REVIEW ARTICLE

DIGITAL TWINS FOR SICKLE CELL PATIENTS: INTEGRATING BIOINFORMATICS, ARTIFICIAL INTELLIGENCE, AND CLINICAL DATA

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Abstract

Sickle cell disease is a genetically inherited blood disorder characterized by considerable clinical variability and frequent complications, including vaso-occlusive crises, strokes, and organ damage. Conventional care methods frequently struggle to forecast personal disease pathways or customize timely interventions. In this scenario, digital twin technology a real-time, data-centric virtual representation of a patient presents a unique chance to revolutionize disease management by combining genomics, clinical information, and computational intelligence. This review examines the convergence of bioinformatics and artificial intelligence in creating digital twins that can accurately model SCD pathophysiology. Bioinformatics tools derive insights from multiomics data, uncovering genetic factors and molecular pathways that affect disease severity. AI and machine learning algorithms subsequently evaluate intricate clinical and biometric data, facilitating immediate risk assessment, treatment modeling, and dynamic care planning. When connected to wearable devices and electronic health records, these technologies improve the responsiveness and personalization of care delivery.
Keywords: Artificial intelligence, digital twins, sickle cell disease, bioinformatics, precision medicine.

INTRODUCTION

Sickle cell disease (SCD) is a long-term, genetic blood condition resulting from a mutation in the β-globin gene, which produces abnormal hemoglobin S. This singular genetic alteration has significant systemic effects, including persistent anemia, vaso-occlusive crises, cerebrovascular accident, and multi-organ failure. After many years of study, SCD remains a major global health issue, especially in sub-Saharan Africa, the Middle East, and among individuals of African heritage in the Americas and Europe. The clinical variability of the disease spanning mild anemia to severe complications has rendered its management complicated and highly personalized[1-3]. Conventional methods for managing SCD typically adhere to reactive models, where treatment starts only after symptoms or complications appear. Although hydroxyurea, blood transfusions, and bone marrow transplants have enhanced results for certain patients, they are not consistently effective or readily available. Additionally, these treatments fail to tackle the erratic nature of the illness or the differing responses seen in individuals. There is an urgent demand for more accurate, anticipatory, and preventive healthcare approaches that can adjust to the individual biological and clinical characteristics of every patient[4].

New digital health technologies are ready to fill this gap. A highly promising innovation is the creation of "digital twins" virtual representations that mirror the physiological and pathological conditions of specific patients in real time. Initially developed for the aerospace and engineering sectors, digital twins are now being tailored for application in healthcare, aiming to provide personalized, ongoing, and data-informed treatment. In the realm of SCD, a digital twin might emulate the progression of the patient's illness, predict complications, and suggest personalized interventions based on real-time data inputs[4]. The development of digital twins in healthcare depends on the incorporation of various data sources, such as genomics, transcriptomics, electronic health records (EHRs), outputs from wearable devices, and lifestyle elements. Bioinformatics is essential for analyzing high-throughput omics data, discovering biomarkers, and charting molecular pathways that affect disease severity and treatment responses. These insights establish a biologically based foundation for the digital twin, enhancing its accuracy and responsiveness to shifts in patient condition[5].

AI and machine learning algorithms are both vital for analyzing and deriving insights from extensive and intricate datasets. These instruments can uncover concealed patterns, create forecasting models, and consistently enhance the twin's actions according to fresh data. For instance, AI can detect minor signs of an approaching vaso-occlusive crisis prior to the onset of clinical symptoms, allowing for prompt intervention. The collaboration between AI and bioinformatics enables digital twins to evolve into effective, flexible systems for simulating treatment responses and improving care[6]. Integrating real-time clinical and physiological data is also fundamental to the operation of digital twins. Progress in mobile health, biosensors, and remote tracking has enabled the monitoring of metrics including oxygen saturation, heart rate variability, hydration level, and environmental factors. These ongoing data streams not only provide real-time status updates for the digital twin but also establish a feedback loop that can influence tailored care plans and facilitate remote clinical decision-making[5].

This narrative review seeks to investigate the growing significance of digital twin technology in the management of sickle cell disease by analyzing the integration of bioinformatics, artificial intelligence, and clinical data to create patient-specific virtual models. The evaluation aims to emphasize the capability of digital twins to improve tailored care, foresee complications, and refine treatment approaches for those affected by sickle cell disease. Furthermore, it seeks to recognize existing challenges, ethical issues, and prospective pathways in the deployment of digital twin systems in both resource-rich and resource-poor healthcare environments.

METHODS

This narrative review was conducted to synthesize current knowledge on the integration of digital twin technology, bioinformatics, and artificial intelligence in the management of sickle cell disease. A comprehensive literature search was performed using electronic databases including PubMed, Scopus, Web of Science, and Google Scholar. Keywords and MeSH terms such as "digital twins," "sickle cell disease," "bioinformatics," "artificial intelligence," "precision medicine," and "clinical data integration" were used in various combinations to identify relevant peer-reviewed articles, reviews, and conference procee-dings published up to July 2025. Inclusion criteria encompassed studies and reviews focusing on the application of digital health technologies in hematologic disorders, especially sickle cell disease, and those discussing computational modeling, machine learning, genomics, and real-time data analytics in clinical care. Articles not available in English, non-peer-reviewed sources, and those unrelated to human health applications were excluded. Additional relevant literature was identified through manual reference checks of key articles. The collected data were thematically organized to explore the conceptual framework, technological components,

and clinical applications of digital twins in SCD management. Ethical, practical, and infrastructural challenges were also considered. Due to the narrative nature of this review, no formal quality assessment or meta-analysis was performed.

Understanding digital twins in healthcare
Digital twins are virtual models of physical objects that imitate their structure, function, and behavior in real-time via ongoing data integration. Initially created for aerospace and manufacturing sectors, digital twin technology has swiftly expanded into healthcare, where it has the potential to transform patient care through dynamic, personalized, and predictive medicine. In the medical setting, a digital twin is an ever-evolving, computational representation of an individual patient that can replicate physiological functions, track disease advancement, and assess treatment approaches with great accuracy[7]. At its essence, a healthcare digital twin combines multiple data sources, such as electronic health records (EHRs), imaging, lab results, wearable sensor information, genetic and molecular profiles, along with patient-reported outcomes. These datasets are processed by algorithms typically driven by artificial intelligence (AI) and machine learning that enable the model to "learn" from fresh data and adjust as needed. This establishes a feedback loop in which the virtual twin reflects the patient's current condition and anticipates probable results in various scenarios. For instance, it can model how a particular drug could influence disease advancement or foresee the development of complications prior to the appearance of clinical signs[8].

The application of digital twins in medicine has already shown promise in areas such as cardiology, oncology, orthopedics, and intensive care. In these domains, digital twins have been used to model cardiac electrophysiology, personalize cancer treatments, simulate orthopedic implant performance, and manage critical care interventions. The growing use of high-throughput bioinformatics tools, combined with advancements in real-time monitoring technologies and AI-driven analytics, now paves the way for their use in managing chronic, complex diseases like sickle cell disease (SCD), where inter-patient variability and acute exacerbations pose unique challenges (Table 1)[9,10].

Role of bioinformatics in digital twin construction
Bioinformatics plays a foundational role in the development of digital twins by providing the tools and methodologies necessary to extract, process, and interpret complex biological data. In the context of SCD, bioinformatics enables the integration of high-throughput omics data including genomics, transcriptomics, proteomics, and metabolomics into dynamic computational models that form the biological core of a digital twin. These data-driven insights allow the digital twin to accurately represent a patient's molecular and cellular state, thus improving its capacity for real-time prediction and personalized simulation[11,12]. Genomic data, particularly the identification of the β-globin gene mutation responsible for hemoglobin S (HbS), form

the starting point for modeling the disease at the molecular level. However, disease severity and clinical manifestations in SCD are influenced by a variety of genetic modifiers such as BCL11A, MYB, and HBS1L-MYB loci. Bioinformatics tools help in uncovering these modifiers through genome-wide association studies (GWAS) and whole-genome sequencing, thereby facilitating more refined risk stratification. Additionally, transcriptomic analyses during steady-state and crisis conditions can identify gene expression signatures that correlate with inflammation, hemolysis, and endothelial dysfunction key pathological processes in SCD[13].

Table 1: Understanding digital twins in healthcare.

Aspect	Description	Relevance to healthcare
Definition	A virtual, dynamic, and data-driven model that accurately represents a physical system or patient.	Enables personalized simulation and prediction of patient health.
Core Components	Integration of biological data, clinical records, real-time monitoring, and computational models.	Provides a comprehensive, multi-layered understanding of disease.
Purpose	To simulate, predict, and optimize clinical outcomes through continuous feedback and adaptation.	Facilitates precision medicine and proactive healthcare management.
Data Sources	Omics data, electronic health records (EHRs), wearable sensors, patient-reported outcomes.	Enables holistic and real-time patient monitoring and intervention.
Applications	Disease modeling, treatment response prediction, risk stratification, patient engagement.	Improves diagnosis, personalized therapy, and patient empowerment.
Advantages	Real-time updates, personalized insights, predictive analytics, and simulation of interventions.	Enhances clinical decision-making and reduces adverse events.
Challenges	Data integration complexity, privacy concerns, ethical issues, and technological barriers.	Requires multidisciplinary collaboration and robust regulatory frameworks.

Furthermore, bioinformatics enables the integration of heterogeneous data types across multiple layers of biology. For instance, proteomic analyses may reveal altered signaling pathways during vaso-occlusive episodes, while metabolomic profiling can provide insight into oxidative stress and energy metabolism. By synthesizing these multiomics datasets, bioinformatics platforms can construct mechanistic models of disease that enrich the digital twin's capacity to simulate real-world scenarios. This level of biological resolution allows for individualized modeling of treatment responses, such as the effect of hydroxyurea or L-glutamine at the molecular and systemic levels[14,15]. Another crucial function of bioinformatics is data preprocessing and quality control. Given the sheer volume and variability of biological data, robust pipelines are needed to filter noise, normalize datasets, and annotate molecular features accurately. These steps are essential to ensure that the digital twin is built on reliable and clinically relevant data. Moreover, bioinformatics supports the interoperability of data across different platforms and institutions, which is especially important for collaborative digital twin development and validation in diverse populations (Table 2)[16,17].

Table 2: Role of bioinformatics in digital twin construction.

Bioinformatics function	Description	Contribution to digital twin
Data Preprocessing & Quality Control	Cleaning and normalizing raw omics and clinical data to ensure accuracy and reliability.	Ensures high-quality input data for accurate modeling and analysis.
Multiomics Integration	Combining genomic, transcriptomic, proteomic, and metabolomic data to create a comprehensive profile.	Captures complex biological interactions underlying sickle cell disease.
Feature Extraction & Selection	Identifying the most relevant biomarkers and data features that influence disease progression.	Reduces data complexity and improves predictive power of the model.
Network and Pathway Analysis	Mapping molecular pathways and interactions to understand disease mechanisms and identify targets.	Reveals biological processes critical for personalized interventions.
Biomarker Identification	Detecting molecular signatures that correlate with clinical phenotypes or treatment response.	Enables early detection, prognosis, and therapy optimization.
Model Input Preparation	Formatting and structuring data into usable forms for machine learning and simulation algorithms.	Facilitates seamless integration with AI components in the digital twin.

Artificial intelligence and machine learning integration

Artificial intelligence (AI) and machine learning (ML) are critical enablers in the construction and operationalization of digital twins, particularly in diseases like SCD that are marked by complex, dynamic, and heterogeneous clinical patterns. AI and ML algorithms are uniquely capable of analyzing large, multi-dimensional datasets spanning genomics, clinical records, wearable sensor outputs, and patient-reported outcomes to uncover hidden patterns, make predictions, and support clinical decision-making in real time[18]. In the context of SCD, AI algorithms can be trained to detect early warning signs of complications such as vaso-occlusive crises, acute chest syndrome, or stroke by continuously analyzing biometric and clinical data streams. Supervised learning models can predict the likelihood of an acute event based on historical data, laboratory trends, and environmental factors. For instance, machine learning models may detect subtle shifts in hemoglobin levels, oxygen saturation, or hydration status that precede a pain crisis. These predictive insights can be used by the digital twin to simulate potential outcomes and prompt timely interventions, such as medication adjustments or hospitalization alerts[19,20].

Unsupervised learning algorithms further enhance the utility of digital twins by discovering novel patient subtypes based on phenotypic or genotypic clusters. This approach is particularly valuable in SCD, where traditional classification systems (e.g., HbSS vs. HbSC) do not fully explain clinical variability. By identifying data-driven subgroups with distinct risk profiles, AI can facilitate more nuanced, stratified care strategies within the digital twin framework. Reinforcement learning a form of AI where algorithms learn from trial-and-error interactions with their environment can be used to simulate personalized treatment regimens, optimize therapeutic responses, and continuously improve clinical recommendations[21]. Natural language processing (NLP), a branch of AI, allows digital twins to incorporate unstructured data from clinical notes, patient narratives, and social determinants of health. This is especially relevant in chronic disease management, where psychosocial factors, adherence patterns, and patient preferences significantly influence outcomes. By extracting and contextualizing this information, AI enables the digital twin to become a more holistic and human-centered tool for care planning[22,23]. AI also plays a crucial role in model validation and adaptability. As patient data evolves over time, machine learning algorithms allow the digital twin to continuously learn and recalibrate its predictions. This self-improving capacity enhances the digital twin's accuracy and reliability, ensuring that it remains clinically relevant in dynamic, real-world settings. Moreover, explainable AI (XAI) approaches are emerging to ensure transparency and clinician trusts in the model's recommendations an essential factor in clinical adoption[24].

Clinical data and real-time monitoring

Clinical data and real-time physiological monitoring are integral components of digital twin functionality, particularly in the management of chronic and unpredictable conditions like SCD. The value of a digital twin lies not only in its biological and computational sophistication but also in its ability to reflect the current and evolving clinical state of an individual patient. To achieve this, continuous data integration from electronic health records (EHRs), wearable devices, and remote monitoring tools is essential[25]. In SCD, the clinical course can change rapidly, with acute episodes such as vaso-occlusive crises, infections, or acute chest syndrome arising with little warning. Real-time data from wearable biosensors such as heart rate variability, oxygen saturation, skin temperature, hydration levels, and activity patterns can offer early indicators of physiological stress. When integrated into a digital twin model, these data streams allow for dynamic updates and predictive alerts, enabling clinicians and patients to intervene before complications fully develop. This proactive approach contrasts with the reactive nature of traditional care, potentially reducing hospitalizations, emergency visits, and disease-related morbidity[26].

Electronic health records provide a rich, longitudinal view of a patient's medical history, including laboratory values, medication use, transfusion history, imaging, and comorbid conditions. Integrating this structured data into the digital twin enhances its contextual accuracy and allows for retrospective modeling of disease patterns. Additionally, incorporating unstructured clinical notes via natural language processing enables the twin to reflect nuanced information such as clinician impressions, symptom evolution, and psychosocial concerns. Together, these datasets empower the twin to offer more precise therapeutic recommendations and simulations[27]. Mobile health platforms further expand real-time data collection by capturing patient-reported outcomes, pain scores, medication adherence, and environmental exposures (e.g., temperature, air quality, humidity) that influence SCD severity. For instance, sudden changes in weather or altitude can precipitate a crisis, and digital twins equipped with geolocation and weather data can incorporate these variables into predictive algorithms. This level of real-world integration supports a more comprehensive, life-centered model of care[28,29]. Importantly, real-time monitoring also fosters patient engagement and self-management. By visualizing their digital twin and receiving personalized feedback, patients may become more proactive in recognizing early signs of deterioration and adhering to preventive measures. In remote and underserved settings, where frequent hospital visits are impractical, these technologies offer an opportunity to extend continuous, high-quality care through telemedicine and decentralized monitoring systems[30,31].

Ethical, legal, and social considerations

The integration of digital twin technology into the clinical management of SCD raises complex ethical,

legal, and social issues that must be thoughtfully addressed to ensure responsible and equitable implementation. At the forefront are concerns related to patient privacy and data security, as digital twins rely on vast amounts of sensitive personal health information including genomic, clinical, and real-time monitoring data. Safeguarding this data against unauthorized access or breaches is critical to maintain patient trust and comply with regulations such as HIPAA, GDPR, and other local data protection laws[32]. Informed consent represents another key ethical challenge. Patients must clearly understand how their data will be used, stored, and shared within the digital twin ecosystem, including potential secondary uses such as research or commercial applications. Given the complexity of digital twin technology, providing comprehensible explanations that allow for truly informed decisions can be difficult[32].

Equity and access constitute significant social considerations. The populations most affected by SCD often marginalized or under-resourced may face barriers to accessing the necessary technologies, such as wearable devices, smartphones, or reliable internet connections, required for digital twin-based care. There is a risk that digital twin innovations could exacerbate existing health disparities unless deliberate efforts are made to ensure inclusivity, affordability, and culturally sensitive implementation. Moreover, disparities in data representation could lead to biased algorithms that perform less accurately for minority groups, underscoring the need for diverse and representative datasets in model training[33,34]. The legal landscape surrounding digital twins is still emerging. Questions about liability and accountability arise when AI-driven models make clinical recommendations or decisions. Determining responsibility in cases of adverse outcomes whether it lies with clinicians, software developers, or healthcare institutions requires clear legal frameworks. Regulatory bodies are beginning to develop guidelines for AI and digital health tools, but harmonized standards and oversight mechanisms are needed to ensure patient safety and foster innovation[35].

Explainable AI (XAI) techniques that provide insight into model decision-making processes help build trust and facilitate informed clinical judgment. Without transparency, there is a risk of over-reliance on "black-box" models that may obscure errors or biases[36]. The psychosocial impact of digital twins on patients warrants attention. While digital twins can empower patients through personalized insights and engagement, they may also induce anxiety or dependence if predictions are perceived as deterministic or overwhelming. Sensitive communication strategies and supportive clinical environments are necessary to ensure digital twin technologies enhance, rather than undermine, patient well-being[37].

CONCLUSIONS

Digital twin technology offers a revolutionary method for handling sickle cell disease by combining bioinformatics, artificial intelligence, and real-time clinical information into an adaptive, individualized model of patient health. By utilizing ongoing data assimilation and advanced computational algorithms, digital twins can potentially forecast disease progression, enhance treatment plans, and predict acute complications prior to their clinical appearance. This change in approach transitions sickle cell treatment from reactive to proactive, improving the accuracy and promptness of interventions. The effective creation and application of digital twins depend on strong bioinformatics systems to analyze intricate molecular patterns, AI and machine learning to understand multi-faceted datasets, and smooth incorporation of clinical and real-time monitoring information. Collectively, these elements form a dynamic virtual replica that mirrors the distinct biological and clinical circumstances of every patient.

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AUTHOR'S CONTRIBUTION

Obeagu EI: conceived the idea, writing the manuscript, literature survey. **Ezeala CC:** formal analysis, critical review. Final manuscript was checked and approved by the both authors.

DATA AVAILABILITY

Data will be made available on request.

CONFLICT OF INTEREST

None to declare.

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