HARNESSING ARTIFICIAL INTELLIGENCE: INNOVATIVE APPROACHES TO MANAGING SICKLE CELL DISEASE

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ABSTRACT

Artificial Intelligence (AI) is revolutionizing the management of sickle cell disease (SCD), as it provides innovative solutions for early diagnosis, treatment and personalized care. Early detection of SCD is important in prevention of and improvement of patient outcomes. The research utilized a systematic and qualitative literature review method, which includes evaluating and contrasting pertinent authors and their results. The PRISMA guidelines were closely followed. The search strategy incorporated the research objectives and established and inclusion criteria for identifying relevant existing studies. The review examined articles on innovative management approaches for sickle cell disease, including both qualitative and quantitative studies. Inclusion criteria required outcomes related to diagnosis, prediction, or monitoring of the disease. Excluded studies were those not specifically about sickle cell disease, lacking AI-based models, unpublished in peer-reviewed sources, or with inadequate data and unclear methodology, as well as those focusing on other hematological disorders. Results revealed that AI-driven models significantly enhance the diagnosis, prediction and monitoring of SCD. AI and machine learning models identified sickle cells in blood smears with 84% to 98% accuracy, exceeding 99% with ensemble models. CRISPR-Cas9 therapies showed promise in restoring red blood cell function in ongoing trials. Wearable devices recorded 83% to 92% accuracy in predicting vaso-occlusive crises. Precision medicine models improved fetal hemoglobin levels to 30–40%. AI integration in SCD management improves risk stratification and personalized care. It facilitates SCD progression monitoring via real-time data and predictive analytics. Investment in AI technologies is essential for diagnosis enhancement, while regulatory bodies must ensure safe use, and researchers should refine tools for patient monitoring. The research will be of particular interest to technology developers and innovators working in the healthcare sector. This study will be important to scholars as they would better understand AI, medicine and healthcare innovation.

Keywords: Artificial intelligence, Innovative approaches, Sickle cell disease

I. INTRODUCTION

Background of the study

Artificial Intelligence (AI) is revolutionizing the management of sickle cell disease (SCD), as it provides innovative solutions for early diagnosis, treatment and personalized care (Koua *et al*.,2024). Early detection of SCD is important in prevention of and improvement of patient outcomes (Singh & Thakkar, 2020). Traditional diagnostic methods such as complete blood counts, sickle cell assays and hemoglobin electrophoresis require skilled professionals and advanced laboratory infrastructure, which may not be readily available, particularly in low-resource settings (Obeagu *et al*.,2024). AI-driven systems can assist in automating the analysis of blood samples, identifying sickled cells and abnormal hemoglobin patterns more efficiently (Lanzkron *et al*.,2022). Machine learning algorithms can help detect these abnormalities from lab results or blood smear images, enabling faster and more accurate diagnoses, even in remote areas where trained experts may be scarce (Goswami *et al*.,2023).

AI's potential extends beyond diagnosis into predictive analytics, where it can forecast disease progression and complications (Nembaware *et al*.,2020). Sickle cell disease is often associated with unpredictable and painful episodes known as vaso-occlusive crises, which can lead to severe pain, organ damage, and reduced quality of life (Gollapalli & Alfaleh, 2022). AI can help predict when a patient might experience a crisis or other

complications. This allows healthcare providers to adjust treatment plans, provide preventive interventions and better manage pain (Dong & McGann, 2021).

Moreover, AI can enhance treatment strategies for SCD by personalizing care plans based on individual patient data (Mayo *et al*.,2021). Machine learning models can analyze responses to various treatments like hydroxyurea, bone marrow transplants, or gene therapy, providing valuable insights into the most effective therapeutic options for each patient (Ndakotsu & Balarabe, 2019). AI tools can identify patterns in how different patients respond to medications and interventions, allowing for more tailored and evidence-based treatment regimens (Kumar & Das, 2021). This helps reduce trial and error, ensuring patients receive the most effective care for their specific needs and conditions (Issom *et al*.,2020).

AI-driven technologies have the potential to revolutionize the way SCD patients are monitored and managed over time. Through wearable devices and mobile health applications, AI can continuously track vital signs, pain levels and other relevant health data in real-time (Gimbert *et al*.,2024). This allows clinicians to monitor patients remotely and provide timely interventions when required (Summers *et al*.,2024). Additionally, AI-powered platforms can facilitate communication between patients and healthcare providers, ensuring that patients have continuous access to support and guidance (Nembaware *et al*.,2020). This systematic review assesses AI in management of SCD.

Objectives

i. To evaluate the effectiveness of AI-based models in predicting sickle cell disease
ii. To investigate the effect of AI models in diagnosing sickle cell disease
iii. To assess the potential of AI in predicting and monitoring sickle cell disease

Research questions

i. How effective are AI-based models in predicting sickle cell disease?
ii. What is the effect of AI models on diagnosing sickle cell disease?
iii. How can AI be used to predict and monitor sickle cell disease?

Significance of the study

This study will be important to healthcare providers, including doctors, nurses and specialists as the implementation of AI-based models will provide a more efficient and accurate way to diagnose and predict SCD. Consequently, providers can make faster, data-driven decisions, reducing the chances of misdiagnosis and enabling timely interventions.

The study will be important to patients, as it will indicate how the use of AI models could improve their quality of life. AI tools that predict disease crises or monitor disease progression could lead to more personalized treatment plans, better management of symptoms and fewer hospitalizations. In addition, early detection and timely interventions can help minimize complications.

This study may provide evidence to support the integration of AI technologies into national health strategies for chronic diseases. The could lead to a reduction in healthcare burdens, such as emergency room visits, inpatient admissions, and long-term care costs. Policy makers could incorporate AI solutions into public health frameworks for more equitable access to high-quality care.

The research will be of particular interest to technology developers and innovators working in the healthcare sector. The study will be a guide for further advancements in AI applications in medicine. Technology companies focused on healthcare solutions can use these findings to refine existing AI models or create new ones for SCD. This study will be important to scholars as they would better understand AI, medicine and healthcare innovation. The study will form a basis for further research on the use of AI in other chronic or genetic diseases. This could lead to the development of standardized protocols for AI-driven healthcare solutions.

II. METHODOLOGY

Study Design

Systematic reviews are carried out to gather information that is relevant to the research. Systematic reviews adhere to a planned and strict methodology, employing particular standards to either include or dismiss studies. This guarantees thorough inclusion of all pertinent studies related to the subject being examined. The research utilized a systematic and qualitative literature review method, which includes evaluating and contrasting pertinent authors and their results. The PRISMA guidelines were closely followed.

Search Strategy

The search strategy incorporated the research objectives and established and inclusion criteria for identifying relevant existing studies. Online databases such as the Google Scholar, Mendeley, EBSCOhost and Cochrane Library were searched for articles published between 2020 and 2025. The screening and selection of studies were carried out based on the predefined selection criteria for data extraction. The search employed combinations of key terms, that included " artificial intelligence “, " innovative approaches " and " sickle cell disease ". Multiple keyword combinations were used in the process. Data analysis was enables through Microsoft Excel, which included articles’ title, author(s), objecives, methodology, findings, conclusions and recommendations.

Selection Criteria

The review searched articles that focused on innovative approaches to managing sickle cell disease. Qualitative and quantitative studies were considered. Only studies that reported outcomes related to the diagnosis, prediction, or monitoring of sickle cell disease were considered for inclusion in the review.

Studies were excluded if they did not specifically focus on sickle cell disease or did not involve AI-based models or technologies. Articles that were not published in peer-reviewed journals or reputable sources were excluded to ensure the quality and reliability of the data. Additionally, studies with insufficient data, unclear methodology, or those that focused on other hematological disorders were excluded.

Data extraction

A total of 48 studies were included in the final analysis, covering diverse areas such as the use of artificial intelligence and machine learning in the diagnosis and prognosis of sickle cell disease, innovations in gene therapy and CRISPR-Cas9 technology, and the application of mobile health and wearable technologies for monitoring and management. The studies also explored the adoption of precision and personalized medicine approaches, as well as global and regional implementation frameworks aimed at improving the treatment and management of the condition. This is summarised in Figure 1: -

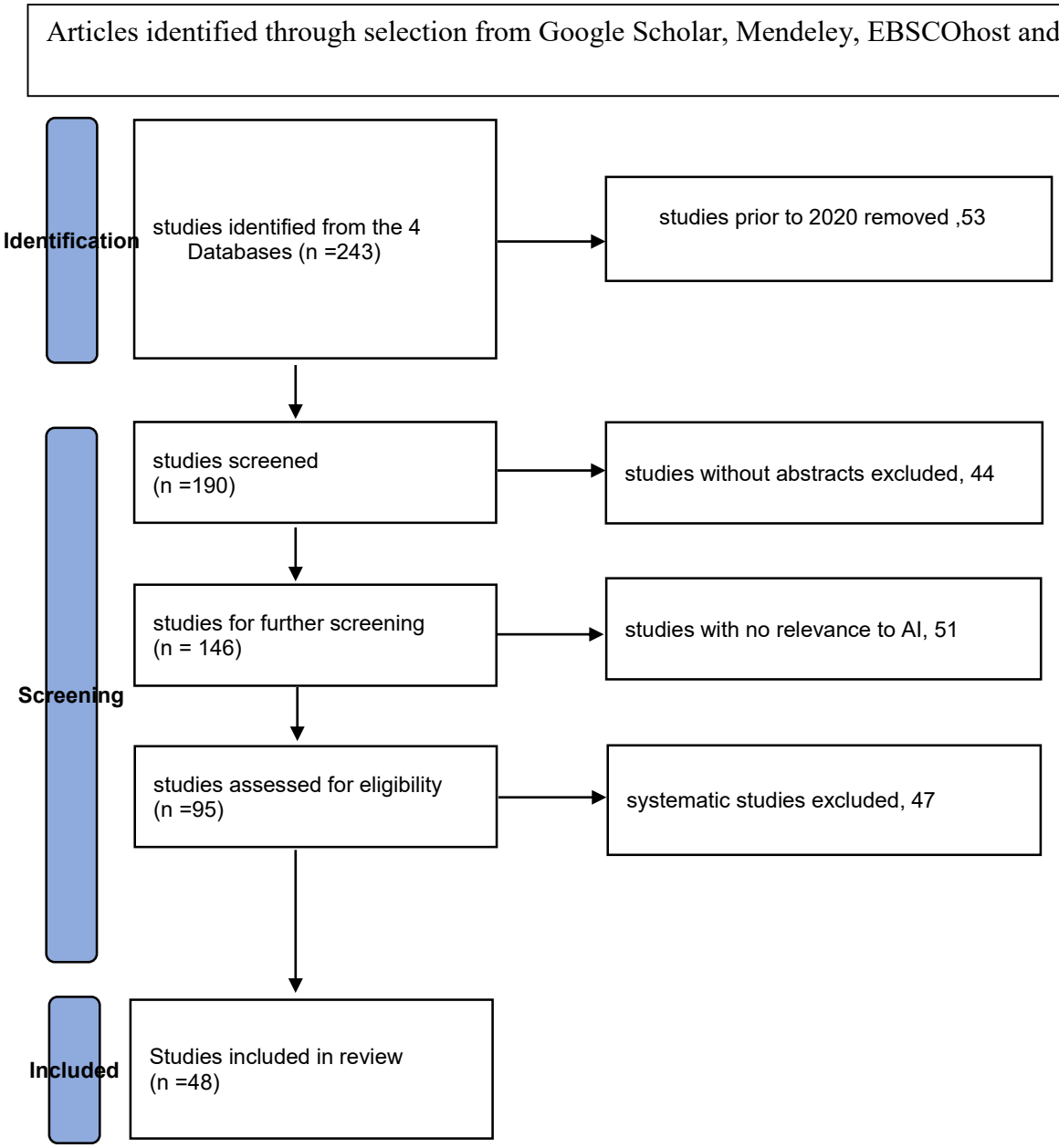

Figure 1: Flow chart

Ethical issues

Ethical considerations in secondary research focus on security, confidentiality and responsible data use (Hoover & Cohen, 2021). This study ensured that all secondary sources were properly acknowledged. Articles sources were valid, reliable and credible. Proper citation and referencing helped maintain transparency and academic integrity. Systematic data searches ensured objectivity and minimized bias. The research followed ethical guidelines to uphold originality and impartiality.

III. FINDINGS

Sickle cell anemia is a genetic blood disorder. It affects hemoglobin, the protein in red blood cells. This causes the cells to become sickle-shaped. Normal red blood cells are round and flexible whereas sickle cells are stiff and sticky (Vuong *et al*.,2023). They can block blood flow in small vessels, which leads to pain and organ damage. Diagnosis of sickle cell disease requires blood tests. Electrophoresis helps identify abnormal hemoglobin. Additionally, chromatography detects hemoglobin changes (Tariq *et al*.,2024). On the other hand, isoelectric focusing separates different types of hemoglobin. A complete blood count checks red blood cell level. A peripheral blood smear shows sickle-shaped cells under a microscope (Petrović *et al*.,2020). Early diagnosis is important for managing the disease. Treatment includes pain relief, blood transfusions and medications (Lanzkron

et al.,2022).

Balde *et al*. (2023) study summarized the current state of the art in sickle cell disease detection and diagnostic algorithms that include picture segmentation, feature extraction and classification. To identify sickle cells in pictures of blood smears taken at a microscopic level, they used computer vision techniques, machine learning, and convolutional neural networks. The authors identified challenges associated with segmentation techniques when handling microscopic images that feature overlapping cells.

On the other hand, Kumar and Das (2021) examined relevance and practicality of these mHealth applications for managing SCD in India. It was indicated that SCD is a persistent hereditary condition that requires continuous treatment and observation. Inadequate drug adherence and insufficient monitoring could result in a rise in health issues and reduced quality of life. In this digital era, many mHealth apps are being tested to see whether they might help people with SCD take their medicine as prescribed.

People with SCD encounter challenges because of vaso-occlusive crises (VOCs), resulting in hospitalizations, organ harm, and an increased risk of mortality. Timely identification of these crises is essential. Consequently, Summers *et al*. (2024) expanded on VOC predictor model, emphasizing advancements in AI approach to enhance patient outcomes and quality of life. Their approach incorporated a smartwatch for continuous physiological data collection and electronic patient-reported outcomes (ePROs). Participants granted permission for extensive data gathering via an FDA-approved device, monitoring daily metrics such as physical activity, sleep quality, heart rate and blood oxygen levels. Two VOC prediction models were created: Model 1 was assessed in 186 patients during one month, whereas Model 2 employed a novel algorithm with 399 patients over a period of six months. Model 1 reached 84% sensitivity and 83% specificity, while Model 2 enhanced sensitivity to 92% without losing specificity. This AI model efficiently forecasts VOCs, hence an immediate alert mechanism.

Additionally, Stojancic *et al*. (2023) evaluated the effectiveness of the Apple Watch in forecasting pain scores in SCD patients. Following approval from institutional review board, they enrolled patients over 18 years of age who were admitted for VOCs. Participants donned an Apple Watch Series 3 that gathered information on heart rate, heart rate variability, and calories burned. Medical records were consulted for pain ratings and vital signs. The data was analysed using three machine learning models: random forest, multinomial logistic regression, and gradient boosting. Two null models were also used to compare their accuracy. The research involved 20 participants, mainly Black or African American. It was possible to use Apple Watch to forecast SCD-related pain quickly and affordably. The random forest model achieved an accuracy of 84.5% with a root-mean-square error of 0.84.

Likewise, Bushra and Shobana (2021) examined advanced deep learning models developed for the early identification of sickle cells in pediatric patients. These models utilize advanced neural network techniques in Artificial Intelligence to classify defective cells and detect unusual patterns in RBC images. Following the pre-processing of blood sample images, deep neural networks help in detecting sickle cell disease in particular geographic regions that are significantly impacted by this condition.

A study by Elsabagh et al. (2023) examined merits and demerits of using AI resources in clinical practice to enhance management of SCD. Using existing literature on both developed and emerging AI applications that can improve management of SCD by advancing diagnosis of SCD and its complications, enhancing risk stratification and assessing effect of AI in developing a personalized strategy for managing SCD patients going forward.

On the other hand, Ikwuka *et al*. (2023) examined existing literature and continuous clinical trials regarding CRISPR-Cas9 genomic editing as a novel approach in treating SCD. Using search terms such as sickle cell disease, genome editing, genetics, new medicines, haematopoietic stem cell transplantation, gene therapy, and CRISPR-Cas9, researchers were able to enquire about active clinical studies that use CRISPR-Cas9 as a treatment. Included in the list of references are research that have been previously analysed, as well as new studies, online summaries, literature reviews, retrospective analyses, case series, and presentations given at academic conferences. CRISPR-Cas9 genome editing emerges as a groundbreaking, inventive technique capable of treating SCD in both children and adults while minimizing adverse effects.

Additionally, Obeagu *et al*. (2024) investigated methods that aim to enhance survival rates and overall well-being for those diagnosed with SCA. Hope is centered on genetic treatments such as CRISPR-Cas9 gene editing and gene therapy with lentiviral vectors to correct genetic defects in SCD. These approaches have been shown to increase the production of healthy red blood cells, reducing sickle cell crises and the need for transfusions. New medications like voxelotor, crizanlizumab and L-glutamine can inhibit hemoglobin polymerization, reduce vaso-occlusive events, and lower oxidative stress. Transfusions have improved with automated techniques and better matching systems. Comprehensive care models, including telemedicine and patient education, enhance adherence and health outcomes, highlighting the need for continued research on these innovations in SCD treatment.

De Ligt *et al*. (2024) developed an AI-based assessment to quantify atypical red blood cells in SCD patients as an objective indicator of the disease. Blood samples from 172 patients with different genotypes (HbSS, HbSβ0, HbSC, HbSβ+) were analyzed under varying oxygen conditions using imaging flow cytometry. Statistical analyses revealed that HbSS and HbSβ0 patients had higher sickle cell proportions and lower discocytes at 21% O2, with VOC increasing holly leaf and granular cells while reducing discocytes. Hydroxyurea reduced sickle cells in HbSS and HbSβ0 patients under hypoxic conditions. The study demonstrated AI's potential in assessing erythrocyte morphology, aiding SCD severity prediction and future research.

Additionally, Vuong *et al*. (2023) evaluated practicality by tracking patients for 30 days after discharge and enhancing ML models for predicting pain. Participants 18 years and older who were eligible and admitted for VOC received Nanpar app along with an Apple Watch. They conveyed their daily pain levels via the app while using watch that monitored physiological metrics. Five ML classification models were created utilizing self-reported pain scores and physiological data, assessed based on accuracy, F1-score, RMSE and AUC. A total of nineteen patients took part, with a median age of 30 years. The group primarily included Black or African American patients with the HbSS genotype. Although dataset was imbalanced and yielded comparable metrics among models, random forest model achieved the highest performance (accuracy 0.89, AUC 0.83). Absence of a correlation with Apple Watch data emphasized difficulties in reporting pain after discharge, signifying a necessity for enhanced data gathering in upcoming research.

In yet another study, Dong and McGann (2021) formulated and prospectively assessed a personalized dosing model for children with SCA, employing a precision medicine strategy to enhance hydroxyurea dosage and clinical outcomes. Innovative lab techniques and a minimal sampling approach was employed that needs just 10 µL of blood taken 15 min, 60 min and 180 min following a test dose. To find the best starting dosage of hydroxyurea and to evaluate exposure, they use Bayesian adaptive control. Conventional weight-based dosing and gradual dosage increases have been surpassed by this dosing strategy, which has yielded HbF responses reaching 30-40%. Millions more SCA patients throughout the world might benefit from improved outcomes if this hydroxyurea dosage strategy were widely used.

A study by Roy *et al*. (2024) used sophisticated healthcare informatics and machine learning methods to examine long-term blood pathology information. Concentrating on key hematological factors provides us with important understanding of the pathophysiology of SCD. Integrating spectroscopic insights into research reveals molecular specifics, enhancing the comprehension of the disease's intricacies and facilitating more refined and focused interventions. They developed prediction models using this data, which allowed for more precise healthcare management and tailored therapies. Results demonstrated that Random Forest outperformed competing algorithms with 88% accuracy, 82% recall, and 92% specificity. This thorough assessment highlighted model's dependability in forecasting both positive and negative cases. Results presented an encouraging direction for improving disease forecasting, management and treatment strategies, providing essential insights for clinical practice regarding sickle cell disease.

Smith *et al*. (2023) advocated for personalized medicine, pharmacogenomics, and integrative medicine as goals to enhance pain management in SCD. Their findings give new information that revises Richard Melzack's neuromatrix theory of pain, establishing it as a comprehensive paradigm for classifying pain subphenotypes and processes in SCD and guiding the selection of targeted interventions. They concluded that subphenotype people with SCD may benefit from using the updated neuromatrix model to improve the selection of individualised multimodal treatment strategies. They laid up all the current pharmacologic and non-pharmacologic treatments

for SCD pain, sorted according to their targets and action processes in the updated neuromatrix model.

Li *et al*. (2024) developed a risk stratification process tailored for adults with SCD receiving HCT, employing patient information from National Institutes of Health Clinical Center from 2004 to 2020. The research examined 73 possible covariates as factors influencing mortality and transplant failure, concentrating on all-cause mortality as the main outcome. Utilizing a two-phase statistical ML approach, significant covariates for mortality were identified, resulting in the creation of a risk score founded on stepwise Cox regression. A further analysis including 111 SCD patients, with a median age of 31.8 years, validated this risk score. Seventeen fatalities were recorded during a follow-up period of 6.9 years. The model accurately forecasted risk of transplant failure, suggesting different disease progression predictions across various risk levels, thus providE essential insights for managing SCD patients in connection with HCT.

Danter (2023) evaluated SCD management outcomes such as VOE, HbA, HbF, quality of life (QoL), RBC haemolysis, and pain, using the DeepNEU© platform v8.2 and aiHumanoid simulations with data from 25 virtual patients in six therapy groups. The combination of Crizanlizumab and Endari showed significant improvements in primary and secondary outcomes. When paired with Voxelotor, these treatments further reduced VOE and RBC haemolysis while enhancing QoL. Results indicated that combination therapies could lessen multi-organoid toxicity, improving patient outcomes and reducing healthcare costs. Meanwhile, Goswami *et al*. (2024) discussed AI's transformative role in SCD healthcare, enhancing diagnostic accuracy with Grad-CAM and transfer learning.

Alharbi *et al*. (2020) developed machine learning models for SCD data analysis, focusing on therapy effectiveness, patient prognosis, and clinical consequences. Alfaleh and Gollapalli (2020) emphasized the importance of early diagnosis in enhancing patients' QoL, lowering healthcare costs, and reducing hospital visits. Gollapalli and Alfaleh (2022) examined AI models trained using five different classifiers: PART, Naive Bayes, Neural Networks (NN), and Support Vector Machine (SVM). The data came from healthcare records collected between 2008 and 2020. By comparing models based on accuracy kappa statistics and classification time, they were able to determine the optimal classification approach. They looked at accuracy, sensitivity, specificity, F1 score, and area under the curve (AUC) as performance indicators. They used naive Bayes classifier, which outperformed other classifiers with an accuracy of 92.22%, to find commonalities in the demographics and inheritance patterns of SCD patients. This AI-driven project enhanced illness treatment via community awareness-raising, particularly among mothers and to enable hospital physicians and practitioners understand the link between disease inheritance and numerous circumstances.

John *et al*. (2022) highlighted that low-income and middle-income countries (LMICs), primarily in sub-Saharan Africa (SSA), face significant challenges from sickle cell disease (SCD). The frequent acute and chronic complications lead to increased healthcare usage, stressing already vulnerable health systems, with alarmingly high mortality rates among children lacking healthcare access. While cellular therapies such as allogeneic hematopoietic stem cell transplant (HSCT) show promise as potential cures in well-resourced settings, LMICs suffer from limited access due to financial issues, insufficient trained staff, and a lack of HSCT technology. Despite these barriers, progress is being made in implementing HSCT for SCD within these nations. A targeted program to develop cell-based therapies in LMICs is essential, given their high disease burden, sky-high treatment costs, and poor long-term quality of life.

Tengshe *et al*. (2021) indicated that SCA is an inherited disorder resulting from a change in one of the genes responsible for producing hemoglobin. This leads to normally round RBCs adopting a sickle shape and blocking the blood vessels. SCD impairs the delivery of oxygen to various body regions and results in significant anemia. Although there is currently no cure for SCD, early diagnosis and treatment may greatly improve patients' quality of life and length of survival. Unfortunately, feature-based automatic categorization using machine learning and image processing is inefficient and easily fooled by small changes in blood cell size, shape and colour. Researchers concluded that sickle-shaped cells may be more accurately diagnosed in blood samples if deep neural networks were used to detect their existence. There were three types of red blood cells: normal, sickle-shaped, and other. A data augmentation approach is used to overcome the shortage of dataset, and histogram equalization is used for preprocessing. Using a CNN with just 5 convolutional layers, they achieved a testing accuracy of 94.57%.

Gimbert *et al*. (2024) employed AI models to assess SCD advancement and treatment reactions. The initial comprehensive SCD dataset in the EU encompasses clinical, laboratory, and research information from 100 patients, utilizing standardized methods across five nations. A quality management strategy guarantees the reliability of datasets. An examination of 1,150 patients showed age distribution (29.5% aged 0-11, 45.6% aged 18-54) and a gender balance, with frequent sub-diagnoses comprising 75% SS and 13% SC variants. The uptake of hydroxyurea and hemoglobin levels were greater than previously observed. The RADeep project oversees 26,892 SCD patients across 324 locations in 12 EU nations, with the goal of qualifying datasets with the EMA and incorporating patient-reported outcomes to improve SCD care pathways.

Tariq, Khurshid, Khan, Dilshad, Zain, Rasool and Akbar (2024) examined promise of CRISPR/Cas9 in addressing SCD and assessed its effectiveness, safety and long-term results in relation to conventional treatment methods. An extensive effort to address the complexities of SCD with emerging technologies was shown by the recent FDA endorsement of Casgevy, a gene therapy using CRISPR/Cas9 technology. To establish CRISPR/Cas9's overall usefulness, complete evaluation of its safety, effectiveness and inclusiveness required long-term, extensive study.

Ala *et al*. (2024) highlighted that sickle cell disease (SCD) is an inherited disorder resulting from a mutation in the β-globin gene, leading to the production of sickle haemoglobin (HbS). This condition, inherited in an autosomal recessive manner, causes polymerisation of HbS under low oxygen conditions, resulting in haemolysis, pain, and impaired blood circulation. Despite progress in understanding SCD's pathophysiology, effective and affordable treatments remain elusive due to issues like patient tolerance and side effects of existing medications. The study emphasized the need for further research on drug efficacy and safety, including clinical trials for various medication combinations, while analyzing current and investigational treatment options for SCD.

Issom *et al*. (2020) evaluated patients' perceived value of the information given by a chatbot that they created based on patient-important needs gathered during earlier research. Participants evaluated chatbot and filled out a post-test questionnaire. Nineteen patients were recruited, and two dropped out. Fifteen respondents (15/17, 88%) rated the statement "The chatbot contains all the information I need" with a score of 3/4 or higher. Findings indicated that mHealth coaching applications may help enhance the understanding of advised health practices linked to preventing the primary symptoms of SCD.

Mayo-Gamble *et al*. (2021) investigated user preferences for a mHealth app that would help individuals with SCD and their caretakers manage their condition on their own. The software would target both urban and rural users. Forty-three individuals with SCD participated across urban and rural areas, with 4 to 15 attendees per session. They were asked about their self-care knowledge, satisfaction with current SCD management information, support levels, and desired mHealth app features. A content analysis revealed seven main themes: current self-management information methods, sought-after information, suggestions for conveying SCD management details, disease management challenges, types of support received, helpful and hindering mHealth app characteristics, and user-desired features. Participants showed openness to using mHealth applications for SCD self-management. The findings suggest that developing a user-friendly, patient-focused mHealth app could improve access to resources for families in rural areas affected by SCD, enhancing disease self-management.

Goswami *et al*. (2023) examined a deep learning model for identifying presence of sickle cells in the bloodstream, thus categorizing them. Among these models, ResNet50 stands out for its impressive 93.88% test accuracy. Effective validation, cell overlap, data accessibility, bias mitigation, interpretability, adherence to regulations, workflow incorporation, and ethical factors are crucial elements that need to be thoroughly evaluated when employing AI in blood smear analysis. Classification of sickle cells is an area where AI has been slow to respond. Due to the lack of a cure, sickle cell disease therapy focusses on symptom management and the prevention of complications. It may be time-consuming and error-prone to manually detect and categorize sickle cells in pictures of blood smears. Therefore, it is essential to have automated techniques for categorizing sickle cells and addressing these issues.

Aliyu *et al*. (2020) noted that patient displays various cell shapes that exhibit significant biomechanical traits. This research focuses on efficiently categorizing irregularities in sickle cell anemia (SCA) using a two-stage

method. It begins with automated extraction of red blood cells (RBCs) from blood smear images to identify regions of interest. Anomalies in SCA patients are detected using the AlexNet deep learning network, utilizing data from 130 patients and nearly 9,000 RBC images. The study aims to quantitatively assess RBC shapes, successfully categorizing fifteen RBC morphologies. The model achieved sensitivity of 95.22%, specificity of 77%, accuracy of 98.82%, and precision of 90%.

Lanzkron *et al*. (2022) outlined the primary goals of GRNDaD, which include: improving care adherence based on guidelines; creating a platform for continuous quality improvement across different sites; facilitating real-time exploration of therapies; and collaborating widely to tackle research enquiries using GRNDaD as a common platform. The search for precision medicine for Sickle Cell Disease (SCD) relies on large databases, requiring willing, well-phenotyped individuals in joint registries. The GRNDaD registry was established by global SCD physicians to create a significant multisite registry. Its strength lies in extensive participation from individuals with SCD, collaborative researchers, and opportunities for quality improvement initiatives.

Singh and Thakkar (2020) reviewed research on SCD focusing on risk stratification systems, forecasting disease severity, predicting dosage needs, and anticipating clinical complications associated with the disease. To improve clinical outcomes and therapeutic treatments in SCD, several studies have used blood characteristics of patients collected from complete blood count (CBC) or high-performance liquid chromatography (HPLC) testing. The correlation and association between pathological characteristics and clinical symptoms may be evaluated by statistical significance assessment. How much medication to provide and how to divide up risks are two applications of machine learning methods.

Petrović *et al*. (2020) suggested a method for choosing classification technique and features, grounded in the latest advancements that yields optimal performance for diagnostic assistance via peripheral blood smear images of red blood cells. People with sickle cell disease provided blood samples to evaluate a proposed system's reliability. The research involved separating and analyzing images for high-quality features. Machine learning was employed to classify blood cell shapes, utilizing established methods for feature extraction. Optimal parameters for each classifier were determined through Randomized and Grid search methods. The team shared raw data, confusion matrices, code libraries and classifier configurations to assist other researchers. Validation was achieved using the public erythrocytesIDB dataset, achieving superior results with interpretable model classifiers.

Mohammed *et al*. (2020) evaluated hypothesis that machine learning physiomarkers can predict organ dysfunction in adult SCD patients hospitalized in intensive care units (ICUs). Employing various machine learning and statistical techniques, we examined 63 SCD patients across 163 encounters (average age 30.7, SD 9.8 years), with 22.7% showing risk of organ failure according to evaluation criteria. Signal processing characteristics from heart rate, blood pressure and respiratory rate distinguished individuals at risk of sudden deterioration. A multilayer perceptron model effectively forecasted organ failure as early as 6 hours prior, reaching 96% sensitivity and 98% specificity. This retrospective analysis underscored the promise of machine learning in forecasting acute organ failure among SCD patients, opening the door to novel treatment approaches for at-risk groups.

Ayoade *et al*. (2023) assessed separate ML algorithms and ensemble models for forecasting SCD through the examination of RBC shapes. Three machine learning algorithms were chosen for comparison, and group models were created, using metrics such as accuracy, sensitivity, and ROC-AUC for assessment. The research utilized Python for analysis, uncovering individual accuracies of MLR=87%, XGBoost=90%, and RF=93%, while hybrid models produced RF-MLR=92% and RF-XGBoost reached 99% accuracy. The exceptional performance of RF-XGBoost emphasizes the advantages of combined ML algorithms in medical datasets, tackling problems such as variance, accuracy, and biases. The research supports the use of ensemble classifiers to improve predictions for SCD.

Nembaware *et al*. (2020) outlined key takeaways and insights from fourth SCDO workshop, which initiated efforts aimed at influencing planetary health, while focusing on enhancing and fostering multisite SCD collaborative research. The Sickle Africa Data Coordinating Center (SADaCC) hosted a workshop with 44

participants from 14 countries, including 2 virtual attendees. The workshop focused on innovative strategies to utilize the Sickle Cell Data Outline (SCDO) for harmonizing data across diverse studies. Participants uploaded data from continuous or previous SCD research via an online platform, fostering collaborative initiatives like multisite cohorts and global clinical trials. The potential of SCDO in enhancing data standards for global SCD collaboration was highlighted, promoting advancements in SCD pathophysiology and planetary health.

Oikonomou *et al*. (2021) developed a model to forecast the HbF% in patients utilizing the three regulatory genes associated with the condition. Various techniques of this kind are investigated in order to improve the model's accuracy via the use of a machine learning approach. An early version of the K-nearest neighbours method is created and tested once it is chosen. The algorithm has been refined, allowing our enhanced model to forecast a patient's HbF% with an accuracy of 87.25%, which represents a significant advancement compared to the current alternative that has a mean error of 336.33%. Model is a reliable tool for small and medium-sized clinical trials because it can quickly predict HbF% and account for genetic background variations that might affect test results. Additionally, 93.45% of our forecasts have a total error of less than 0.5.

Koua *et al*. (2024) introduced an innovative approach employing deep learning (DL) and AI, all while maintaining human supervision during the procedure. They employed convolutional neural networks (CNNs) to examine IEF gel images, attaining more than 98% accuracy in recognizing diverse SCD profiles, significantly exceeding constraints of conventional techniques. By including a new "Unconfirmed" category for cases where there was uncertainty, the approach eliminated guesswork and gave physicians the data they needed to make educated judgements. An effective, efficient, and accurate solution for SCD screening was provided by an AI-driven application, SCScreen, which skillfully integrated machine learning with medical expertise. The formerly challenging task of diagnosing newborns with significant sickle cell syndromes (SDM) was taken care of by SCScreen. The treatment of SCD may be revolutionized by this research. Infants with SCD may have a greater chance of survival and a higher quality of life thanks to SCScreen, which improves screening methods and, maybe, reduces costs.

Farota *et al*. (2022) conducted study to address challenges posed by current early detection and follow-up methods, they proposed a novel targeted screening strategy utilizing artificial intelligence. For the purpose of sickle cell status prediction, they tested and evaluated five different machine learning algorithms. Starting off, it seemed like they could tell whether a particular infant had a risky profile because to the very high prediction accuracy shown by the majority of the models.

Ndakotsu and Balarabe (2019) indicated that Vasoocclusive painful crisis is primary clinical occurrence in SCD patients, with almost all individuals with SCD enduring this episode at some point in their lives. Acute vasoocclusive pain episodes can eventually develop into chronic pain, leading to a diminished quality of life linked with other health issues such as anxiety, depression, and reliance on pain relief medications. The survival rate of people with SCD has increased because of medical breakthroughs that have resulted in new treatments and therapeutic approaches. Even though these patients have a shorter average lifespan than the general population. A specific and thorough prescription and monitoring approach is required to guide pain management. Precision medicine, which is centred on the practical application of human genetics, provides a growing variety of translational research goals for pain management in sickle cell disease, which may help accomplish this.

Arji *et al*. (2023) explored effective strategies to reduce the morbidity and mortality linked to sickle cell disease in children living in sub-Saharan Africa. The interventions identified through the Joanna Briggs scoping review framework included pharmacotherapy, newborn screening, comprehensive healthcare, disease-modifying agents, nutritional supplements, systemic treatments, and patient education. A total of 36 studies, primarily from West African nations, showed that these evidence-based interventions effectively decreased common complications of sickle cell disease, such as stroke, vaso-occlusive crises, and severe anemia. Despite facing challenges like limited resources and availability, the establishment of specialized sickle cell clinics and consistent treatments with hydroxyurea, sulphadoxine-pyrimethamine, L-arginine, and Omega-3 supplements could significantly reduce mortality and morbidity in sub-Saharan Africa.

IV. DISCUSSION

Research by Balde *et al*. (2023) highlighted the use of convolutional neural networks and machine learning techniques for image segmentation, feature extraction, and classification in identifying sickle cells in blood smear images. Additionally, Roy *et al*. (2024) employed healthcare informatics and machine learning to analyze long-term hematological data, improving disease forecasting and management. Their findings indicate that AI models, particularly Random Forest algorithms, achieve high accuracy, specificity, and recall in predicting sickle cell cases. AI-based models have demonstrated high accuracy in predicting sickle cell disease (SCD). Studies such as Goswami *et al*. (2023) and Ayoade *et al*. (2023) indicate that deep learning models, including ResNet50 and ensemble techniques like RF-XGBoost, achieve high classification accuracy in detecting sickle cells from blood smear images. Additionally, Mohammed *et al*. (2020) highlighted the potential of machine learning physiomarkers in predicting organ dysfunction in SCD patients, showcasing AI's predictive power in clinical settings. However, challenges such as data bias, model interpretability, and workflow integration remain areas requiring further improvement.

AI models have a transformative effect on diagnosing sickle cell disease. Studies by Bushra and Shobana (2021) demonstrated the application of deep learning models for early detection, particularly in pediatric patients. Moreover, Elsabagh *et al*. (2023) outlined the benefits of AI in clinical practice, enhancing risk stratification and aiding in personalized patient management. These advancements suggest that AI can significantly improve diagnostic accuracy and efficiency, reducing reliance on traditional microscopy methods. AI has significantly enhanced SCD diagnosis through image analysis, risk stratification, and patient management support. Petrović *et al*. (2020) and Aliyu *et al*. (2020) demonstrated that AI models effectively classify red blood cell morphologies, aiding in early diagnosis. Additionally, Lanzkron *et al*. (2022) emphasized AI's role in creating large-scale SCD registries like GRNDaD, which improve diagnosis and precision medicine. Despite these advancements, Singh and Thakkar (2020) highlighted the need for further validation of AI models in real-world clinical environments to ensure accuracy, fairness, and regulatory compliance.

AI has a huge potential in predicting and monitoring sickle cell disease. Studies by Summers *et al*. (2024) and Stojancic *et al*. (2023) demonstrated the use of wearable technologies, such as smartwatches, for real-time physiological monitoring and pain prediction in SCD patients. Their research showed that AI models could effectively forecast vaso-occlusive crises (VOCs), enabling early interventions. Similarly, Li *et al*. (2024) developed a risk stratification model for SCD patients undergoing hematopoietic stem cell transplantation (HCT), improving patient outcomes through predictive analytics. Additionally, Vuong *et al*. (2023) leveraged machine learning models to predict post-discharge pain in SCD patients, emphasizing the role of AI in continuous patient monitoring. AI has shown great potential in monitoring and managing SCD progression through real-time data analysis and patient-centered applications. Issom *et al*. (2020) and Mayo-Gamble *et al*. (2021) found that AI-powered mHealth apps and chatbots enhance patient understanding and self-management. Moreover, Gimbert *et al*. (2024) demonstrated how AI-driven large datasets, such as the RADeep project, contribute to better monitoring of SCD patients across multiple nations. However, concerns about data quality, security and long-term effectiveness highlight the need for continuous research and development in AI-driven SCD management.

V. CONCLUSIONS AND RECOMMENDATIONS

Conclusions

AI-driven models significantly enhance the diagnosis, prediction and monitoring of SCD. Convolutional neural networks and machine learning techniques effectively segment images, extract features, and classify sickle cells with high accuracy. Additionally, advanced algorithms such as Random Forest and deep learning models, including ResNet50 and RF-XGBoost, improve disease classification and forecasting. These technologies support early diagnosis, enabling timely interventions and personalized treatment strategies. However, challenges such as data bias, model interpretability, and workflow integration must be addressed to optimize AI's clinical applicability.

The integration of AI in clinical practice revolutionizes SCD management by enhancing risk stratification and personalized patient care. AI-powered systems reduce dependency on traditional microscopy, streamlining

diagnostic workflows and improving efficiency. Large-scale SCD registries and databases further enhance precision medicine, enabling more effective treatment plans. Despite these advancements, real-world validation of AI models remains crucial to ensuring their accuracy, fairness, and regulatory compliance. Continuous refinement of AI algorithms will be essential to promote widespread clinical adoption and acceptance.

AI aids in monitoring and managing SCD progression through real-time data analysis and predictive analytics. Wearable technologies and mobile health applications provide continuous physiological monitoring, allowing early detection of vaso-occlusive crises and improved patient self-management. AI-driven risk stratification further enhances treatment outcomes, particularly for patients undergoing complex procedures such as hematopoietic stem cell transplantation. While AI demonstrates promising potential, concerns regarding data quality, security, and long-term efficacy emphasize the need for continuous research and development to refine and standardize AI-driven approaches in SCD care.

Recommendations

Healthcare institutions should invest in AI-driven technologies to enhance the diagnosis and monitoring of SCD. Machine learning models should be integrated into clinical workflows to improve accuracy and efficiency. Efforts must be made to address challenges such as data bias and model interpretability.

Regulatory bodies should establish guidelines to ensure the safe and ethical use of AI in SCD management. AI models should undergo rigorous validation before clinical adoption. Standardized protocols should be developed to enhance reliability and compliance.

Researchers should focus on improving AI-driven tools for real-time patient monitoring. Wearable technologies and mobile health applications should be optimized for better patient self-management. Further studies should address data security and long-term effectiveness to ensure sustainable AI solutions in healthcare.

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