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Healthcare development and innovation in the Arabian Gulf

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Research Article

Artificial Intelligence Applications in the Intensive Care Unit for Sepsis-Associated Encephalopathy and Delirium: A Narrative Review

Mutaz I. Othman[1,2*], Abdulqadir J. Nashwan[1], Ahmad A. Abujaber[1], Mohamad Y. Khatib[2]

[1]Nursing Department, Hamad Medical Corporation, Doha, Qatar
[2]Critical Care Department, Hamad Medical Corporation, Doha, Qatar

*Email: mothman8@hamad.qa

ABSTRACT

Background: Sepsis, a life-threatening condition triggered by an altered immune response to infection, poses significant challenges in clinical management.
Aim: This review discusses the role of Artificial Intelligence (AI) in predicting Sepsis-Associated Encephalopathy (SAE) and Sepsis-Associated Delirium (SAD).
Methods: A thorough search encompassing PubMed, CINAHL, Medline, and Google Scholar yielded studies published from 2013 to 2023.
Results: The narrative review emphasizes AI's potential in the early identification and prognosis of SAE and SAD, specifically through machine learning and deep learning methods, such as XGBoost.
Conclusion: This review underscores the importance of early detection in sepsis and emphasizes how AI can improve prediction accuracy, offering promise in transforming the management of these complex neurological complications within the intensive care unit (ICU).

Keywords: Artificial Intelligence (AI), Sepsis, Sepsis-Associated Encephalopathy (SAE), Sepsis-Associated Delirium (SAD), Machine Learning (ML), Intensive Care Unit (ICU)

1. INTRODUCTION

Sepsis is a severe condition caused by the body's response to an uncontrolled infection, leading to inflammation and organ failure[1]. It is a significant global health issue, resulting in substantial rates of illness and death[2]. Sepsis management can be particularly challenging due to the potential for neurological complications. The incidence of neurological complications can vary significantly, ranging from 8% to over 70%, depending on factors such as severity, patient profile, and diagnostic criteria[3]. Two complications of sepsis are Sepsis-Associated Encephalopathy (SAE) and Sepsis-Associated Delirium (SAD). These complications occur in approximately 50% of cases[4]. SAE is characterized by changes in mental state, cognitive function, and electroencephalogram (EEG) patterns, whereas SAD is associated with sudden and varying alterations in attention and cognition[5]. Early detection and management of both conditions are crucial due to their significant impact on patient outcomes.

Efficient sepsis care requires timely identification and a high level of suspicion for severe adverse events and systemic inflammatory response syndrome[6]. Timely diagnosis and treatment are crucial in sepsis management, as delays can have a detrimental impact on patient outcomes. Traditional

http://doi.org/10.5339/avi.2023.11

Submitted: 18 December 2023
Accepted: 30 December 2023

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Cite this article as: Othman MI, Nashwan AJ, Abujaber AA, Khatib MY. Artificial Intelligence Applications in the Intensive Care Unit for Sepsis-Associated Encephalopathy and Delirium: A Narrative Review, Avicenna 2023(2):11 http://doi.org/10.5339/avi.2023.11

delirium assessments use validated tools to detect and treat patients, ensuring early diagnosis and timely treatment. Popular tools include the Confusion Assessment Method (CAM), the Delirium Rating Scale, and the Cognitive Test for Delirium[7]. Trained physicians administer these assessments to confirm diagnoses, determine causes, manage symptoms, and create treatment plans for delirium patients.

Prompt recognition of SAE and SAD enables healthcare providers to initiate appropriate interventions, including antibiotics and supportive treatments. Furthermore, early detection of SAE and SAD can help prevent or reduce long-term neurological harm and enhance the recovery of patients[8].

Large language models (LLMs) are deep learning algorithms that use large amounts of data to perform natural language processing (NLP) tasks[9]. LLMs are known for their ability to understand and generate human language and have various applications in various industries. Furthermore, LLMs can improve search engine responses, customer service, marketing, legal, healthcare, and science. LLMs can perform tasks like answering questions, summarizing documents, translating languages, and completing sentences, but some require external tools or additional software. In the healthcare sector, LLMs play a crucial role in various areas, including vaccine development, disease treatment, and preventive care[7].

Early detection and prediction of SAE and SAD not only have the potential to save lives but also help reduce the long-term complications associated with this medical condition.

This narrative review aimed to evaluate the status of Artificial Intelligence (AI) applications in predicting two critical conditions associated with sepsis: SAE and SAD. This evaluation was done through a deep review to analyze the methodologies used in recent studies, summarize essential findings, and offer insights into the potential of AI in detecting and curing neurological complications at an early stage.

2. OVERVIEW OF ARTIFICIAL INTELLIGENCE (AI) IN HEALTHCARE

AI is transformative in healthcare, encompassing machine learning, deep learning, and more approaches, enabling computers to analyze extensive datasets, identify patterns, and generate predictions[10].

AI has been utilized in various tasks in healthcare, including medical imaging analysis, discovering new medicines, and disease prediction[11]. AI's ability to rapidly and accurately analyze extensive data makes AI a valuable asset for enhancing patient care and clinical decision-making[12].

AI holds considerable potential in predicting conditions such as SAD and SAE[12]. AI algorithms can detect early signs of neurological complications by analyzing diverse data sources, such as electronic health records, vital signs, laboratory results, and neuroimaging data. Additionally, AI can potentially support healthcare providers in classifying the risk, enabling them to allocate resources and interventions more efficiently[13].

Incorporating AI into sepsis management can enhance early detection, improve patient outcomes, and ultimately save lives in the battle against these complex neurological conditions associated with sepsis[12].

2.1 Diagnostic and Imaging Support

AI-driven diagnostic tools have the potential to assist healthcare practitioners in analyzing and interpreting various medical imaging modalities, including X-rays, magnetic resonance imaging (MRI), and computed tomography (CT) scans. These AI algorithms can identify deviations from the norm, facilitating the timely detection of medical conditions such as cancer or neurological illnesses. For instance, in analyzing medical images like CT scans, AI aids radiologists in detecting cerebral hemorrhages[14]. Prioritizing critical cases and delivering more efficient diagnoses using AI algorithms could significantly enhance patient outcomes.

AI is crucial in healthcare data analytics, particularly algorithmic tissue segmentation, and disease categorization techniques. The practical advantages of employing in-silico modeling and three-dimensional (3D) reconstruction applications are noteworthy. Integrative analytics approaches have the potential to significantly impact imaging informatics by improving the accuracy of diagnosis and treatment planning[15].

2.2 Predictive Analytics

AI utilizes patient data, including medical records and vital signs, to forecast the occurrence and progress of diseases[12]. This tool is used for identifying patients at risk of developing numerous health issues, such as sepsis, diabetes, and heart disease. Predictive analytics foresees patient readmissions, identifies high-risk individuals, and effectively tailors intervention plans to reduce readmission rates[16].

2.3 Personalized Treatment Plans

AI can provide customized treatment strategies by considering an individual's genetic profile, medical history, and behavioral data. Precision medicine offers personalized treatment plans based on an individual's genetic profile, medical history, and behavioral data. AI plays a significant role in developing these personalized medicines by analyzing patient data and identifying treatment targets. The benefits of using AI in customized treatment plans include improved treatment effectiveness, earlier diagnosis and better treatment, resource optimization, clinical trial optimization, and patient engagement[17]. However, limitations include the need for massive amounts of data and a receptive healthcare ecosystem[17].

Despite these challenges, the convergence of AI and precision medicine is expected to accelerate personalized care objectives, leading to enhanced treatment outcomes[15]. AI systems provide personalized cancer treatment plans by analyzing patient data and recommending treatments based on individual profiles and the latest medical research for oncology patients[18].

2.4 Natural Language Processing (NLP)

NLP facilitates the ability of AI systems to derive valuable information from unstructured clinical notes. This capability enhances the quality of medical documentation and expedites the process of data analysis for both research purposes and patient care[19]. For example, employing NLP to transcribe physician-patient interactions improves the efficiency of clinical documentation, enabling precise and swift updates to patient records.[20].

2.5 Robotics and Automation

Surgical robots and AI-assisted robotic systems play a crucial role in facilitating the performance of minimally invasive procedures by surgeons, offering enhanced accuracy and dexterity. Robots can also aid with monotonous jobs, such as prescription dispensing in pharmacies[21]. The robotic system aids surgeons in performing precise, minimally invasive surgeries, enhancing vision, agility, and control, thereby reducing patient recovery times[22].

2.6 Healthcare Administration

AI supports healthcare companies by facilitating administrative functions such as appointment scheduling, invoicing, and claim processing. This integration of AI technology has been shown to improve operational efficiency and reduce organizational challenges within healthcare[23]. Revenue Cycle Management (RCM) automation enhances healthcare financial processes by automating claim processing, billing, revenue optimization, and reducing administrative burdens on vendors. This transformation streamlines operations, making them more efficient and time-saving[24].

2.7 Challenges and Considerations

AI in healthcare presents several challenges and considerations that need to be addressed. One of the main concerns is the ethical implications of using AI algorithms[11]. There is a risk of bias in these algorithms, which can lead to unfair treatment or discrimination against certain groups of patients. Transparency in decision-making is also crucial, as healthcare professionals and patients need to understand how AI systems arrive at their conclusions. Another important consideration is data privacy and security, as patient data is highly sensitive and must be protected. AI systems must comply with privacy regulations and have robust security measures to prevent unauthorized access or breaches[25].

3. METHODS

3.1 Search Strategy

The literature search involved exploring published articles related to AI applications in predicting two essential conditions associated with sepsis: SAE and SAD. The investigations utilized the following

Table 1. Search Strategy and Search Operators used.

Query	Result
("Artificial Intelligence" OR "AI") AND ("ICU" OR "Intensive Care Unit") OR ("Sepsis") OR ("Sepsis-Associated Encephalopathy" OR "SAE" OR "Sepsis-Associated Delirium" OR "SAD")	**97**
("ICU" OR "Intensive Care Unit") AND ("Artificial intelligence" OR "AI") AND ("Sepsis") OR ("Sepsis-Associated Encephalopathy" OR "SAE") OR ("Sepsis-Associated Delirium" OR "SAD")	**65**
("AI" OR "Artificial Intelligence") AND ("ICU" OR "Intensive Care Unit") AND ("Sepsis-Associated Encephalopathy" OR "SAE") AND ("Sepsis-Associated Delirium" OR "SAD")	**11**

databases: Embase, Medline, CINAHL (Cumulative Index to Nursing and Allied Health Literature), PsychInfo (Psychology Information), and PubMed. Additionally, the Google Scholar search engine was used to identify further studies.

Articles were included in the review based on the following inclusion criteria: studies published between 2013 and 2023, research focusing on AI, machine learning, deep learning, and natural language processing to predict SAE and SAD in critical care settings. The abstracts of all studies identified by the search strategies were examined, with a preference for works in English. Full-text versions of those that met the eligibility criteria were then obtained**.** Furthermore, the reference lists of selected papers were checked for additional related studies. While several studies were identified, only those that met the criteria were selected for the final analysis of the review. Two reviewers were involved to ensure transparency in the study selection process and maintain the reliability of the review results, as outlined in Table 1.

Studies unrelated to artificial intelligence, those with irrelevant content, those conducted in non-healthcare settings, and those involving pediatric populations were excluded. Only studies that met the established criteria were selected for the final analysis of the review. The studies resulting from the identified search strategy were thoroughly discussed, and four studies that offered valuable insights were chosen based on how well they aligned with the study goal.

4. DISCUSSION

Previous research findings suggest that AI and machine learning have the potential to be employed in the timely identification of SAE and SAD. However, specific challenges must be addressed to harness its capabilities thoroughly.

In one study, the goal was to develop a machine learning (ML) model for the early prediction of SAD. The study analyzed data from the Medical Information Mart for Intensive Care (MIMIC-IV) and the electronic intensive care unit Collaborative Research Database (eICU-CRD). Various methods, including logistic regression, support vector machines, decision trees, random forests, and extreme gradient boosting (XGBoost), were used to construct prediction models. The XGBoost model demonstrated superior performance in predicting SAD, surpassing traditional delirium assessments and enabling earlier diagnosis in patients who are difficult to assess using standard methods[26].

Another study focused on evaluating the predictive performance of the MySurgeryRisk AI system, which demonstrated accurate early-stage prediction of SAD. The study analyzed data from the MIMIC-IV and eICU-CRD databases and constructed various prediction models using multiple methods. The XGBoost model was chosen as the final model, showing superior performance in predicting SAD. The system uses an automated Electronic Health Records (EHR) platform for predictive purposes, accurately predicting postoperative complications and delivering these predictions to surgeons. The study included all adult patients aged 18 years or older admitted for any inpatient surgical procedure. The study also examined the validation and matching of surgeons' predictive accuracy[27].

Conversely, work is underway to develop interpretable ML models to predict SAE in sepsis patients admitted to the intensive care unit (ICU). Six ML classifiers were used to predict SAE occurrences, with Bayesian optimization adjusted for model hyperparameters. The optimal algorithm was chosen based on predicted efficiency. The study found significant variations in SAE occurrence among individuals with pathogen infections, with creatinine identified as the optimal risk factor. The most optimal model identified mechanical ventilation and the duration of mechanical ventilation as significant factors. The XGBoost model demonstrated high predictive accuracy, and visual explanations were used to convey information. The interpretable model underwent evaluation by expert physicians, assisting in predicting SAE likelihood more intuitively[28].

Another study sought to develop an ML model to assess the likelihood that patients with SAE (Serious Adverse Events) would experience mortality within 30 days. The models were validated using the MIMIC-IV database and evaluated using metrics like AUC, accuracy, sensitivity, specificity, and predictive values. Out of 6994 patients, 17.62% died due to SAE. The recursive feature elimination method identified 15 variables for selection. These variables included Acute Physiology Score III (APSIII), Glasgow Coma Score (GCS), Sepsis-related Organ Failure Assessment (SOFA), Charlson Comorbidity Index (CCI), Red Blood Cell Volume Distribution Width (RDW), Blood Urea Nitrogen (BUN), Age, Respiratory Rate, PaO2, Temperature, Lactate, Creatinine (CRE), Malignant Cancer, Metastatic Solid Tumor, and Platelet (PLT). The study demonstrated that ML models can assess SAE prognosis in the ICU, and online calculators could improve predictive model dissemination[29].

5. THE ROLE OF AI IN PREDICTION MODEL FOR SAD AND SAE IN ICU

AI is a critical tool in developing prediction models for SAD and SAE in ICUs. It integrates data and provides real-time analysis, early detection, personalized predictions, and continuous monitoring[30]. AI models can assign risk scores, identify high-risk individuals, and offer customized assessments. However, careful integration of ethical, regulatory, and clinical aspects is necessary to optimize AI's benefits in healthcare fully[31]. Figure 1 summarizes how AI can enhance prediction for SAD and SAE in ICUs. The XGBoost algorithm, known for its effectiveness in machine learning, is crucial in improving predictive models for SAE and SAD.

The XGBoost algorithm is a robust machine-learning technique that integrates boosting, decision trees, regularization, gradient descent, and an objective function for optimization[32]. The process begins with data collection, preprocessing, feature selection, model training, assessment, and prediction. Boosting combines weak learners (decision trees) to create a strong learner, enabling precise prediction. XGBoost is known for its scalability and efficient handling of large-scale datasets. This open-source tool uses gradient boosting for supervised learning, employing decision tree ensembles as its base learner and incorporating regularization techniques to mitigate overfitting. Model parameters are optimized using gradient descent to minimize the reduction in operations and enhance accuracy. While XGBoost is effective and efficient, achieving optimum performance requires substantial computational resources and meticulous hyperparameter tuning[33].

Complex neurological disorders, like SAE and SAD, may exhibit limited symptoms[4]. Diverse methods can enhance symptom characterization, including standardized assessment tools, multimodal data collection, continuous monitoring, neuroimaging procedures, ML algorithms, remote monitoring, patient-reported outcomes, and AI-based NLP. Effective interdisciplinary collaboration among intensivists, neurologists, and neuropsychologists is crucial for patient care and decreased mortality rates[34].

Strategies involve employing specialized assessment tools such as the Confusion Assessment Method (CAM) or the Richmond Agitation-Sedation Scale (RASS), utilizing multiple data sources for comprehensive data collection, continuously monitoring vital indicators, employing neuroimaging techniques like MRI and EEG, developing machine learning models to identify patterns in patient data, utilizing remote monitoring technologies to track patients after they leave the ICU, encouraging patients to report any changes in cognitive function and mental status, and employing AI and NLP techniques to analyze clinical notes that lack structure[35].

Effective collaboration between intensivists, neurologists, and neuropsychologists is crucial to understanding symptom characterization for SAE and SAD[36]. Timely prompts and alerts from clinical decision support systems, coupled with education and training, equip healthcare professionals with the necessary knowledge to recognize initial symptoms and appreciate the significance of prompt diagnosis[37]. Quality improvement programs aim to maintain a standardized approach to evaluating and improving the identification of symptoms and the early detection of serious adverse events.

Incorporating AI into healthcare can significantly reduce costs, especially in predicting and diagnosing conditions such as SAE and SAD[38]. AI-powered prediction models can enable early interventions, optimize resources, implement preventive measures, minimize diagnostic errors, enhance treatment pathways, and improve operational efficiency. By precisely identifying patients at risk, healthcare providers can optimize resource allocation. AI can assist in customizing treatment pathways using predictive models, thereby reducing the utilization of less efficient treatments and medications[39]. This individualized approach can result in financial benefits and enhanced patient outcomes[38].

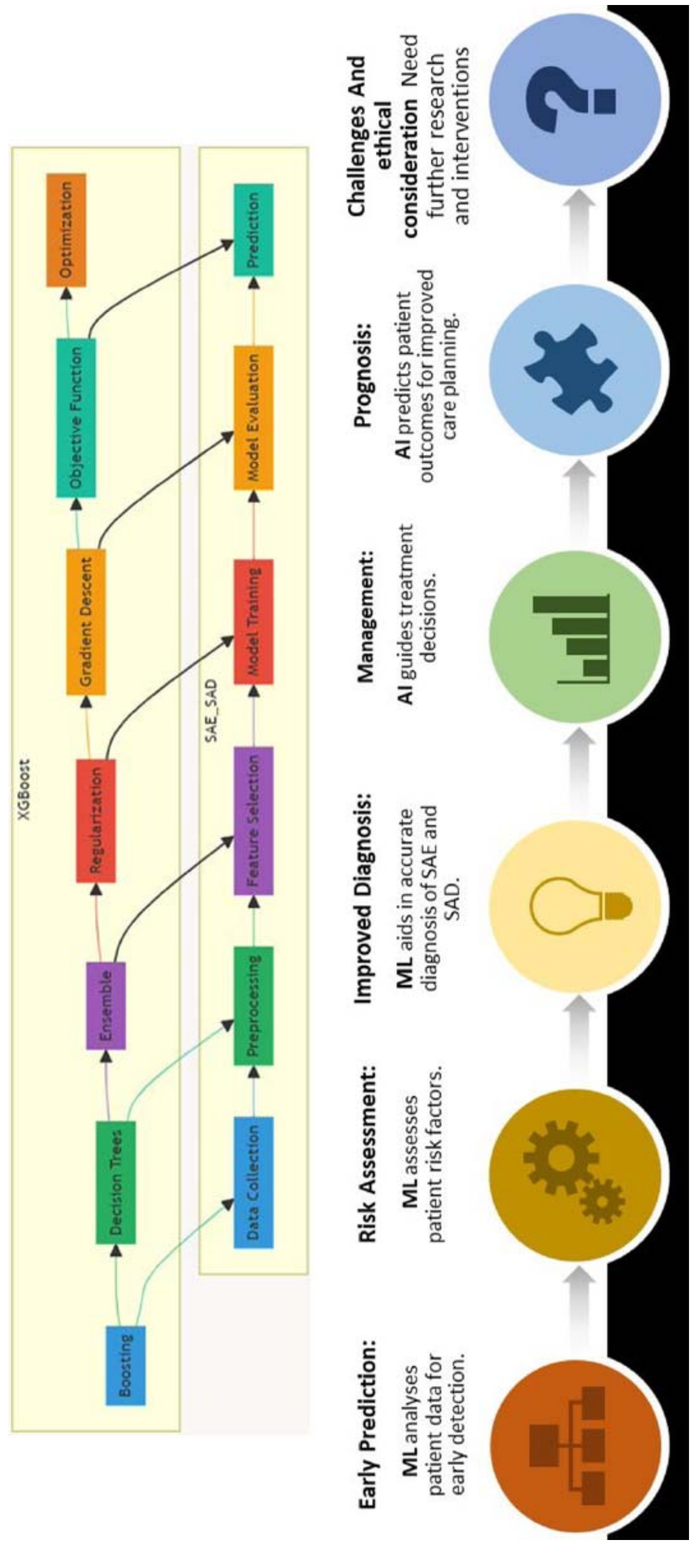

Figure 1. AI in Sepsis-Associated Encephalopathy (SAE) and Sepsis-Associated Delirium (SAD) Summary, (source: author).

6. CHALLENGES CURRENTLY FACED AND FUTURE DIRECTIONS FOR AI-DRIVEN EARLY PREDICTION OF SAD AND SAE

Developing a prediction model for SAD and SAE in the ICU is a challenging process that requires careful analysis. Challenges in this area include data quality, imbalanced data, feature selection, temporal data, clinical variability, interpretability, data privacy and security, ethical considerations, and generalizability[40]. Effective collaboration among data scientists, clinicians, and domain experts is essential for a comprehensive understanding of the clinical context. Validation is necessary to apply the model effectively in practical settings[41]. Timely predictions are crucial for practical application, and seamless integration into the clinical workflow is paramount. Adopting a patient-centric approach is vital, with regulatory compliance playing a critical role[41]. Transparency and accountability are crucial in fostering trust within the healthcare community[3]. Improvement is essential to effectively respond to evolving patient populations and clinical practices. Emphasizing the importance of patient safety, data privacy, and ethical standards is vital when developing a valuable tool to enhance patient care in the ICU[3].

As shown in Table 2, AI in SAE and SAD has benefits such as early prediction and intervention, improved diagnosis, and real-time management support. Challenges include false alarms, data privacy, algorithm bias, and integration complexities. For example, inadequate data protection measures can result in breaches and compromises of sensitive patient information, raising ethical concerns about patient consent and confidentiality. Biased algorithms can contribute to ongoing healthcare disparities and face challenges when applying predictions to a wide variety of patients, impacting the accuracy of outcomes. Inadequately integrated AI systems might disturb established workflows and lead to inefficiency in patient care. Additionally, challenges in compatibility may impede the smooth integration of AI systems and consequently need to be of the highest priority problems to address to ensure the efficient and ethical implementation of AI in healthcare management. Therefore, healthcare providers should invest in technology, ensure ethics and transparency, collaborate with regulators, and train staff.

7. IMPLICATIONS AND CONCLUSION

This review evaluates AI's effectiveness in predicting sepsis-associated conditions, SAE, and SAD, analyzing methodologies, findings, and potential for early neurological complications like SAE and SAD detection and treatment. The studies reviewed in this summary highlight the potential of AI and machine learning in predicting and diagnosing SAD and SAE. Machine learning models, notably the XGBoost algorithm, have shown superior performance in predicting SAD and SAE compared to traditional methods. These models have been developed and validated using data from the MIMIC-IV and eICU-CRD databases. Additionally, the studies emphasize the importance of interpretable machine learning models that can provide visual explanations and assist physicians in making more intuitive predictions. Furthermore, machine learning models have also been utilized to estimate the likelihood of mortality in patients with SAD and SAE, demonstrating their potential in assessing prognosis in the ICU setting. Overall, these findings suggest that AI has the potential to improve the timely identification and prognosis of SAD and SAE.

Using AI in the ICU for SAE and SAD presents several challenges that must be addressed. These challenges include ensuring the quality and availability of data, interpreting and explaining the models used, integrating AI systems with existing infrastructure, maintaining privacy and security, validating and ensuring the reliability of AI algorithms, and effectively managing resources. However, further research and addressing specific challenges are necessary to fully utilize AI's abilities and solve particular problems before it can reach its full potential. AI's future applications in the ICU for SAE and SAD involve early prediction and diagnosis, personalized treatment plans, monitoring and real-time intervention, enhanced decision-making, and streamlined clinical processes.

DECLARATIONS

Ethics approval and consent to participate: Not applicable.
Consent for publication: Not applicable.
Availability of data and materials: All data generated or analyzed during this study are included in this published article.
Competing interests: The authors have no conflicts of interest to disclose.
Funding: None.

Table 2. Use Cases for AI in SAE and SAD: Advantages, Disadvantages, and Solutions.

	Advantages	Disadvantages	Solutions
Early Prediction	- Timely detection of SAE and SAD symptoms.	- Potential for false alarms leading to unnecessary interventions.	- Implement smarter AI algorithms that consider multiple data sources to reduce false alarms.
	- Early intervention and treatment.	- Reliance on data quality and accuracy.	- Improve data quality through data cleaning and validation processes.
	- Improved patient outcomes and reduced mortality.	- Ethical and privacy concerns with continuous monitoring.	- Develop transparent and ethical AI practices with patient consent and data protection in mind.
Improved Diagnosis	- Enhanced symptom characterization and pattern recognition.	- Initial implementation costs.	- Invest in AI technology and training for healthcare staff to ensure optimal utilization.
	- Utilizes various data sources for comprehensive assessment.	- Need for specialized training of healthcare staff.	- Offer training and education programs for healthcare staff to enhance their AI usage skills.
	- Accurate and rapid diagnosis, reducing delays.	- Potential algorithm bias and fairness concerns.	- Address algorithm bias through regular audits and diverse dataset usage to ensure fairness.
Prognosis	- Accurate assessment of prognosis for patients with SAE and SAD.	- Interpretability challenges for clinicians.	- Develop AI models with interpretability features, such as visual explanations, for easier clinical understanding.
	- Identifies patients at risk of developing complications.	- Data privacy and security concerns with patient data.	- Ensure compliance with data privacy regulations and implement robust security measures.
	- Customized treatment strategies based on prognosis.	- Potential resistance from clinicians in adopting AI-based recommendations.	- Promote education and awareness among clinicians regarding the benefits of AI-driven personalized treatment.
Risk Assessment	- Risk stratification for effective allocation of resources.	- Limited access to data from electronic health records (EHR).	- Work on improving data sharing practices among healthcare institutions to enable comprehensive AI models.
	- Identifies high-risk individuals and enables preventive measures.	- Ethical considerations in utilizing patient data for AI models.	- Establish clear ethical guidelines for data usage and involve patients in the consent process.
	- Supports personalized assessments and care plans.	- Generalizability of AI models to diverse patient populations.	- Collaborate across diverse healthcare settings to ensure AI models are adaptable to different patient profiles.
Management	- Real-time monitoring and alerts for healthcare providers.	- Integration of AI into existing healthcare systems can be complex.	- Develop seamless integration strategies that align with existing healthcare systems and workflows.
	- Consistent and standardized evaluation of symptoms.	- Ensuring AI compliance with healthcare regulations.	- Collaborate with regulatory bodies to establish guidelines for AI integration and compliance in healthcare.
	- Supports quality improvement programs for better patient care.	- Resistance to technology adoption by healthcare institutions.	- Showcase successful AI implementations and share best practices to ease institutional resistance.

Table of Abbreviations

ICU	Intensive Care Unit
SAE	Sepsis-Associated Encephalopathy
SAD	Sepsis-Associated Delirium
AI	Artificial Intelligence
XGBoost	extreme gradient boosting
LLMs	Large language models
MIMIC-IV	Medical Information Mart for Intensive Care
eICU-CRD	Electronic Intensive Care Unit Collaborative Research Database
EHR	Electronic Health Records

Authors' contributions: MIO: Conceptualization. MIO, AJN, AAA, MYK: Literature search, Manuscript preparation. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Acknowledgments: None.

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