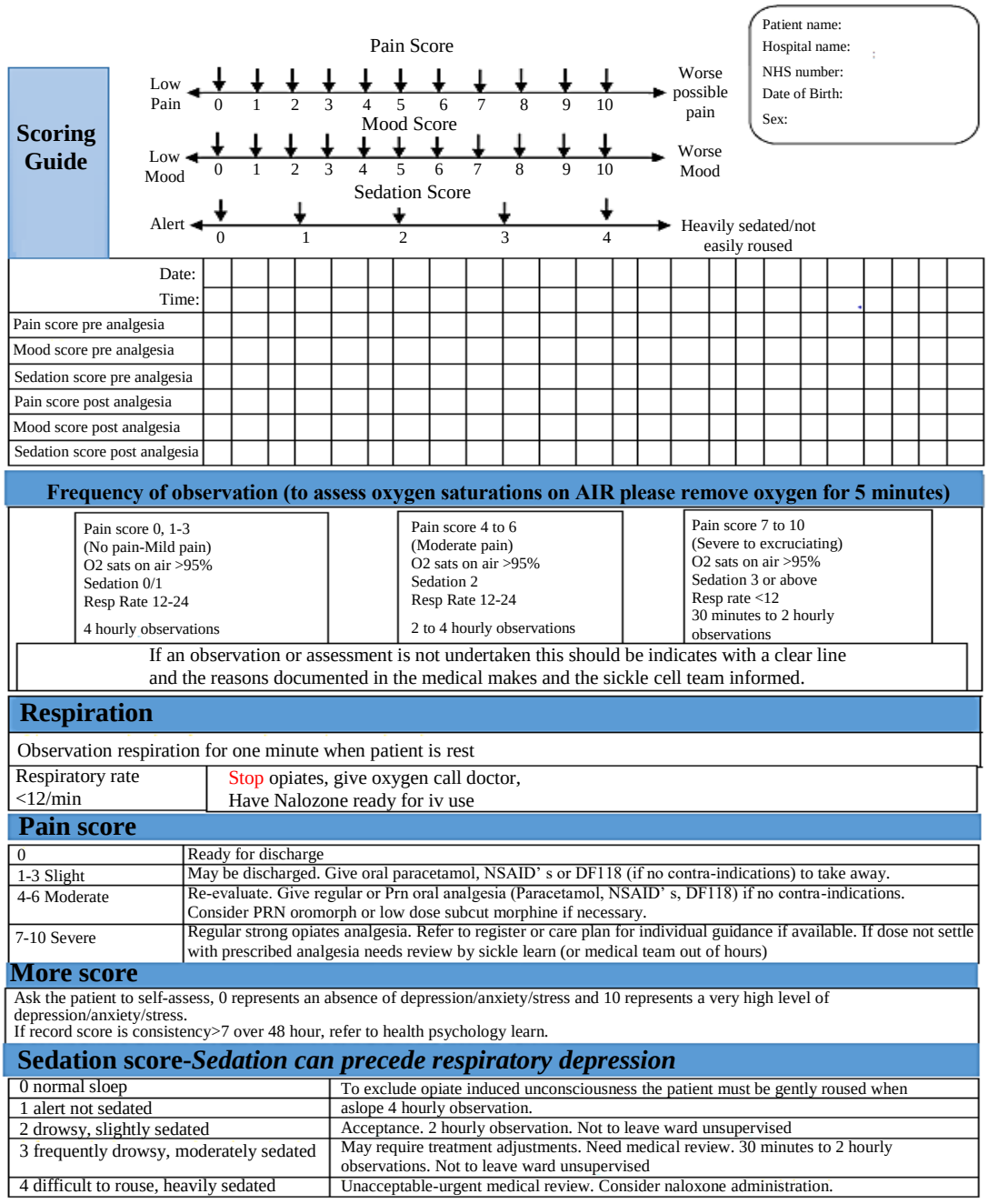


**Fig. 4:** Pain assessment scale (Howard and Telfer, 2015)

## Materials and Methods

ANN's ability to learn can be used to implement the algorithm capable of learning and optimizing processes involved in the management of pain in SCD patient. Data are collected by hospitals and healthcare centers having records of the entire SCD patients that have been diagnosed and treated. With this data we can determine a patient that has greater risk by processing and analysing the data collected. Neural Network can help to process and analyze patients with sickle cell and those that need immediate attention. The use of ANN can help predict the best practice in management of pain during crisis based on the symptoms. Elsalamony (2016) presented an algorithm to identify healthy and unhealthy sickle cell patient using ANN as structured in Fig. 5. This was a neural network which has input layer, output layer and hidden layer (between input and output layers), but not trained to optimize the processes in the management of pain in SCD.

**Table 4:** Related works in neural network based approach to sickle cell disease-related pain management

| Author | Methods/ Techniques | Research Focus | Limitation |
|---|---|---|---|
| Xu *et al*. (2017) | Convolutional neural network | The paper focused on the modeling of deep convolutional networks in classification of different structure of the red blood cell compared with method of independent structure. Both methods gave a good prediction and could assist in the pain of SCD patients. | No focus on pain management of the Sickle cell diseases-related and the number of datasets used were small in classifying the SCD. |
| Hirimutugoda and Wijayarathna (2010) | Artificial Neural Network (ANN) | The paper gave an idea of the possible accurate and faster diagnosis method of disorder in red blood cell (RBC) | Unable to manage pain in sickle cell anaemia when a patient is being faced with crisis. |
| McCartney *et al*. (2014) | ANN | Develop a secure web-based system for facial pain diagnosis and evaluate the performance having higher accuracy. | The research did not focus on Sickle cell Diseases in recognizing and optimizing pain. |
| Pombo *et al*. (2014) | ICT Technologies | The paper reviewed the application of computer information and technologies for pain management using an automated database. | No techniques to learn and optimize the processes in management of pain. |
| Tomari *et al*. (2014) | Automated system and ANN | Classification of RBC with the assistance identify of computer system to detect and Normal and Abnormal RBC by using ANN classifier. | The automated system was used to train the network in classifying the RBC into normal/abnormal but not for management of pain of the SCD. Few datasets were used to classify using ANN. |
| Horn *et al*. (2015) | Cella Vision system and ANN | This paper focussed on detecting RBC by microscopy manual differential to theCella Vision and comparing performance with ANN. | No technique was used to optimize or train network for RBC morphologic abnormalities |
| Schneider *et al*. (2015) | Optical ANN | ANN used for classification of the blood cell for cell imaging. Proposed a label-free technique that uses a discrete numeric holographic microscopy | ANN was not used to train the network but rather to classify using numerical simulations. |
| Argüello *et al*. (2015) | Computational model technique | The research recommended computational model techniques for pain management and to predict for other healthcare areas. | No specific model was used; only suggested a computational model for pain management |
| Coleman *et al*. (2016) | Phenomenological Analysis | The paper focused on the challenges of the painful episodes in SCD, quality of life and timing of their experiences | No Computational Technique was used in optimizing painful sickling episodes. |
| Tyagi *et al*. (2016) | ANN | ANN technique was used to classify the normal and abnormal RBC based on the datasets features. | Optimizing and prediction of the pain in SCD were not considered. |
| Durant *et al*. (2017) | Convolutional Neural Networks | The research showed that Convolutional NN could be used to indicate White Blood Count (WBC) with higher accuracy and optimize performance in a clinical and health care sector. | Morphologic profile of blood cells relies heavily on manual smear processing techniques and visual inspection |
| Khalaf *et al*. (2017) | Machine learning Methods/ANN | ANN was used for classification of medical data for prevention and guidelines for diseases in Sickle Cell. | No training of datasets. It only provided manual approaches to sickle cell therapy. |
| Rahmat *et al*. (2018) | Self-Organizing Map Neural Network. | The paper classified normal and abnormal RBC of the sickle cell diseases in digital image using self-organizing map neural network. | System developed could not optimize the process of pain management in SCD |

From Table 4, various researchers acknowledged the fact that there is a demonstrated need for management of pain in SCD. Equally and importantly accepted is the need to optimize the processes of the pain management for better healthcare services.

## *Training Data for Sickle Cell Disease*

Currently, there is no standardization for pain management in SCD. This paper attempts to develop a neural network model capable of promoting higher-quality care by optimizing the processes in managing sickle cell patients during pain-induced crisis. This will help to improve the quality of life of the patient with attendant reduction of unnecessary spending, patient illness and pressure for the healthcare practitioners in terms of emergency cases they need to attend to per time. The SCD attributes adapted from Khalaf *et al*. (2016) in Table 4 were enhanced for consideration with Age, Educational Background and Location items. Monte Carlo Random Number Generation technique has been used in this research to generate dataset using the fifteen attributes of Table 5. This approach developed a scientific framework that facilitates hypothetical generation of a big dataset without necessarily going through the time-consuming Ethical Approval Committee process of Institutional Review Board.

**Table 5:** Sickle cell Disease Datasets attributes as enhanced from Khalaf *et al*. (2016)

| S/N | Attributes | Meaning |
|---|---|---|
| 1. | Age | Length of time that the patient has lived |
| 2. | Weight | A body relative mass of that patient |
| 3. | Educational Background | Highest educational background of the patient to know the level of literacy |
| 4. | Haemoglobin | The protein found in the Red Blood Cell (RBC) that carries oxygen to every part of the body. |
| 5. | Location | Geographical area and address where the patient lives. |
| 6. | Mean corpuscular volume (MCV) | The measure of the size of the red blood cells in the body of the patient. |
| 7. | Platelets (PLTS) | Thrombocytes: refer to components of blood whose function is to stop bleeding. |
| 8. | Neutrophils (WBC NEUT) | Neutrophils helps to fight infections |
| 9. | Neutrophils count (RETIC A) | Real number of White Blood Cells (WBC) present in the patient. |
| 10. | Reticulocyte count (RETIC %) | Measures the rate at which reticulocytes are made in the bone marrow and enter the bloodstream. |
| 11. | Alanine Aminotransferase (ALT) test | The blood test that checks for liver damage. It's an enzyme mostly in liver and kidney cells |
| 12. | Body Bio Blood (BIO) | BodyBio wellness Report is a revolutionary report that lets you get the most from the companion blood test. |
| 13. | Fetal Hemoglobin (HbF) | The RBC that carries oxygen round the body. |
| 14. | Bilirubin | Helps to find the cause of health conditions, like jaundice, liver disease and anaemia. |
| 15. | Lactate Dehydrogenase (LDH) | An enzyme involved in the energy production that is found in almost the body's entire cell. |

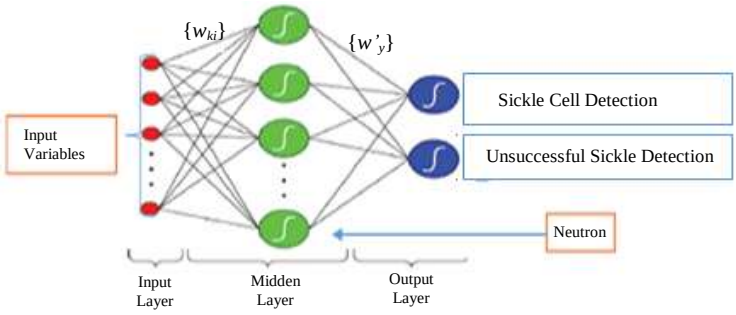


**Fig. 5:** Multilayer perceptron of the neural network (Elsalamony, 2016)

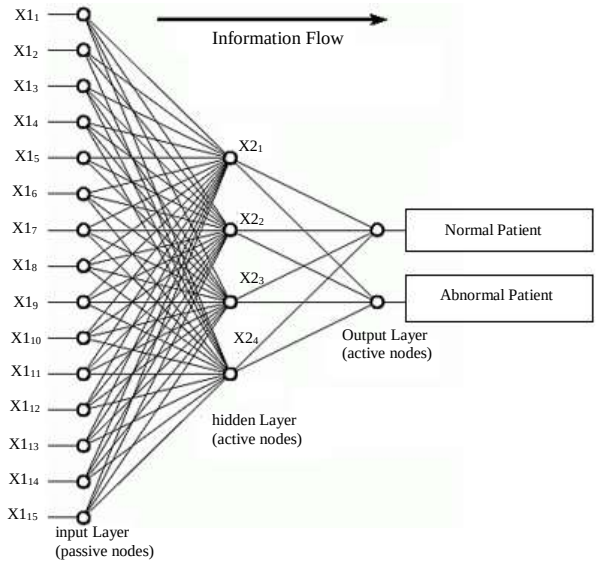


**Fig. 6:** ANN framework for SCD-Related Pain Management; adapted from Karan *et al*. (2012)

Figure 6 presents the neural network to manage the pain in sickle cell patient to be able to determine between normal and abnormal patient in the processes, using the attributes in Table 5.

About 515 datasets were generated using Monte Carlo a Simulation Techniques to Generate Random Number for items in Table 5.

## Results

For the purpose of the work we classified pain into four: low acute pain, severe acute pain, low chronic pain and severe chronic pain (crisis). Our target output percentages are as presented in Table 6.

Our results using Figs. 6 and 7 are presented in Table 7.

To validate the system, we have a training dataset and testing dataset on classifier model. The evaluation of the neural network was based on some certain parameters such as sensitivity, specificity, precision, the F1 score, Youden's J statistic and the classification accuracy. Table 8 shows the formula to evaluate the performance.

Where TP, TN, FP and FN stand for true positive, true negative, false positive and false negative respectively for the evaluation performance. Back-propagation method was used for training the datasets. The activation function was determined by the weight of the network, the gradient of the loss function fed into the network to the back-propagation to update the weights of the function in order to reduce the loss function. This was done using a supervised form of learning in ANN. The ANN could learn from the datasets and be able to recommend the best processes in management of pain of sickle disease patient.

| S/N | Age | Weight | Edu Backgd | Haemoglobin | Location | MCV | PLTS | WBC | Neutrophils Count | Reticulocyte Count | ALT Test | Body Bio Blood | Fetal Haemoglobin | Bilirubin | Bilirubin Dehydrogenase | Pain Classification |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 1 | 2 | 3 | 4 | 2 | 3 | 2 | 3 | 1 | 3 | 4 | 4 | 3 | 2 | 1 | 2 |
| 2 | 2 | 2 | 1 | 3 | 3 | 4 | 1 | 1 | 1 | 2 | 3 | 3 | 3 | 3 | 1 | 3 |
| 3 | 1 | 2 | 4 | 3 | 4 | 2 | 4 | 3 | 2 | 2 | 1 | 2 | 3 | 2 | 3 | 1 |
| 4 | 1 | 3 | 1 | 4 | 2 | 3 | 3 | 3 | 2 | 2 | 4 | 1 | 1 | 2 | 2 | 4 |
| 5 | 1 | 2 | 4 | 3 | 1 | 1 | 4 | 2 | 3 | 4 | 2 | 2 | 4 | 3 | 3 | 3 |
| 6 | 2 | 2 | 2 | 2 | 4 | 2 | 2 | 2 | 2 | 3 | 1 | 1 | 2 | 2 | 3 | 2 |
| 7 | 1 | 4 | 1 | 4 | 3 | 3 | 3 | 3 | 2 | 4 | 2 | 3 | 3 | 2 | 3 | 2 |
| 8 | 2 | 3 | 1 | 4 | 4 | 1 | 2 | 3 | 4 | 2 | 2 | 1 | 4 | 4 | 1 | 4 |
| 9 | 2 | 4 | 3 | 4 | 2 | 4 | 2 | 2 | 1 | 3 | 2 | 3 | 1 | 2 | 4 | 4 |
| 10 | 1 | 1 | 2 | 3 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 1 | 1 | 4 | 3 | 4 |
| 11 | 3 | 1 | 1 | 1 | 1 | 3 | 3 | 3 | 2 | 2 | 2 | 2 | 1 | 2 | 3 | 2 |
| 12 | 1 | 1 | 3 | 2 | 4 | 4 | 1 | 1 | 1 | 2 | 4 | 2 | 1 | 4 | 1 | 4 |
| 13 | 3 | 3 | 1 | 1 | 1 | 1 | 3 | 1 | 4 | 3 | 1 | 1 | 3 | 3 | 1 | 1 |
| 14 | 1 | 2 | 2 | 3 | 3 | 3 | 1 | 2 | 3 | 3 | 3 | 3 | 1 | 2 | 1 | 4 |
| 15 | 1 | 2 | 3 | 4 | 4 | 2 | 4 | 2 | 2 | 4 | 3 | 4 | 1 | 2 | 1 | 4 |
| 16 | 3 | 2 | 1 | 3 | 3 | 4 | 4 | 4 | 4 | 3 | 4 | 1 | 1 | 2 | 1 | 3 |
| 17 | 2 | 3 | 3 | 1 | 1 | 2 | 2 | 2 | 2 | 4 | 3 | 1 | 1 | 1 | 1 | 4 |
| 18 | 3 | 4 | 4 | 1 | 2 | 2 | 2 | 3 | 4 | 4 | 1 | 1 | 1 | 1 | 3 | 1 |
| 19 | 3 | 3 | 1 | 3 | 3 | 1 | 2 | 1 | 2 | 3 | 3 | 3 | 4 | 1 | 1 | 3 |
| 20 | 3 | 1 | 1 | 1 | 3 | 3 | 3 | 2 | 4 | 2 | 4 | 4 | 2 | 1 | 1 | 2 |
| 21 | 1 | 3 | 1 | 1 | 4 | 2 | 1 | 3 | 4 | 1 | 3 | 1 | 3 | 2 | 3 | 3 |
| 22 | 1 | 1 | 3 | 1 | 2 | 4 | 3 | 1 | 1 | 1 | 4 | 2 | 2 | 2 | 1 | 2 |

**Fig. 7:** Sample of data generated

**Table 6:** Target output percentage

| Pain classification | Percentage classification | Class number |
|---|---|---|
| Less acute pain | 0-25% | 1 |
| Severe acute pain | 26-50% | 2 |
| Less chronic pain | 51-75% | 3 |
| Severe chronic pain | 76-100% | 4 |

**Table 7:** Attributes classification

| | Attributes classification | 0-25% | 26-50% | 51-75% | 76-100% |
|---|---|---|---|---|---|
| S/N | Class number | 1 | 2 | 3 | 4 |
| 1 | Age | 0-25 years | 26-50 years | 51-75 years | 76-100 years |
| 2 | Weight | Under Weight | Normal Weight | Over Weight | Obesity |
| 3 | Educational Background | Illiterate | High School | Graduate | Post Graduate |
| 4 | Haemoglobin | Low | Normal | High | Very High |
| 5 | Location | Rural | Urban | Sub-urban | Exurban |
| 6 | Mean corpuscular Volume(MCV) | Low | Normal | High | Very High |
| 7 | Platelets (PLTS) | Low | Normal | High | Very High |
| 8 | Neutrophils (WBC) | Low | Normal | High | Very High |
| 9 | Neutrophils Count | Low | Normal | High | Very High |
| 10 | Reticulocyte Count | Low | Normal | High | Very High |
| 11 | Alamine Aminotransferase (ALT Test) | Low | Normal | High | Very High |
| 12 | Body Bio Blood | Low | Normal | High | Very High |
| 13 | Fetal Haemoglobin | Low | Normal | High | Very High |
| 14 | Bilirubin | Low | Normal | High | Very High |
| 15 | Bilirubin dehydrogenase | Low | Normal | High | Very High |

**Table 8:** Performance metric calculation, adapted from (Karayiannis and Venetsanopoulos, 2013)

| Metric name | Calculation |
|---|---|
| Sensitivity | TP/(TP+FN) |
| Specificity | TN/(TN+FP) |
| Precision | TP/(TP+FP) |
| F1 Score | 2 * (Precision * Recall)/(Precision + Recall) |
| Youden's J statistic (J Score) | Sensitivity + Specificity – 1 |
| Accuracy | (TP + TN)/(TP + FN + TN + FP) |
| Area under ROC | 0 ⇐ Area under the |
| Curve (AUC) | ROC curve ⇐ 1 |

## Discussion

Back-Propagation Neural Network (Multilayer Perceptron) with supervised learning model has been applied in SCD pain management processes in promoting higher-quality care. The datasets features of the SCD patients were used to train the neural network according to the pain encountered in identifying and treating the patient as fast as possible. Performance evaluation metric of the training datasets would help determine the accuracy and effectiveness of the Neural Network for utmost result.

## Conclusion

Sickle cell disease includes a group of inherited disorders of haemoglobin production. Haemoglobin S polymerises when deoxygenated, causing rigidity of the erythrocytes, blood hyperviscosity and occlusion of the microcirculation with resultant tissue ischaemia and infarction. Literature has ascertained that haemoglobin polymerization which leads to erythrocyte rigidity and vaso-occlusion is central to the pathophysiology of SCD. Equally established is the importance of chronic anaemia, haemolysis and vasculopathy. Clinical management is basic and few treatments have a robust evidence base. This paper provides a solution to SCD pain management during VOC. Painful episodes can easily be managed by the healthcare sectors to serve as a great relief. The development of this framework would help solve some of the challenges that are faced in the healthcare system in SCD-related pain management.

## Acknowledgement

We acknowledge the sustained mentorship by: Professor Charles Onuwa Uwadia (University of Lagos, Lagos, Nigeria), Professor Victor W. Mbarika (Southern University and A&M College of Business, Baton Rouge, Louisiana, USA) and Professor Sunday O. OJO, Tshwane University of Technology, Pretoria 0001, South Africa).

## Funding Information

No funding was involved in this research work as it forms an extract from the second author's postgraduate degree programme pursuit being supervised by the first author.

## Author's Contributions

**Zacchaeus Omogbadegun:** Originated and prepared the conceptual framework for the work. He wrote the Abstract, contributed to the Literature Review, edited the work and supervised the work.

**Israel Ogundele:** Besides contributing to the Literature Review, wrote the initial draft of the work and also used Monte Carlo technique to generate the hypothetical random numbers (test data) for the work based on the expanded attributes.

**Olufunke Oladipupo:** Reviewed the conceptual framework for the work. Provided cognate materials for the Literature Review, wrote the Conclusion section, and co-supervised the work.

Each of the authors read and agreed with the contents.

## Ethics

To prevent ethical issues that may arise after the publication of the manuscript, Monte Carlo Random Number Generation technique has been used in this research to generate dataset using enhanced fifteen attributes. This approach developed a scientific framework that facilitated hypothetical generation of a big dataset without targeting a particular patient or necessarily going through the usual time-consuming Ethical Approval Committee process of Institutional Review Board. We have also run the manuscript through a plagiarism/similarity check (Turnitin) to ensure the originality and uniqueness of the research work. We have ensured every item in the References List has been properly cited and vice versa. In addition, we have made a direct and substantial contribution to the research.

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