Journal of Multiscale Neuroscience

Original Research

Artificial intelligence coupled with the *Internet of Things* targeting neurodevelopmental challenges in preterm neonates

Syed Taimoor Hussain Shah[1,†], Syed Adil Hussain Shah[1,2,†], Konstantinos Panagiotopoulos[1], Janet Pigueiras-del-Real[3], Kainat Qayyum[4], Syed Baqir Hussain Shah[5], Shahzad Ahmad Qureshi[6], Angelo Di Terlizzi[2], Giacomo Di Benedetto[7], Marco Agostino Deriu[1,*]

[1]Politecnico di Torino, Department of Mechanical and Aerospace Engineering, PolitoBioMed Lab, Corso Duca degli Abruzzi 24, Torino, 10129, Italy

[2]GPI SpA, Department of Research and Development (R&D), Via Ragazzi del '99, Trento 38123, Italy

[3]University of Cádiz, Department of Condensed Matter Physics, Cádiz 11510, Spain

[4]Tianjin Polytechnic University, School of Artificial Intelligence, Binshui West Road No. 399, Tianjin 300387, PR China

[5]COMSATS University Islamabad (CUI), Wah Campus, Department of Computer Science, Grand Trunk Road, Wah 47040, Pakistan

[6]Pakistan Institute of Engineering and Applied Sciences (PIEAS), Department of Computer and Information Sciences, Islamabad 45650, Pakistan

[7]7HC SRL, Rome 00198, Italy

[†]Equal Contributions

*Correspondence: marco.deriu@polito.it

DOI: https://doi.org/10.56280/1680389540

Received: 7 February 2025 Accepted: 19 February 2025 Online published: 12 March 2025

Abstract

Preterm neonates face significant neurological risks due to incomplete brain development at birth. The third trimester is critical for brain maturation, and premature birth disrupts essential developmental processes, leading to long-term cognitive, motor, and sensory impairments. Key vulnerabilities include cortical underdevelopment, white matter damage, and immature neurotransmission, contributing to neurodevelopmental disorders such as cerebral palsy, attention deficits, and learning difficulties. While advances in Neonatal Intensive Care Units (NICUs) have improved survival rates, early detection and continuous monitoring of complications remain challenging. The integration of *Internet of Things* (IoT) technology in neonatal care presents a transformative approach, enabling real-time physiological monitoring, predictive analytics, and automated alerts for timely interventions. IoT-driven neonatal monitoring systems enhance clinical decision-making, reduce caregiver burden, and improve patient outcomes. In parallel, Artificial Intelligence (AI) is revolutionizing neonatal healthcare by processing multimodal data, including clinical records, physiological signals, and imaging to provide real-time insights, predictive diagnostics, and risk assessments. Machine learning (ML) and deep learning (DL) techniques aid in disease prediction, anomaly detection, and precision diagnostics, significantly enhancing neonatal monitoring. However, challenges such as AI interpretability, data security, and integration into clinical workflows must be addressed to ensure adoption. Explainable-AI (XAI) tools such as SHAP, LIME, and Grad-CAM are crucial in making AI-driven decisions more transparent and actionable. The future of neonatal AI lies in developing multimodal frameworks that integrate physiological signals and facial, vocal, and motion data for comprehensive neonatal health monitoring. Addressing the technical and ethical challenges associated with AI and IoT adoption will be critical to fully realizing their potential in neonatal care and improving outcomes for preterm infants.

Keywords: Preterm neonates, brain development, neurodevelopmental disorders, neonatal intensive care unit, Internet of Things, artificial intelligence, machine learning, deep learning, explainable-AI, predictive analytics

1. Introduction

Neonates refer to newborn infants within the first 28 days of life, a period marked by profound physiological transformations. This phase is critical for survival and long-term health, as neonates must adapt to life outside the womb. These adaptations involve significant changes in respiratory, cardiovascular, metabolic, and immune systems, making neonates particularly vulnerable to complications (Lawn et al.,2005; Moster et al., 2008; Blackburn, 2017; Anef, 2019). Neonatal development is a critical period categorized into distinct stages based on the gestational age of the infant, as illustrated in **Figure 1**. Each stage reflects varying degrees of physiological, neurological, and developmental maturity, as discussed below. These stages are crucial for determining the medical and technological interventions required to support neonates, especially those born preterm (Goldenberg *et al.*, 2008; Blencowe *et al.*, 2013, 2013; Tana *et al.*, 2023):

(i) Extremely Preterm Neonates (22–28 Weeks): Infants born at this stage face the most significant challenges due to incomplete organ development. They typically require advanced life-support systems, such as mechanical ventilation, and constant monitoring for survival. The central nervous system (CNS), lungs, and gastrointestinal system are underdeveloped, increasing the risk of conditions like intraventricular hemorrhage (IVH) and chronic lung disease (Jobe & Ikegami, 2000; Behrman et al., 2007; Mally et al., 2010; Kusuda, 2025).

(ii) Very Preterm Neonates (29–31 Weeks): This group represents infants with a slightly higher gestational maturity than extremely preterm neonates. While their survival rates are better, they still require intensive care in neonatal intensive care units (NICUs) to support respiratory and thermal regulation. Neurological development is ongoing, and these neonates are at risk for neurodevelopmental disorders (Pani & Panda, 2012; Grunau, 2013; Vrancken et al., 2018).

(iii) Moderate Preterm Neonates (32–34 Weeks): Infants born during this period exhibit more stable physiological functions but still face risks associated with feeding difficulties, respiratory instability, and jaundice. Their neurological and organ development has progressed, reducing but not eliminating the risk of long-term developmental challenges (Sharma *et al.*, 2019; Karnati et al., 2020; Vuppu & Iragamreddy, 2023).

(iv) Late Preterm Neonates (32–34 Weeks): Often referred to as "near-term," these infants have a higher degree of maturity. However, they still require careful monitoring for potential issues such as transient tachypnea, hypoglycemia, and thermoregulation problems. While many late preterm neonates can thrive with minimal intervention, they remain at risk for mild developmental delays (Pulver *et al.*, 2010; Sharma *et al.*, 2019; Karnati et al., 2020).

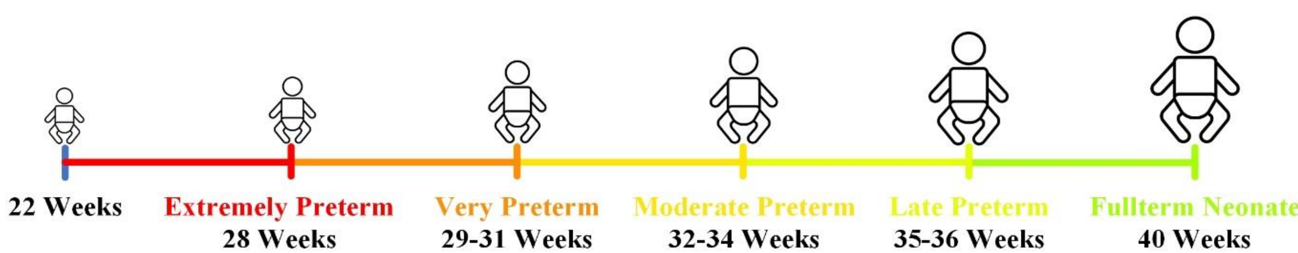

Figure 1 The classification of neonates into distinct stages based on their gestational age at birth. The stages range from Extremely Preterm Neonates (born at 22–28 weeks) to Full-Term Neonates (born at or beyond 37 weeks). Each stage highlights the varying degrees of developmental maturity, from severely underdeveloped organ systems in extremely preterm neonates to fully matured systems in full-term neonates. Key stages include Very Preterm Neonates (29–31 weeks), requiring intensive medical support, and Moderate and Late Preterm Neonates (32–36 weeks), who display progressively greater physiological and neurological stability but may still face mild complications. This classification is critical for guiding clinical interventions, particularly in NICUs, where care is tailored to the specific needs of neonates in each stage.

Preterm neonates are at heightened risk of neurological complications due to incomplete brain development at birth (Paneth, 2018). These issues can have immediate and long-term consequences, affecting motor, cognitive, and sensory functions. In addition, the third trimester of pregnancy is a critical period for brain development, during which the neonatal brain undergoes rapid growth and structural refinement (Dubois *et al.*, 2020; Fenn-Moltu *et al.*, 2022). This process is significantly interrupted in preterm births, resulting in a cascade of developmental vulnerabilities.

The interruption of these vital developmental processes underscores the fragility of the preterm brain and its heightened risk of injury. Understanding these challenges is essential for developing tailored interventions that support neural growth and mitigate the long-term consequences of preterm birth. In this way, the article delves into the neurological vulnerabilities of preterm neonates, emphasizing how incomplete brain development at birth increases the risk of motor, cognitive, and sensory impairments. It explores key challenges such as cortical underdevelopment, white matter damage, and immature neurotransmission, all of which contribute to long-term neurodevelopmental disorders like cerebral palsy and attention deficits. The discussion extends to common neurological conditions affecting preterm neonates, including intraventricular hemorrhage, periventricular leukomalacia, and hypoxic-ischemic encephalopathy, highlighting their causes and long-term implications. Given these vulnerabilities, the critical role of Neonatal Intensive Care Units (NICUs) is examined, showcasing their specialized interventions for stabilizing preterm infants and managing complications related to respiratory distress, infections, and thermoregulation. However, despite advancements in NICU care, the challenges associated with intensive monitoring, caregiver burden, and the need for real-time clinical decision-making persist.

The heightened neurological risks faced by preterm neonates due to incomplete brain development underscore the need for continuous monitoring and timely interventions. Despite significant advancements in Neonatal Intensive Care Units (NICUs), challenges persist in ensuring early detection and personalized care. The integration of technology, particularly the Internet of Things (IoT) and Artificial Intelligence (AI), offers promising solutions to bridge these gaps by enabling real-time physiological monitoring and predictive analytics. AI is transforming clinical decision-making, especially in fields such as neonatal care, where early and accurate insights are crucial for the well-being of vulnerable patients. AI technologies enable advanced predictive analytics, facilitate real-time monitoring, and provide sophisticated decision-support tools in neonatal intensive care units (NICUs) (Pigueiras-del-Real *et al.*, 2024). Utilizing diverse data sources (Shah et al., 2022; Qureshi *et al.*, 2024), including clinical records, physiological signals, and multimodal data (e.g., ECG (Gentile *et al.*, 2023), facial (Shah *et al.*, 2023), vocal (K *et al.*, 2021), and motion data (Abbasi *et al.*, 2023)), AI in neonatal care has the potential to improve health outcomes by capturing a comprehensive view of a neonate's health status. Yet, to be adopted effectively in clinical settings, these AI models must be interpretable and transparent, providing clinicians with clear insight into the reasoning behind their predictions. This interpretability ensures that AI-driven insights are clinically actionable, and fosters trust among healthcare providers.

Considering the challenges and the growing need for AI in NICUs, this article delves into the critical neurological challenges faced by preterm neonates, particularly those born before completing their full gestational development. It highlights the significance of the third trimester in brain maturation and how its disruption leads to long-term impairments. Despite advancements in Neonatal Intensive Care Units (NICUs), challenges persist in ensuring continuous monitoring and timely interventions. The integration of Internet of Things (IoT) technologies and Artificial Intelligence (AI) into neonatal care is transforming early detection, monitoring, and decision-making in NICUs. IoT facilitates real-time data collection from various sensors, while AI-driven models analyze multimodal data, including physiological signals, clinical records, and imaging, to predict risks and improve outcomes. However, these technological advancements come with challenges, including data security, model interpretability, and clinical workflow integration. This paper explores these aspects in detail, offering insights into how IoT and AI can revolutionize neonatal healthcare while addressing their limitations.

The article is structured into several key sections, each designated with a specific section number for clarity. Section 2 examines the role of Neonatal Intensive Care Units (NICUs) in stabilizing and supporting preterm infants, outlining specialized interventions for managing complications such as respiratory distress and infections. Section 3 explores the challenges in neonatal care, including the burden on caregivers, the limitations of traditional monitoring systems, and the need for continuous, real-time physiological assessment. Section 4 delves into the role of IoT in neonatal monitoring, detailing its architecture, advantages, and the challenges associated with its implementation in clinical settings. Section 5 presents the integration of AI in NICUs, highlighting predictive modeling, machine learning applications, image and signal processing, and the necessity of explainability tools such as SHAP, LIME, and Grad-CAM to enhance trust and clinical adoption. Section 6 introduces a multimodal AI framework that combines ECG, facial, vocal, and motion data for a comprehensive approach to neonatal monitoring. Section 7 discusses ethical considerations, data security concerns, and interoperability challenges associated with AI and IoT in neonatal healthcare. Finally, Section 8 concludes the article by summarizing key findings, discussing future research directions, and emphasizing the potential of AI and IoT in transforming neonatal care.

2. Neurological issues and long-term impacts

Preterm neonates, particularly those born extremely or very preterm, are at a heightened risk of developing various neurological complications due to the immaturity of their central nervous system and the challenges associated with their early birth. Some of the most common neurological conditions affecting preterm neonates are as follows:

One of the primary areas affected by preterm birth is cortical development. The cerebral cortex, responsible for higher-order functions such as sensory processing, motor coordination, and cognitive abilities, remains underdeveloped in preterm neonates (Back & Miller, 2014; Heuvel *et al.*, 2014). This underdevelopment is often attributed to the disruption of normal cell migration, differentiation, and synapse formation. Consequently, preterm neonates frequently exhibit difficulties in sensory processing, such as visual and auditory perception, as well as motor coordination challenges that may persist into later life stages (Molnár, Luhmann & Kanold, 2020; Wallois et al., 2020).

Another critical issue in preterm neonates is the vulnerability of white matter. White matter, essential for effective neural communication, undergoes significant maturation during the third trimester, particularly through the process of myelination. In preterm neonates, incomplete myelination leaves white matter highly susceptible to injury from factors such as hypoxia, inflammation, or intraventricular hemorrhage. Damage to white matter can lead to disrupted neural signaling, resulting in motor deficits, cognitive delays, and long-term neurodevelopmental impairments, including conditions like cerebral palsy.

In addition, neurotransmission, the process by which neurons communicate via synapses, is also compromised in preterm neonates due to the immaturity of their neural networks. During the third trimester, the brain undergoes critical processes such as synaptic pruning and the maturation of neurotransmitter systems. These processes are disrupted in preterm births, leading to inefficient neural network formation. (Basu *et al.*, 2021; Petanjek *et al.*, 2023). The impaired development of excitatory and inhibitory neurotransmitter systems may further contribute to challenges in regulating neural activity, which can manifest as difficulties in attention, memory, and emotional regulation later in life (Scheuer *et al.*, 2021; Yan & Rein, 2022).

Intraventricular hemorrhage (Honnorat *et al.*, 2023; Périsset *et al.*, 2023) is a significant concern in very preterm infants, characterized by bleeding into the brain's ventricular system. This condition often occurs within the first few days of life due to the fragility of blood vessels in the developing brain and fluctuations in cerebral blood flow. IVH is graded on a severity scale from I to IV, with higher grades associated with more severe neurological consequences, including hydrocephalus and long-term neurodevelopmental impairments.

Periventricular leukomalacia (Martinez-Biarge *et al.*, 2019; Petri & Tinelli, 2023) refers to the damage or softening of the white matter surrounding the brain's ventricles, primarily due to a lack of oxygen or blood flow (ischemia). PVL is one of the leading causes of motor impairments, such as cerebral palsy in preterm infants. The condition disrupts the development of myelination, which is crucial for efficient nerve signal transmission, and often results in spasticity, poor coordination, and other motor deficits.

Hypoxic-ischemic encephalopathy (Nabetani et al., 2021; Tetorou *et al.*, 2021) is a type of brain injury that occurs due to insufficient oxygen supply (hypoxia) or reduced blood flow (ischemia) during or shortly after birth. While HIE can affect term infants, preterm neonates are particularly vulnerable due to their underdeveloped brain structures. Depending on the severity, HIE can result in a range of outcomes, from mild developmental delays to severe conditions such as epilepsy or cerebral palsy.

Preterm neonates are at increased risk of long-term neurodevelopmental delays, which may manifest as cognitive, motor, and behavioral challenges during infancy and later in childhood (Jois, 2019; Gamarra-Oca *et al.*, 2021). These delays often stem from a combination of perinatal brain injury, altered neurodevelopmental trajectories, and environmental factors. Cognitive impairments can include difficulties with attention, memory, and executive function, while motor challenges may involve delayed milestones or abnormal muscle tone. Behavioral issues, such as hyperactivity or autism spectrum disorders, are also more prevalent in this population (Linsell *et al.*, 2018; You *et al.*, 2019).

The neurological challenges faced by preterm neonates often extend far beyond the neonatal period, leading to lifelong consequences that significantly impact their quality of life. Due to the immaturity of their brain at birth and the high vulnerability to injuries during critical developmental stages, preterm neonates are predisposed to a range of long-term neurodevelopmental complications.

Motor impairments are among the most common long-term effects in preterm neonates, with cerebral palsy being a predominant condition. Cerebral palsy results from damage to the motor control centers of the brain, often due to conditions like periventricular leukomalacia (PVL) or intraventricular hemorrhage (IVH). Children with cerebral palsy may experience spasticity, muscle weakness, poor coordination, or even complete loss of motor function in severe cases, requiring lifelong physical therapy and assistive devices for mobility (Hong & Rha, 2023; Martini & Corvaglia, 2023).

Cognitive challenges are frequently observed in individuals born prematurely. These deficits may include learning disabilities, difficulties in language processing, attention disorders, and impaired executive functioning, such as problem-solving and decision-making. Memory-related issues are also common, stemming from disruptions in hippocampal development, a brain region critical for memory consolidation (Vandormael *et al.*, 2019; Cainelli *et al.*, 2020). Such impairments often result in academic challenges and necessitate individualized educational support during school years.

Preterm neonates are at an increased risk of developing behavioral disorders as they grow older. Among these, attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorders (ASD) are particularly prevalent. ADHD in former preterm infants may manifest as difficulties with attention regulation, impulsivity, and hyperactivity, while ASD is often associated with social communication challenges and repetitive behaviors (Makris *et al.*, 2023; Rubin *et al.*, 2023). The etiology of these disorders is multifactorial, involving a combination of perinatal brain injuries and altered neurodevelopmental pathways.

Addressing these neurological challenges requires timely medical interventions and long-term multidisciplinary support, including physical therapy, occupational therapy, and neurodevelopmental assessments, to optimize outcomes for preterm neonates. Also, the long-term impacts emphasize the critical need for early detection, targeted therapeutic interventions, and sustained multidisciplinary care. Addressing these challenges proactively can enhance functional outcomes and improve the overall quality of life for individuals born prematurely.

3. Role of NICUs in neonatal care

NICUs are specialized hospital units dedicated to the care of critically ill newborns. These environments are equipped to handle a range of complications that arise in premature or high-risk infants, such as respiratory distress syndrome, infections, jaundice, and congenital disorders (Bulut *et al.*, 2022; De Paula Fiod Costa & De Paula Fiod Costa, 2022; Shah *et al.*, 2022). NICUs are designed to create controlled, supportive environments that cater to neonates' unique medical needs, primarily focusing on stabilizing vital functions while addressing the specific complications associated with underdeveloped organs.

NICU serves as a critical care environment specifically designed to meet the unique needs of newborns who require specialized medical attention. These units provide a tiered system of care categorized into levels based on the complexity of services offered (Bourque *et al.*, 2024; Goodman *et al.*, 2024). Level I NICUs cater to healthy newborns requiring minimal monitoring and support, while Level II facilities manage moderately ill or premature infants needing more focused care, such as short-term respiratory assistance or intravenous therapy. Level III NICUs offer advanced interventions for critically ill neonates, including mechanical ventilation, advanced imaging, and specialized treatments. At the highest level, Level IV NICUs are equipped for the most complex cases, including surgical procedures and treatments for life-threatening conditions, supported by a multidisciplinary team and cutting-edge technology. This tiered approach ensures that newborns receive care tailored to their specific medical needs, promoting better outcomes through a combination of expert staff, advanced equipment, and specialized protocols.

NICUs are designed to address a range of medical conditions commonly encountered in newborns, particularly those born prematurely or with underlying health issues. These include hypothermia, where an infant's body struggles to maintain a stable temperature due to underdeveloped thermal regulation, and respiratory distress syndrome caused by immature lung development (Shah *et al*., 2022; Goodman *et al.*, 2024). Other critical conditions include hypoxia, characterized by insufficient oxygen in the bloodstream, and sepsis, a severe infection that can rapidly become life-threatening. Each condition is treated using specialized interventions, such as mechanical ventilation for respiratory support or antibiotics to manage infections, ensuring that neonates receive timely and effective care to stabilize their health and support their development (Alhumaid *et al*., 2024).

NICUs are equipped with a range of advanced medical devices and technologies designed to address the unique healthcare needs of critically ill newborns. Incubators play a central role by providing a controlled and thermally regulated environment that protects neonates from temperature fluctuations and external stressors, crucial for their fragile systems (Hodson, 2018; Chandrasekaran *et al.*, 2021; Vitale *et al.*, 2021). Mechanical ventilators are employed to assist or completely support breathing in neonates with underdeveloped or impaired lungs, ensuring adequate oxygen delivery and carbon dioxide removal (Gupta *et al.,* 2021). Oxygen hoods deliver a precise concentration of oxygen to infants who require respiratory support without invasive intubation, while phototherapy units are used to treat jaundice by breaking down excess bilirubin in the skin through exposure to specific wavelengths of light (Sashi-Kumar *et al*., 2016).

3.1. Challenges in neonatal Care

Providing care for neonates, particularly those born prematurely or with critical health conditions, poses significant challenges due to their physiological vulnerabilities and the demanding nature of delivering precise, real-time care in a high-stakes environment. Neonates have fragile health owing to underdeveloped organs, immature physiological systems, and a heightened susceptibility to infections, making them prone to rapid health deterioration. The delicate balance required to stabilize and support these infants highlights the complexities of neonatal care.

One of the primary challenges stems from the physiological vulnerabilities of neonates. Premature infants often have underdeveloped cardiovascular systems, leading to issues such as hypotension and poor perfusion. Their respiratory function is similarly compromised due to immature lungs lacking sufficient surfactant, resulting in conditions like respiratory distress syndrome (RDS) (Kharrat & Jain, 2022; Brett & Robinowitz, 2023; Shah *et al.*, 2024). Additionally, their immune systems are underdeveloped, making them highly susceptible to infections that can escalate quickly. These physiological weaknesses demand constant vigilance and specialized medical interventions to prevent or address complications as they arise.

Another critical aspect is the need for intensive monitoring to detect subtle changes in a neonate's condition. Monitoring systems in NICUs are designed to track vital signs such as heart rate, respiratory rate, oxygen saturation, and temperature in real time. However, these systems are not without limitations (Khanam *et al.*, 2021; Maurya *et al.*, 2021; Cay *et al.*, 2022; Al-Beltagi *et al.*, 2024). Traditional monitoring devices can sometimes produce data inaccuracies or false alarms, complicating clinical decision-making. Furthermore, these systems are often manually intensive, requiring caregivers to frequently adjust settings, interpret data, and respond promptly to alarms, adding to the already demanding nature of NICU care (Villarroel *et al.*, 2019; Gandhimathi Alias Usha & Bharathi, 2024).

The burden on caregivers further compounds the challenges of neonatal care. NICU staff must manage multiple patients simultaneously, closely monitoring vital signs, administering treatments, and making quick decisions in response to health fluctuations. This constant need for vigilance often leads to information overload, as caregivers must process large volumes of fragmented data from various monitoring devices. The overwhelming number of alarms, many of which may be false or non-critical, can result in alarm fatigue, where caregivers become desensitized to alarms, potentially reducing their responsiveness to genuine emergencies.

4. Role of IoT in neonatal monitoring

The integration of IoT technology into NICUs represents a groundbreaking advancement, revolutionizing neonatal care by enabling interconnected devices to gather, analyze, and communicate data in real time, as shown in Figure 2. By utilizing IoT in healthcare, particularly in neonatal monitoring, NICUs can significantly enhance the quality, precision, and responsiveness of care. This innovation facilitates the continuous collection of physiological and environmental data, enabling clinicians to make informed decisions and intervene promptly in critical situations.

IoT refers to the network of interconnected devices that communicate autonomously through a shared network. These devices collect, transmit, and process data using sensors, cloud-based servers, and analytical platforms (Atzori et al., 2010; Alharbe & Almalki, 2024). In healthcare, IoT operates through a multi-layered architecture comprising sensing devices, network gateways, cloud computing, and user interfaces. Sensors attached to neonates or positioned within the NICU environment capture vital signs such as heart rate, respiratory rate, and oxygen saturation, along with external parameters like temperature and humidity (Islam *et al.*, 2015; Rahmani *et al.*, 2018). This data is transmitted to cloud servers, where it is analyzed in real time and presented to clinicians through user-friendly dashboards or alerts. Such continuous monitoring ensures uninterrupted oversight of neonatal health, reducing the likelihood of missing critical health deteriorations.

The advantages of IoT in NICU settings are manifold, primarily revolving around improved patient outcomes and operational efficiency. IoT-enabled systems can detect early warning signs of complications, such as respiratory distress or sepsis, by identifying subtle deviations in vital signs that may not be immediately evident to caregivers. By automating data collection and analysis, IoT reduces the manual burden on health-care providers, allowing them to focus on clinical decision-making rather than routine monitoring. Moreover, IoT systems facilitate seamless data integration across various devices, eliminating fragmented data silos and creating a cohesive view of a neonate's condition. Real-time insights provided by IoT reduce response times, enabling faster and more targeted medical interventions, which are critical for the fragile health of preterm or critically ill infants.

The IoT ecosystem in NICUs comprises various devices and technologies, all working synergistically to enhance neonatal care. Wearable sensors attached to neonates monitor physiological parameters such as heart rate variability, respiration patterns, and body temperature, illustrated in Figure 2. Environmental sensors ensure optimal NICU conditions by tracking ambient temperature, humidity, and noise levels, which are crucial for maintaining the neonates' fragile stability (Pigueiras-del-Real *et al.*, 2024). Smart devices such as infusion pumps, ventilators, and phototherapy units can also be integrated into the IoT network to provide automated adjustments based on real-time patient data. These interconnected devices create a comprehensive ecosystem that monitors and predicts potential health risks, ensuring timely interventions.

The adoption of IoT in NICU settings heralds a new era in neonatal care, combining technological innovation with clinical expertise to address the unique

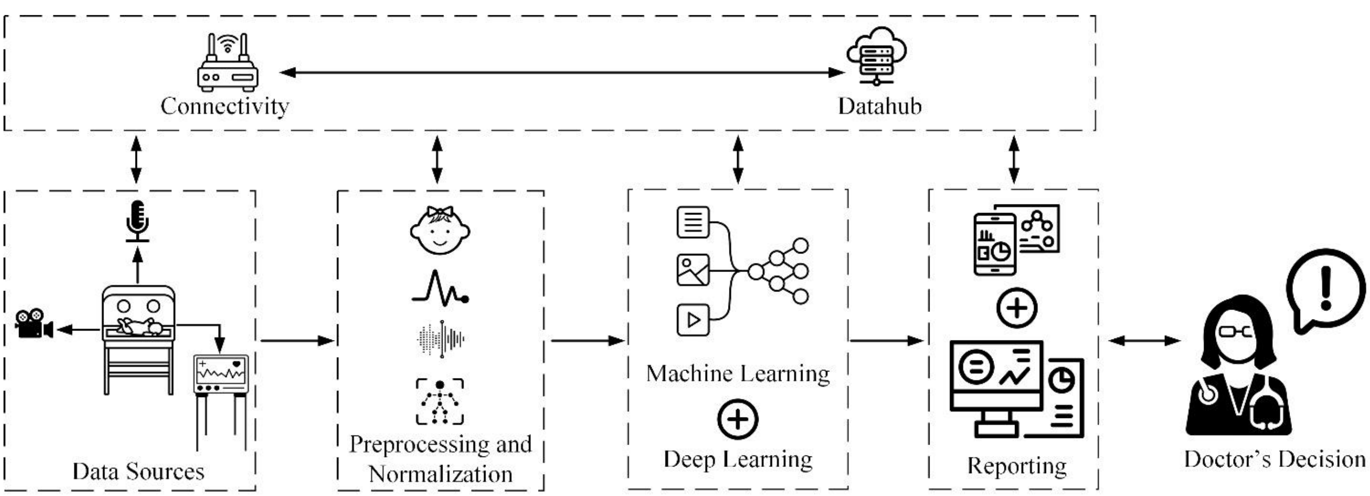

Figure 2 AI-enabled NICU workflow integrates multimodal data sources, preprocessing, machine learning, and decision-support systems to assist healthcare professionals in making informed clinical decisions.

challenges of caring for vulnerable neonates. By offering real-time, data-driven insights and streamlining clinical workflows, IoT has the potential to save lives, reduce caregiver fatigue, and pave the way for more personalized and proactive neonatal healthcare solutions.

4.1. IoT systems and devices in the NICU

The integration of IoT systems and devices in NICUs has revolutionized the way real-time clinical data is gathered, monitored, and utilized to ensure optimal care for premature and critically ill infants. These devices, specifically tailored for NICU environments, continuously monitor key clinical parameters, including temperature, heart rate, respiratory rate, and blood oxygen levels, providing healthcare professionals with actionable insights to improve neonatal outcomes. The deployment of IoT technologies in NICU workflows encompasses wearable sensors, smart incubators, and advanced contactless monitoring systems, each contributing uniquely to neonatal care.

Wearable and implantable sensors form the backbone of IoT applications in the NICU, enabling the continuous capture of critical physiological data without disturbing the infant. Examples of such devices include ECG patches for cardiac monitoring, temperature sensors for thermal regulation, and pulse oximeters for oxygen saturation measurement. These sensors are designed with high sensitivity and comfort in mind, ensuring that even the most delicate neonates can be monitored effectively. By providing uninterrupted data streams, these devices allow healthcare providers to detect abnormalities early, reducing the risk of adverse outcomes and minimizing the need for invasive procedures (Grooby *et al.*, 2023; Wilgocka *et al.*, 2023; Zhou *et al.*, 2024b).

Smart incubators represent a pivotal innovation in NICU environments, integrating IoT technologies to monitor and control crucial environmental factors such as temperature, humidity, and noise levels (Singh *et al.*, 2023; Jameel *et al.*, 2024). Built-in sensors within these incubators maintain a stable microenvironment that mimics the womb, promoting neonatal health and recovery. Temperature regulation is critical to avoid hypothermia or hyperthermia, while maintaining optimal humidity levels prevents dehydration and supports skin integrity. Noise control reduces stress and fosters proper neurological development. These incubators often feature data connectivity, allowing healthcare teams to remotely monitor and adjust settings in real-time, ensuring the infant remains in a consistently therapeutic environment.

Contactless monitoring technologies are emerging as a game-changer in NICU care, offering non-invasive solutions for tracking physiological parameters. (Singh *et al.*, 2023; Jameel *et al.*, 2024). Infrared thermography, for example, enables temperature monitoring without requiring skin contact, reducing the risk of infection and skin irritation. Video monitoring systems can track respiratory movements, while radar-based sensors measure vital signs like heart rate and respiration with remarkable precision. These systems provide a layer of convenience and safety, allowing clinicians to monitor neonates without physical disruption, which is particularly beneficial for extremely fragile infants. Furthermore, these advancements align with the growing emphasis on minimally invasive care practices, enhancing both patient comfort and clinical efficiency.

4.2. Data collection and management in IoT-enabled NICU systems

The implementation of IoT-enabled systems in NICUs generates vast amounts of real-time data, necessitating an advanced and reliable data management framework that prioritizes data security and patient privacy. The architecture for collecting, storing, processing, and retrieving data forms the backbone of these systems, enabling actionable insights for clinicians while ensuring compliance with regulatory standards such as HIPAA, GDPR, and local data protection laws (Madhusudhan & Pravisha, 2023; Qureshi *et al.*, 2024). This section examines the flow of data from acquisition to integration, emphasizing the technologies and processes that ensure efficient, secure, and privacy-preserving data management.

IoT devices deployed in NICUs continuously gather data from a variety of sources, including incubators, ventilators, wearable sensors, and physiological monitors (Grooby *et al.*, 2023; Wilgocka *et al.*, 2023; Zhou *et al.*, 2024b; Pigueiras-del-Real *et al.*, 2024; Pigueiras-del-Real *et al.*, 2024). These devices measure critical parameters such as temperature, respiratory rate, oxygen saturation, and environmental conditions like humidity and noise, contributing to a comprehensive, real-time health profile of neonates. The collected data streams are integrated into a secure, unified database, reducing information silos and enhancing clinical decision-making through consolidated insights (Singh *et al.*, 2023; Jameel *et al.*, 2024). Secure APIs and standardized communication protocols, such as HL7 and FHIR, facilitate seamless data interoperability while maintaining encryption standards to safeguard sensitive patient information (Du *et al.*, 2024).

The enormous volume of data generated in IoT-enabled NICUs requires robust, encrypted storage solutions to ensure accessibility and protection against unauthorized access. Cloud computing plays a central role by providing scalable, centralized storage with end-to-end encryption that allows healthcare teams to access patient data from secure interfaces (Khazaei *et al.*, 2015; Madhusudhan & Pravisha, 2023). However, to address latency concerns and minimize exposure to cyber threats, edge computing is increasingly employed, processing sensitive data locally on hospital servers or IoT gateways before transmitting only essential insights to the cloud. This hybrid cloud-edge model ensures that critical neonatal health data is processed in real-time while remaining secure against cyberattacks and unauthorized breaches (Du *et al.*, 2024).

Ensuring neonatal data privacy is paramount, requiring adherence to strict compliance frameworks. Data anonymization and pseudonymization techniques are implemented to safeguard personally identifiable information (PII) before storage or external analysis (Qureshi et al., 2024). Access controls, role-based permissions, and multi-factor authentication (MFA) further restrict data access to authorized medical personnel only, preventing unauthorized breaches (Abduhari *et al.*, 2025). Additionally, audit logs and blockchain-based verification systems can be integrated to enhance transparency, track data modifications, and ensure compliance with healthcare security standards (Das *et al.*, 2025).

Before data can be analyzed or utilized, it must undergo preprocessing to address noise, inconsistencies, and potential errors, ensuring accuracy and reliability in decision-making (Shah et al 2022a,b; Qureshi *et al.*, 2024). Preprocessing includes filtering noise from sensor data, normalizing values for consistency, and validating readings against standard clinical benchmarks. Advanced machine learning algorithms detect anomalies and flag suspicious data points, ensuring that medical decisions are based on high-quality, verifiable inputs (Mohammad, 2025).

By integrating secure data collection, encryption, real-time processing, and privacy-preserving mechanisms, IoT-enabled NICU systems enhance neonatal care while ensuring the highest data security and compliance standards. Ongoing security audits, AI-driven anomaly detection, and adherence to evolving regulatory requirements will further fortify patient data protection, fostering trust in AI-driven neonatal monitoring systems.

4.3. Benefits of IoT in enhancing neonatal care

The integration of IoT technologies in NICUs is transforming neonatal care, offering unprecedented opportunities to enhance patient outcomes, streamline workflows, and improve care quality. By utilizing real-time data and automation, IoT-enabled systems allow caregivers to detect health issues early, reduce manual workload, and predict patient trajectories with precision. This section explores the key benefits of IoT in neonatal care, focusing on automated monitoring, reduced administrative tasks, and the application of predictive analytics.

IoT technologies empower NICUs with continuous, automated monitoring systems that track critical parameters such as heart rate, respiratory rate, and blood oxygen levels in real time. This constant surveillance enables early detection of complications like apnea, bradycardia, or sepsis, which are common and potentially life-threatening in neonates (Joshi, 2019). IoT systems equipped with advanced algorithms can identify subtle deviations from normal patterns and alert healthcare providers before symptoms become critical. For example, in NICUs that implemented IoT-driven monitoring, studies have shown a marked improvement in early diagnosis and timely intervention, leading to better survival rates and reduced complications. Such systems also enhance caregivers' confidence in maintaining stable neonatal conditions, even during periods of high patient volume.

Traditionally, NICU staff spend significant time manually recording vital signs and other clinical parameters. IoT systems automate this process by continuously capturing, storing, and displaying data from sensors, monitors, and other connected devices. This automation not only eliminates the risk of human error associated with manual documentation but also frees up caregivers to focus on direct patient care activities such as comforting infants, communicating with families, and implementing treatment plans (Pigueiras-del-Real *et al.*, 2024). For instance, by integrating IoT systems, a NICU can reduce hours spent on routine administrative tasks, allowing nurses and physicians to dedicate more time to addressing the individualized needs of each infant.

IoT-enabled NICUs generate vast amounts of real-time data, which, when analyzed using predictive algorithms, can provide valuable insights into an infant's health trajectory. Predictive analytics can identify early warning signs of complications, such as infection or organ dysfunction, by analyzing subtle trends in physiological data (Varisco, 2023; Tan *et al.*, 2024). For example, by applying machine learning models to IoT data, clinicians can predict the likelihood of an infant developing sepsis hours before clinical symptoms appear, allowing for proactive treatment. Additionally, predictive tools can forecast developmental outcomes or potential long-term challenges, enabling more personalized and preventive approaches to care. These capabilities improve the quality of care and build trust and confidence among families, as healthcare providers can act swiftly and effectively based on data-driven predictions.

4.4. Challenges and limitations of IoT in NICU settings

While the integration of IoT technologies into NICUs offers transformative benefits, it also presents a range of challenges and limitations that can hinder widespread adoption. These challenges span financial, technical, and ethical domains, necessitating careful consideration and strategic solutions to ensure effective and secure implementation. This section discusses the primary barriers to adopting IoT systems in NICUs, focusing on costs, data security, interoperability, and network reliability.

The implementation of IoT systems in NICUs demands significant financial investments in both hardware and software. Advanced sensors, monitors, and IoT platforms that ensure real-time data collection and processing are costly to procure and install. In addition to the initial setup costs, ongoing expenses for system maintenance, upgrades, and technical support can place a considerable financial burden on healthcare institutions. Smaller or resource-constrained hospitals may find it particularly challenging to adopt these systems due to limited budgets, hindering equitable access to advanced neonatal care technologies. These cost considerations underline the need for scalable and cost-effective IoT solutions tailored to different healthcare settings.

One of the most critical challenges in IoT-enabled NICUs is ensuring the security and privacy of sensitive neonatal data. IoT systems involve complex networks with multiple devices transmitting real-time data, which increases the risk of cyberattacks, data breaches, and unauthorized access. This is especially concerning in NICUs, where patient data is highly sensitive and requires strict protection (Tresp *et al.*, 2016; Hudson, 2022). Regulatory frameworks such as the Health Insurance Portability and Accountability Act (HIPAA) in the United States and the General Data Protection Regulation (GDPR) in Europe mandate stringent compliance to safeguard data privacy (Annas, 2003; Rumbold & Pierscionek, 2017; Zaguir et al., 2024). However, meeting these regulations can be technically and financially demanding, requiring robust encryption protocols, secure authentication mechanisms, and continuous monitoring of IoT networks.

A significant technical challenge in adopting IoT in NICUs is the lack of interoperability among devices from different manufacturers. IoT devices often operate on proprietary protocols, creating difficulties in integrating them with existing hospital information systems (HIS) and legacy devices (Nan & Xu, 2023). This fragmentation can lead to data silos, inconsistent data formats, and inefficient workflows, limiting the full potential of IoT-enabled care. Standardized communication protocols and interfaces are essential to ensure seamless data transfer and interoperability between devices and systems. However, achieving standardization requires industry-wide collaboration and regulatory incentives, which remain ongoing challenges.

IoT devices in NICUs rely heavily on stable and reliable network connections to transmit real-time data continuously. Any disruption in connectivity or delays in data transmission can compromise the quality of care, particularly in critical situations where timely interventions are crucial. NICU environments, often characterized by a high density of medical equipment and electronic devices, can experience network congestion and interference, further exacerbating connectivity challenges (Shah *et al.*, 2022a). Hospitals must invest in robust network infrastructures, such as high-speed Wi-Fi and backup systems, to ensure uninterrupted data flow. Additionally, edge computing solutions can help mitigate latency issues by processing data locally and reducing reliance on external networks.

4.5. Ethical considerations in IoT for neonatal monitoring

The integration of IoT systems in neonatal monitoring introduces profound ethical questions surrounding data privacy, ownership, and the implications of automation in clinical decision-making. As these technologies become increasingly sophisticated, healthcare providers and policymakers must navigate the ethical responsibilities associated with their deployment. The unique vulnerabilities of neonatal patients, combined with the sensitive nature of their health data, underscore the need for a robust ethical framework that prioritizes transparency, accountability, and respect for patient rights. This section explores two key ethical considerations: informed consent and data ownership, and the balance between automation and human oversight.

One of the central ethical challenges in IoT-enabled neonatal monitoring is the issue of informed consent. Neonates, by their very nature, cannot provide consent for the collection and use of their health data, leaving this responsibility to their caregivers. This dynamic raises questions about data ownership and the rights of the infant as a patient. Caregivers must be fully informed about how their child's data will be collected, stored, and used, as well as the potential risks and benefits (Colom & Rohloff, 2018). However, the technical complexity of IoT systems often makes it difficult for caregivers to fully understand these processes, potentially compromising informed consent. Furthermore, ethical concerns arise regarding who truly "owns" the data whether it belongs to the healthcare provider, the institution, or the patient. Clear policies must be established to ensure that data is used solely for the benefit of the patient, with safeguards against misuse for commercial purposes or unauthorized sharing with third parties.

While IoT systems offer the potential for more efficient and accurate monitoring, they also raise ethical concerns regarding over-reliance on automation in clinical decision-making. Automated systems, driven by algorithms, may lack the ability to consider contextual factors, nuances, and the complexity of individual cases, which are often critical in neonatal care (Racine *et al.*, 2024). For instance, an IoT system might flag a vital sign anomaly that is a false positive or miss subtle but critical patterns that a seasoned clinician might notice.

One major concern is the impact of false positives incorrectly identifying a critical issue when none exists. In neonatal care, false positives can lead to unnecessary medical interventions, causing distress for both the infant and caregivers. Frequent false alarms may contribute to "alarm fatigue," a phenomenon in which healthcare providers become desensitized to alerts, increasing the risk of overlooking true emergencies. Additionally, false positives can subject neonates to unnecessary tests or treatments, such as unneeded antibiotic administration, which can disrupt gut microbiota (Rozé *et al.*, 2020) and contribute to antimicrobial resistance (Kronn, 2019; Mahdi et al., 2022).

Conversely, false negatives failing to detect a true medical issue pose a potentially greater risk. In neonates, conditions such as sepsis (Pace & Yanowitz, 2022), respiratory distress (Fang *et al.*, 2020), or hypoglycemia (LeBlanc *et al.*, 2018) can progress rapidly, and delayed detection may result in severe complications or mortality. An IoT system that misses subtle but critical patterns could fail to alert clinicians in time, leading to preventable adverse outcomes. False negatives are particularly dangerous because clinicians may place undue trust in technology, assuming that an absence of alerts equates to patient stability. This over-reliance on automated decision-making can erode clinical vigilance, reducing proactive assessments and timely interventions (Awhonn, 2020; Mahdi et al., 2022).

Beyond patient safety, these errors raise broader ethical issues, including the dehumanization of care and the erosion of clinical expertise. If IoT technologies are viewed as authoritative over human judgment, there is a risk of shifting responsibility from trained professionals to algorithms. This shift can compromise personalized care, as neonates require highly individualized treatment plans that consider factors beyond what an algorithm can quantify (Kamleh *et al.*, 2021).

In this way, AI can play a crucial role in improving neonatal monitoring by enhancing the accuracy and reliability of alerts, reducing false positives and negatives, and supporting clinical decision-making rather than replacing it. By integrating advanced machine learning models, real-time data analysis, and clinician-in-the-loop validation, AI can refine alarm systems to distinguish between true and false alerts, minimizing unnecessary interventions while ensuring timely responses to critical conditions. Additionally, AI-driven systems can incorporate predictive analytics to anticipate potential complications before they escalate, allowing proactive care strategies tailored to each neonate's condition. To fully harness AI's potential in NICU settings, it is imperative to develop robust frameworks for continuous learning, clinician oversight, and ethical integration, ensuring that AI enhances neonatal care without undermining the critical role of human expertise and judgment (Xu *et al.*, 2024; Jothi *et al.*, 2025).

5. AI in NICU

This section introduces the foundational methodologies, algorithms, and tools in AI and machine learning (ML) for neonatal care, with a focus on explainability techniques (Shah *et al.*, 2022a) to address transparency in decision-making. Aligned with the thesis objectives, this chapter explores a comprehensive framework integrating multimodal data, interpretable model design, and specialized approaches in image, signal, and motion analysis for neonatal care.

AI encompasses various techniques, including machine learning (ML), deep learning, and signal and image processing, each with unique roles in healthcare applications. By identifying and modeling patterns within vast datasets, AI has demonstrated success in tasks like disease detection, prognosis prediction, and anomaly recognition, even with minimal direct human oversight (Topol, 2019a). In the context of neonatal care, these techniques are applied to monitor physiological signals, analyze visual data, and interpret vocalizations, collectively enhancing the capability of predictive systems.

Machine Learning (ML) (Shah *et al.*, 2021) involves training algorithms on datasets to make predictions or identify patterns. Supervised learning, unsupervised learning, and reinforcement learning are commonly used approaches in healthcare, with supervised learning proving particularly useful in diagnosing and monitoring patients (Litjens *et al.*, 2017).

Deep Learning (DL), a subset of ML, utilizes neural networks with multiple layers to model complex patterns within large volumes of data. Deep learning architectures such as convolutional neural networks (CNNs) and recurrent neural networks (RNNs) have been highly effective in healthcare, especially for image recognition and time-series prediction tasks, respectively (Topol, 2019b).

Image Processing and Signal Processing techniques allow for the extraction and analysis of clinically relevant features from data sources like medical imaging and ECG signals (Obermeyer & Emanuel, 2016). Image processing is key in visual diagnostics, while signal processing plays a significant role in analyzing physiological data, enabling the monitoring and assessment of health parameters in real time.

The integration of these AI methodologies with domain-specific data (clinical, image, and signal data) enables the creation of models that can assess health risks, predict outcomes, and support clinical decisions across diverse healthcare applications, particularly in neonatal care, as illustrated in **Figure 3**. The application of AI in neonatal care spans multiple domains, including predictive modeling, image and signal processing, and decision support for clinical workflows. AI models are trained on diverse datasets comprising electronic health records, real-time physiological signals, and imaging data to detect anomalies and assess neonatal health risks. Deep learning techniques, particularly convolutional neural networks (CNNs) and recurrent neural networks (RNNs), have proven highly effective in processing medical images and time-series data, respectively. Furthermore, integrating AI-driven tools in NICUs enables automated monitoring, early warning systems for critical conditions, and improved treatment precision. However, despite these advancements, AI adoption in neonatal care faces challenges such as data standardization, model interpretability, and ethical concerns, necessitating the development of explainable AI frameworks to enhance clinical trust and usability.

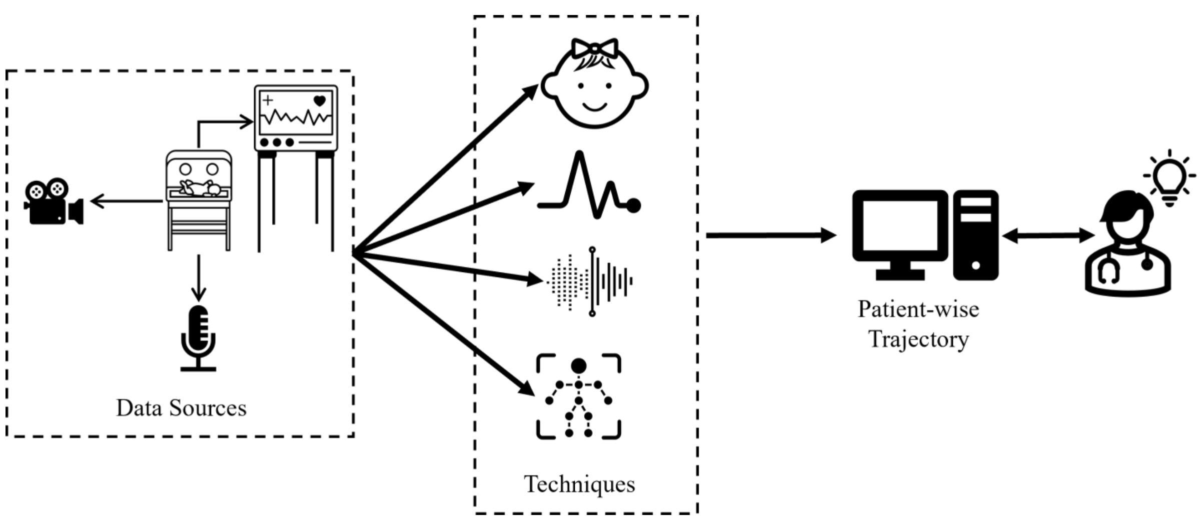

Figure 3 Illustrates integrating data sources and AI in neonatal care for clinical decision-making.

5.1. Image processing techniques in neonatal care

Image processing plays a crucial role in healthcare AI, allowing for the extraction of valuable information from visual data. In neonatal care, images from clinical imaging, facial recognition, and visual monitoring systems are processed to detect conditions associated with specific facial features or anatomical anomalies. Techniques in this field start with noise reduction, contrast enhancement, and normalization, which are essential for improving the quality of images before analysis (Russ, 2016). It is especially important for neonatal facial analysis, where small anatomical features need to be captured clearly.

Facial features and anatomical landmarks are detected through convolutional neural networks (CNNs) and other deep learning methods that can identify specific visual traits related to syndromic or developmental anomalies (Shah *et al.*, 2024). These traits provide early diagnostic insights. Image segmentation isolates regions of interest, like specific facial features, enabling more precise diagnosis (Shah *et al.*, 2021). Classification algorithms categorize images based on identified features, providing a basis for further analysis by healthcare professionals.

Zeng *et al.* (2024) introduces a non-contact video-based monitoring framework for measuring vital signs in preterm and critically ill neonates in the NICU, addressing the limitations of traditional contact-based methods. The research involved 50 preterm infants (average gestational age: 37.5 ± 2.6 weeks) and validated a framework that extracts heart rate (HR), respiratory rate (RR), heart rate variability (HRV), respiratory rate variability (RRV), and actigraphy using remote photoplethysmography (rPPG) and motion-based algorithms. The proposed system achieved HR and RR measurements within clinical acceptance range (±5 bpm), aligning with ANSI/AAMI EC13:2002 standards and NIH recommendations. It demonstrated high concordance with contact-based monitors, particularly for HRV and RRV features (R-value > 0.8), and outperformed ECG-derived actigraphy in classifying movement states. The research highlights AI-driven video monitoring as a scalable, non-invasive alternative for neonatal cardiorespiratory assessment, with future advancements focusing on higher-resolution cameras, improved movement differentiation, and AI-driven sleep staging and pain assessment.

Zhao *et al.* (2024) presents a deep learning-based framework for neonatal pain detection using facial expressions, addressing the limitations of subjective nurse-based assessments. Traditional neonatal pain scales, such as NIPS and N-PASS, rely heavily on clinical judgment, often leading to variability and delayed pain intervention. To overcome this, the proposed framework employs a transfer learning-based end-to-end pain detection neural network that efficiently detects pain events using a single camera, reducing the need for multimodal data collection and extensive computational resources. A manual assessment branch is integrated to handle borderline cases, improving trust and reliability in real-world clinical settings. Experimental results demonstrate that the framework outperforms state-of-the-art methods by at least 25% in accuracy, achieving 77.54% on the MNPAD dataset and 82.35% with manual assessment integration. The study highlights the potential for real-time, automated neonatal pain detection, enabling more timely and precise pain management in NICUs, with future research focused on multimodal classification, dataset expansion, and portable, edge-computable models for broader clinical adoption. The study includes neonates from 27 to 41 weeks gestational age as part of the MNPAD dataset, ensuring a diverse representation of neonatal pain responses.

Manworren *et al.*(2024) investigates the development of a machine learning (ML) model for pain classification in neonates, leveraging the Neonatal Facial Coding System (NFCS), the only observational tool associated with brain-based evidence of pain. Using video sequences from 49 term neonates undergoing heel lance, six experienced NICU nurses labeled pain-related facial expressions, providing a frame-level, nurse-informed dataset. The ML model was trained on these labeled frames and tested using Logistic Regression, Support Vector Machines (SVM), and Random Forest classifiers. Results showed that the best-performing model, a Random Forest classifier, achieved 98% accuracy, 97.7% precision, and 98.5% recall, significantly surpassing NICU nurses' interrater reliability (68%) and AUC (0.68). The most critical pain features identified were lowered brows, closed eyes, and deepened nasolabial furrow, which were difficult to detect in real-time assessments. Unlike traditional observational pain scales, which are inconsistent and prone to subjectivity, the proposed Pain Recognition Automated Monitoring System (PRAMS) offers continuous, automated, and unbiased pain detection. These findings highlight ML's potential in enhancing neonatal pain assessment, enabling timely interventions and reducing the risks of under- or overtreatment associated with current nurse-dependent methods.

5.2. *Signal processing for neonatal health monitoring*

Signal processing is integral to analyzing physiological signals, such as ECG, EEG, and vocal signals, in neonatal care (Olmi *et al.*, 2021; Variane *et al.*, 2022). These signals provide real-time data on vital functions, offering insights into neonates' cardiovascular, respiratory, and neurological health.
Given the high sensitivity of neonatal physiological data, preprocessing steps like noise reduction, filtering, and artifact removal are critical (Sweeney et al, 2012; Rahman *et al.*, 2024). Techniques such as wavelet transforms, Fourier analysis and smoothing filters are applied to enhance signal quality. Signal processing methods capture informative features such as heart rate variability, amplitude, and frequency bands from ECG or EEG signals (Shah *et al.*, 2022; Gentile *et al.*, 2023; Sharma & Meena, 2024). These features are essential in assessing health risks like arrhythmia or potential neurological delays. Time-series analysis techniques, such as long short-term memory (LSTM) networks (Hochreiter, 1997), are used to identify temporal patterns in sequential data, which is particularly useful for understanding developmental trends over time (Abotaleb & Dutta, 2024).

Vaishnavi *et al.* (2024) introduce a novel deep learning framework, EHO-DCGR net, for classifying cry signals from premature infants to support early health monitoring. The approach integrates Mel-Frequency Cepstral Coefficients (MFCC), Power Normalized Cepstral Coefficients (PNCC), Bark-Frequency Cepstral Coefficients (BFCC), and Linear Prediction Cepstral Coefficients (LPCC) to extract key features from infant cries. These features are optimized using the bio-inspired Elephant Herding Optimization (EHO) algorithm, which selects the most relevant attributes for classification. The Deep Convolutional Gated Recurrent Neural Network (DCGR net) then categorizes cry signals into five types—eair, neh, eh, heh, and owh—associated with different infant needs and potential health issues. Experimental results demonstrate that EHO-DCGR net achieves an impressive 98.45% classification accuracy, surpassing existing deep learning models such as MFCC-SVM, DFFNN, SVM-RBF, and SGDM. The proposed model also outperforms traditional CNN and RNN architectures, including AlexNet, DenseNet, LSTM, and GRU, by improving accuracy by up to 12.64%. These findings highlight the efficacy of EHO-DCGR net in precise, non-invasive cry-based health monitoring, with potential applications in neonatal care and early detection of pathological crying patterns. Future research will explore hybrid models and advanced optimization techniques to further enhance classification accuracy and robustness.

Shayegh & Tadj (2025) explores the potential of newborn cry analysis as a non-invasive biomarker for detecting sepsis and respiratory distress syndrome (RDS) in neonates, particularly in resource-limited settings where advanced diagnostic tools are scarce. The research utilized expiratory cry segments from newborns aged 1 to 53 days, employing self-supervised learning (SSL) models—wav2vec 2.0, WavLM, and HuBERT—to extract deep audio features directly from raw cry signals without manual feature engineering. A classifier layer was placed atop these SSL models to categorize newborns into Healthy, Sepsis, or RDS groups, with model fine-tuning performed using linear and annealing learning rate strategies. Results demonstrated that the annealing learning rate consistently outperformed the linear strategy, with wav2vec 2.0 achieving the highest classification accuracy of 89.76%. Among the models, wav2vec 2.0 showed the strongest balance across all conditions, while WavLM excelled in detecting healthy cases, and HuBERT exhibited consistent but slightly lower performance. However, Sepsis detection remained challenging, primarily due to shorter cry durations and complex acoustic variations associated with the condition. These findings highlight the potential for Newborn Cry Diagnosis Systems (NCDSs) to assist clinicians in early disease detection, enabling timely interventions and improved neonatal outcomes, especially in low-resource clinical environments where access to traditional diagnostic tools is limited.

Xiao & Luo(2024) examined the clinical effects of music therapy (MT) on premature infants in neonatal intensive care units (NICUs), focusing on its impact on physiological stability, parent-child attachment, and neurological function. The study included 152 preterm infants, with 78 in the reference group (admitted between January 2021 and January 2022) receiving routine management and 74 in the observation group (admitted between February 2022 and February 2023) receiving MT in addition to standard care. The gestational age of the infants ranged from 31 to 35 weeks. The study assessed brain function using amplitude-integrated electroencephalogram (aEEG), neonatal behavioral neurological assessment (NBNA) scores, and parent-child attachment through the pictorial representation of attachment measure (PRAM). Results indicated no significant differences between the groups in aEEG and NBNA scores ($P > 0.05$), suggesting that MT did not directly enhance neurological development. However, the observation group had a significantly lower PRAM self-baby-distance ($P < 0.05$), indicating improved parent-child bonding. Additionally, pulse and respiratory rate (RR) were significantly lower in the observation group ($P < 0.05$), demonstrating a stabilizing effect on vital signs. MT also reduced the number and duration of crying episodes in premature infants ($P < 0.05$), further supporting its role in improving comfort and emotional regulation. However, no significant differences were observed in temperature or the incidence of complications ($P > 0.05$) between the two groups. The findings suggest that MT is a valuable, non-invasive intervention in NICU settings, particularly for enhancing physiological stability and parent-child attachment, though further research is needed to confirm its long-term benefits on neurodevelopment.

Signal analysis can be extended to vocalizations, where features like pitch, volume, and frequency provide clues to a neonate's state, such as distress or comfort. These features, once extracted, can feed into predictive models to help healthcare providers proactively manage neonatal health risks.

5.3. Machine learning algorithms for health-care predictions

Various machine learning algorithms are applied to neonatal health predictions, each selected based on suitability for different types of data (e.g., image, signal, or tabular data). In this section, the emphasis is on model choices that balance predictive power with interpretability.

Supervised learning algorithms, such as support vector machines (SVMs), decision trees, and ensemble methods (e.g., random forests), are commonly used in neonatal health monitoring due to their ability to predict discrete health outcomes (Shah *et al.*, 2024a). These models learn from labeled data to predict conditions like respiratory distress, jaundice, or sepsis in neonates.

Deep learning models, especially convolutional neural networks (CNNs) and recurrent neural networks (RNNs), are instrumental for processing high-dimensional data such as images and time-series signals (Bairouk, 2023; Galić *et al.*, 2025). CNNs excel in image-based tasks, while RNNs are suited for sequential data, making them ideal for processing ECG data. The models provide high accuracy in prediction tasks, though they often require explainability tools to interpret complex decision pathways.

Jenkinson et al. (2024) presents a narrative review of 11 studies utilizing AI to predict extubation outcomes in preterm neonates. Reported AUC values ranged from 0.7 to 0.87, indicating moderate to high predictive performance, though only two studies conducted external validation, highlighting the need for further research to confirm model generalizability. The patient population consisted of prematurely born infants requiring mechanical ventilation in NICUs, with an average gestational age of 28.12 weeks. The AI methodologies varied and included logistic regression (MLR), decision trees (DT), random forest (RF), gradient boosting machines (GBM), support vector machines (SVM), and artificial neural networks (ANN). The models utilized diverse input features, including birth weight, gestational age, oxygen saturation (SpO_2), and fraction of inspired oxygen (FiO_2), to predict extubation failure and the likelihood of reintubation. While AI has demonstrated potential in improving extubation success predictions, the review emphasizes the necessity of external validation, standardization of input variables, and comparison with traditional clinical predictors to establish efficacy, reliability, and real-world applicability in NICU settings. Future research should address biases in training datasets, enhance model interpretability, and integrate AI tools into clinical workflows to support clinical decision-making while maintaining patient safety.

Tashakkori et al. (2024) utilize machine learning (ML) techniques to predict NICU admission and identify key influencing factors based on a real-world dataset of pregnant women. The research categorizes predictive features into four groups—demographic, pregnancy, neonatal, and delivery factors—to analyze their impact on NICU admission. Six ML models were employed, including Support Vector Machine (SVM), Decision Tree (DT), Gaussian Process (GP), Multilayer Perceptron (MLP), Random Forest (RF), and Bagging, with model ranking performed using the TOPSIS method. The findings reveal that neonatal factors (accuracy: 0.96, AUC: 0.96) are the most predictive for NICU admission, followed by pregnancy and delivery factors (accuracy: 0.91). The study also identifies Bagging as the best model for demographic and pregnancy factors, RF for neonatal factors, DT for delivery factors, and SVM for complete case analysis. By offering early prediction of high-risk neonates, the results can aid healthcare providers in resource allocation, preventive interventions, and improved neonatal outcomes. No specific neonatal age is mentioned in the study.

Ensuring that AI models are interpretable in neonatal care is essential for clinical acceptance. Explainability tools like SHAP (SHapley Additive exPlanations) (Lundberg & Lee, 2017), LIME (Local Interpretable Model-Agnostic Explanations) (Ribeiro et al., 2016), and Grad-CAM (Gradient-weighted Class Activation Map) (Selvaraju *et al.*, 2020) help clinicians understand model outputs, offering transparency and insights into feature importance. These tools enable clinicians to evaluate predictions based on individual patient characteristics, making the AI-driven recommendations more actionable.

5.4. Explainability in clinical AI models

Incorporating AI in clinical decision-making requires that these models not only perform accurately but also offer interpretability. Unlike traditional models, modern deep learning algorithms often operate as "black boxes," making it challenging to understand how inputs influence outputs, as shown in Figure 4. In neonatal care, where clinical decisions are high-stakes, it is essential for AI models to justify their predictions in an interpretable manner (Shah *et al.*, 2024). This need is met through explainable AI (XAI) tools, which translate complex model outputs into insights that clinicians can readily understand, thereby fostering trust and ensuring accountability in clinical settings.

The explainability techniques explored here SHAP, LIME, and Grad-CAM address different aspects of model interpretation:

* SHAP (SHapley Additive exPlanations): SHAP (Lundberg and Lee, 2017) offers a method grounded in game theory to quantify the contribution of each feature in a model's decision-making process. This technique assigns a "Shapley value" to each feature, representing its impact on a specific prediction. The primary strength of SHAP lies in its global interpretability; it provides clinicians with an aggregated view of how individual features, such as heart rate variability or oxygen saturation, influence outcomes across multiple predictions. In neonatal care, SHAP can be particularly useful in analyzing complex time-series data or clinical indicators, offering clinicians a clear view of which features contribute most to the predicted outcomes. This information can assist in refining treatment approaches, as clinicians understand which physiological factors are driving specific health predictions, such as risk levels for hypoxemia or sepsis.
* LIME (Local Interpretable Model-Agnostic Explanations): LIME (Ribeiro et al., 2016) is a local interpretation tool that offers instance-based explanations by creating surrogate models to approximate the behavior of complex AI models around specific predictions. Unlike SHAP, LIME provides insights at a granular level, making it possible for clinicians to interpret individual model predictions on a case-by-case basis. In neonatal healthcare, LIME's ability to focus on specific predictions allows clinicians to analyze each neonate's unique circumstances, such as risk levels for specific complications. This local explainability is especially beneficial for precision medicine, as clinicians can gain detailed insight into how specific risk factors or recent physiological changes contributed to a prediction.

* Grad-CAM (Gradient-weighted Class Activation Mapping): Grad-CAM (Selvaraju *et al.*, 2020) is a visualization-based interpretability tool primarily used in convolutional neural networks (CNNs) for image data. Grad-CAM provides spatial interpretability by creating heat maps that highlight regions in an image that influence model predictions. Grad-CAM is invaluable in image-based analysis, such as detecting facial anomalies in neonates that may indicate underlying syndromic conditions. By highlighting areas of the face that influence predictions, clinicians gain an intuitive understanding of the model's focus, which can enhance the accuracy of visual diagnostics and support early intervention.

Together, they provide a multi-faceted view that allows clinicians to assess model behavior globally (across many predictions) and locally (in individual cases). This level of transparency helps ensure that AI-based recommendations align with clinical observations, making the insights more actionable.

6. Multimodal AI tools integration for neonatal health monitoring

Integrating specialized AI tools designed for clinical, ECG, facial, vocal, and motion data within a unified analytical framework offers a comprehensive and innovative approach to neonatal health prediction.

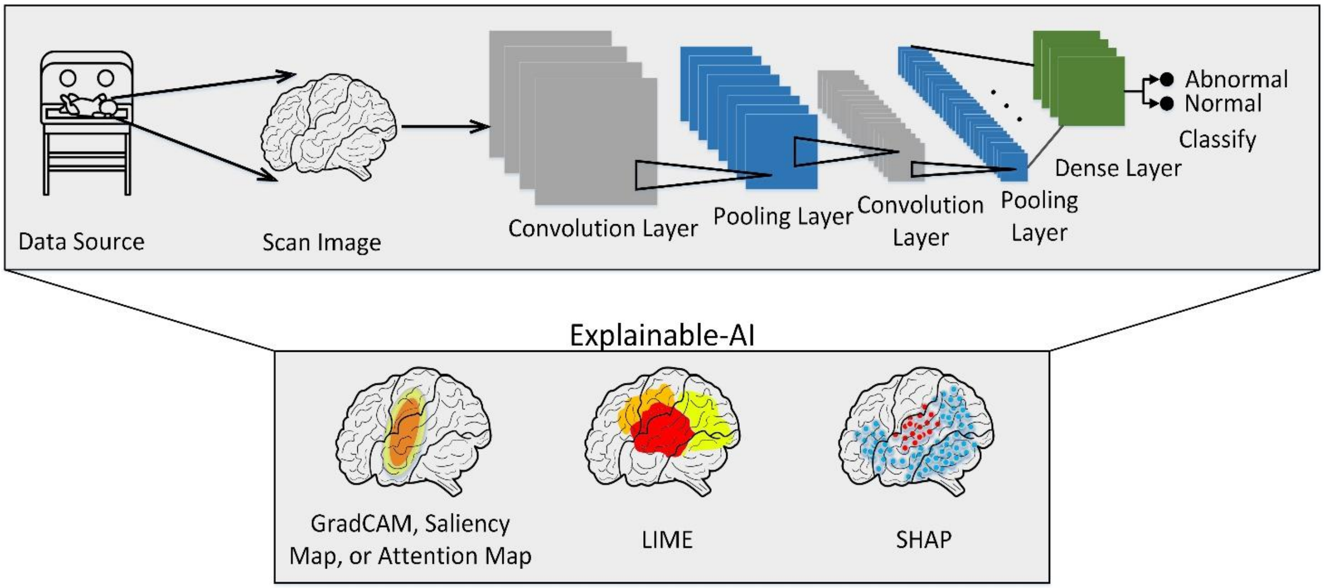

Figure 4 Illustration of a Convolutional Neural Network (CNN) pipeline with an example application for neonatal neurodevelopment. The model processes input images through convolutional and pooling layers to extract features, followed by a fully connected layer for classification tasks (e.g., autism spectrum disorder (Wang *et al.*, 2023)). Explainable AI techniques, including GradCAM, LIME, and SHAP, provide visual interpretations by highlighting critical areas within the image contributing to the model's decision-making, enhancing transparency and clinical trustworthiness.

Each modality-specific AI tool provides unique insights into neonatal well-being: ECG-based models analyze cardiac health, vocal analysis detects stress or pain through cry recognition, motion-based AI tools analysis identifies syndromic features and distress signals. By combining the strengths of these AI tools, evaluate neurodevelopmental progress, and facial the framework enables a holistic understanding of neonatal health, improving prediction accuracy and supporting timely clinical interventions.

The integration of multimodal AI tools leverages advanced fusion techniques, including early, late, and hybrid fusion, to ensure the effective combination of outputs from diverse data modalities. Early fusion involves integrating raw data inputs from various modalities, enabling models to learn cross-modality patterns from the outset. Late fusion merges high-level feature representations generated by individual modality-specific models, focusing on synthesizing insights at a decision-making level. Hybrid fusion combines both approaches, allowing the framework to capture complex interactions and dependencies across modalities (Shah *et al.*, 2023). These strategies ensure that the multimodal framework maximizes the predictive value of each AI tool while maintaining robustness and flexibility in handling complex neonatal data.

Integrating multimodal AI tools presents several challenges, including differences in data formats, temporal misalignments, and noise characteristics across modalities. Effective strategies, such as domain-specific feature engineering, data standardization, and alignment techniques, are employed to address these issues. Advanced preprocessing methods harmonize the inputs, ensuring compatibility and reducing noise, while temporal alignment techniques synchronize data streams for meaningful analysis. These efforts are critical to enhancing the performance and reliability of the multimodal AI framework in clinical scenarios, enabling more accurate, interpretable, and actionable predictions in neonatal health monitoring (Zhou *et al.*, 2024; Shah *et al.*, 2024).

Considering integration, Mukai et al. (2021) presents an automated sleep-wake state classification system for newborns using only body and face videos, eliminating the need for intrusive devices like EEG. Given that premature neonates in NICUs are exposed to excessive light and noise, affecting their circadian rhythms and sleep quality, the authors propose a 3D Convolutional Neural Network (3D CNN)-based method to classify sleep states based on Brazelton's criteria. The study evaluates different approaches, including whole-body video, face-only video, and a fusion of both with time-series smoothing and probability weighting. Experiments conducted on 16 videos of eight newborns (all younger than 37 weeks gestation) showed that integrating whole-body and face-only classification with probability weighting achieved the highest accuracy of 61.1% and a kappa score of 0.623, demonstrating the effectiveness of combining spatial and temporal features. The proposed method outperforms traditional optical flow-based classification. It provides a non-invasive, scalable solution for neonatal sleep-wake monitoring, with future improvements focusing on enhanced feature integration and larger datasets for increased accuracy and robustness.

7. Ensuring accuracy and accountability in AI-driven neonatal care

To mitigate the risks associated with AI misdiagnoses in neonatal care, it is crucial to establish clear protocols for physician intervention, continuous evaluation, and system improvement. When an AI system makes an incorrect diagnosis, clinicians must have predefined response mechanisms, including immediate clinical reassessment, verification through traditional diagnostic methods, and multi-disciplinary consultations to confirm or refute AI-generated predictions. AI should serve as a decision-support tool rather than a sole authority, with human oversight remaining central to patient care (Mitra & Rehman, 2025).

A continuous learning framework must be implemented to enhance the reliability and accuracy of AI-driven clinical decision support systems (CDSS). This includes regular system audits, retrospective analyses of AI-generated recommendations, and real-time feedback loops where clinicians report misclassifications for model refinement. Moreover, AI models should undergo ongoing validation with diverse datasets, ensuring they adapt to varying neonatal conditions, demographic differences, and evolving medical knowledge. Incorporating explainable AI (XAI) techniques can further aid clinicians in understanding AI decisions, allowing them to identify potential biases, errors, or limitations in predictions (Ratta et al., 2025).

AI implementation in NICU settings must follow a dynamic, self-improving approach where errors are systematically reviewed, flagged, and corrected. By integrating clinician feedback, periodic recalibration, and regulatory compliance, AI can become a more reliable partner in neonatal care, enhancing accuracy and trust in automated systems while maintaining the highest patient safety and care quality.

8. Conclusion

Integrating AI and IoT into neonatal care presents a paradigm shift in early detection, continuous monitoring, and clinical decision-making for preterm infants. While NICUs have improved survival rates, AI-driven predictive analytics and IoT-enabled monitoring systems provide an additional layer of precision and efficiency in neonatal healthcare. Machine learning models process multimodal data to identify early warning signs, allowing timely interventions that significantly improve long-term neurodevelopmental outcomes. However, challenges such as data privacy, interoperability, and AI interpretability must be addressed to ensure widespread adoption. Explainability tools are vital in making AI-driven decisions transparent and actionable for clinicians. Moving forward, developing robust, multimodal AI frameworks will be crucial in advancing neonatal care, ultimately enhancing the quality of life for preterm infants through proactive and personalized healthcare solutions.

Conflict of Interest Statement

The authors declare no conflict of interest.

Funding

The present research work has been developed as part of the PARENT and GALATEA projects, funded by the European Union's Horizon 2020 research and innovation program under the Marie Sklodowska-Curie-Innovative Training Network 2020, Grant Agreement N° 956394 (https://parenth2020.com/) and Grant Agreement N° 101183057 (https://cordis.europa.eu/project/id/101183057).

References

Abbasi, H., Mollet, S.R., Williams, S.A., Lim, L. & Battin, M.R. *et al.* (2023) Deep-learning for automated markerless tracking of infants' general movements. *International Journal of Information Technology* **15**, 4073–4083.

Abduhari, E.S., Shaik, T.C., Adidul, A.B., Ladja, J.H. & Saliddin, E.S. *et al.* (2025) Access control mechanisms and their role in preventing unauthorized data access: A comparative analysis of RBAC, MFA, and strong passwords. *Natural Sciences Engineering and Technology Journal* **5**, 418–430.

Abotaleb, M. & Dutta, P.K. (2024) Optimizing long short-term memory networks for univariate time series forecasting: a comprehensive guide. In, *Hybrid Information Systems: Non-Linear Optimization Strategies with Artificial Intelligence*. Ramakant Bhardwaj , Pushan Kumar Dutta , Pethuru Raj , Abhishek Kumar , Kavita

Saini , Alfonso González Briones and Mohammed K.A. Kaabar (Eds.) De Gruyter , Berlin.

Al-Beltagi, M., Saeed, N.K. & Bediwy, A.S. (2024) Pulse oximetry in pediatric care: Balancing advantages and limitations. *World Journal of Clinical Pediatrics* **13**, 96950.

Alharbe, N. & Almalki, M. (2024) IoT-enabled healthcare transformation leveraging deep learning for advanced patient monitoring and diagnosis. *Multimedia Tools and Applications* (in press)

Alhumaid, S., Alabdulqader, M., Al Alawi, Z., Al Ghamdi, M.A. & Alabdulmuhsin, M.A. *et al.* (2024) Clinical characteristics and outcomes of SARS-CoV-2 infection in neonates with persistent pulmonary hypertension of the newborn (PPHN): A Systematic Review. *Children* **11**, 1305.

Anef, C.K. (2019) *Comprehensive Neonatal Nursing Care.* Springer Publishing Company, New Jersery.

Annas, G.J. (2003) HIPAA Regulations — A New Era of Medical-Record Privacy? *New England Journal of Medicine* **348**, 1486–1490.

Atzori, L., Iera, A. & Morabito, G. (2010) The Internet of Things: A survey. *Computer Networks* **54**, 2787–2805.

Awhonn (2020) *Core Curriculum for Neonatal Intensive Care Nursing E-Book*. Elsevier Health Sciences.Amsterdam.

Back, S.A. & Miller, S.P. (2014) Brain injury in premature neonates: A primary cerebral dysmaturation disorder? *Annals of Neurology* **75**, 469–486.

Bairouk, A. (2023) *Astronomical Image Time-series Classification Using Deep Learning*. PhD thesis. Université de Montpellier, France.

Basu, S.K., Pradhan, S. & du Plessis, A.J. (2021) GABA and glutamate in the preterm neonatal brain: In-vivo measurement by magnetic resonance spectroscopy. *NeuroImage* **238**, 118215.

Behrman, R.E., Butler, A.S. & Outcomes, I. (2007) Mortality and acute complications in preterm infants. In, *Preterm Birth: Causes, Consequences, and Prevention*. Richard E. Behrman & Adrienne Stith Butler, (Eds.). National Academies Press, Washington D.C.

Blackburn, S.T. (2017) *Maternal, Fetal, and Neonatal Physiology: A Clinical Perspective*. Elsevier Health Sciences, Amsterdam.

Blencowe, H., Cousens, S., Chou, D., Oestergaard, M. & Say, L. *et al.* (2013) Born too soon: The global epidemiology of 15 million preterm births. *Reproductive Health* **10**, S2.

Bourque, S.L., Murthy, K., Grover, T.R., Berman, L. & Riddle, S. (2024) Cutting into the NICU: Improvements in outcomes for neonates with surgical conditions. *NeoReviews* **25**, e634–e647.

Brett, C. & Robinowitz, D. (2023) Physiology and development of the term and preterm neonate. In J. Lerman (ed.) *Neonatal Anesthesia*. Cham: Springer International Publishing, Switzerland.

Bulut, Ö., Kahraman, K. & Uçar, Ç. (2022) Assessment of cases admitted to the neonatal intensive care unit with lower respiratory tract infection. *Kocatepe Tıp Dergisi* **23**, 75–81.

Cainelli, E., Arrigoni, F. & Vedovelli, L. (2020) White matter injury and neurodevelopmental disabilities: A cross-disease (dis)connection. *Progress in Neurobiology* **193**, 101845.

Cay, G., Ravichandran, V., Saikia, M.J., Hoffman, L. & Laptook, A. *et al.* (2022) An e-textile respiration sensing system for NICU monitoring: design and validation. *Journal of Signal Processing Systems* **94**, 543–557.

Chandrasekaran, A., Amboiram, P., Balakrishnan, U., Abiramalatha, T. & Rao, G. *et al.* (2021) Disposable low-cost cardboard incubator for thermoregulation of stable preterm infant – a randomized controlled non-inferiority trial. *eClinicalMedicine* **31**, 100664.

Colom, M. & Rohloff, P. (2018) Cultural considerations for informed consent in paediatric research in low/middle-income countries: a scoping review. *BMJ Paediatrics Open* **2**, e000298.

Das, S.R., Jhanjhi, N.Z. & Asirvatham, D. (2025) Securing AI-based healthcare systems using blockchain technology. In, *AI Techniques for Securing Medical and Business Practices*. IGI Global Scientific Publishing. Hershey, PA.

De Paula Fiod Costa, H. & De Paula Fiod Costa, E. (2022) Neonatal complications of prematurity. In, R.A. Moreira de Sá and E.B. da Fonseca (eds) *Perinatology: Evidence-Based Best Practices in Perinatal Medicine*. Cham, Springer International Publishing.

Du, Y.-C., Chen, P.-F., Ciou, W.-S., Lin, T.-W. & Hsu, T.-C. (2024) An IoT-based contactless neonatal respiratory monitoring system for neonatal care assistance in postpartum center. *Internet of Things* **28**, 101371.

Dubois, J., Alison, M., Counsell, S.J., Hertz-Pannier, L. & Hüppi, P.S. *et al.* (2020) MRI of the neonatal brain: A review of methodological challenges and neuroscientific advances. *Journal of Magnetic Resonance Imaging* **53**, 1318–1343.

Fang, J.L., Mara, K.C., Weaver, A.L., Clark, R.H. & Carey, W.A. (2020) Outcomes of outborn extremely preterm neonates admitted to a NICU with respiratory distress.

Archives of Disease in Childhood - Fetal and Neonatal Edition **105**, 33–40.

Fenn-Moltu, S., Fitzgibbon, S.P., Ciarrusta, J., Eyre, M. & Cordero-Grande, L. *et al.* (2022) Development of neonatal brain functional centrality and alterations associated with preterm birth. *Cerebral Cortex* **33**, 5585–5596.

Galić, I., Habijan, M., Leventić, H. & Romić, K. (2025) Machine learning empowering personalized medicine: a comprehensive review of medical image analysis methods. *Electronics* **12**, 4411.

Gamarra-Oca, L.F. de, Ojeda, N., Gómez-Gastiasoro, A., Peña, J. & Ibarretxe-Bilbao, N. *et al.* (2021) Long-term neurodevelopmental outcomes after moderate and late preterm birth: a systematic review. *The Journal of Pediatrics* **237**, 168-176.e11.

Gandhimathi Alias Usha, S. & Bharathi, K. (2024) AI-powered vigilance in neonatal vital signs monitoring for optimal health care. In, *Modernizing Maternal Care With Digital Technologies*. IGI Global Scientific Publishing. Hershey,PA.

Gentile, F.R., Shah, S.T.H., Sperti, M., Panagiotopoulos, K. & Primi, R. *et al.* (2023) An innovative medical decision support tool for neurological outcome prediction from post-resuscitation electrocardiograms (MILESTONE). *European Heart Journal*, **44**, ehad655.650.

Goldenberg, R.L., Culhane, J.F., Iams, J.D. & Romero, R. *et al.* (2008) Epidemiology and causes of preterm birth. *The Lancet* **371**, 75–84.

Goodman, D.C., Stuchlik, P., Ganduglia-Cazaban, C., Tyson, J.E. & Leyenaar, J. *et al.* (2024) Hospital-Level NICU capacity, utilization, and 30-Day outcomes in Texas. *JAMA Network Open* **7**, e2355982.

Grooby, E., Sitaula, C., Chang Kwok, T., Sharkey, D. & Marzbanrad, F. *et al.* (2023) Artificial intelligence-driven wearable technologies for neonatal cardiorespiratory monitoring: Part 1 wearable technology. *Pediatric Research* **93**, 413–425.

Grunau, R.E. (2013) Neonatal pain in very preterm infants: long-term effects on brain. neurodevelopment and pain reactivity. *Rambam Maimonides Medical Journal* **4**, e0025.

Gupta, N., Bruschettini, M. & Chawla, D. (2021) Fluid restriction in the management of transient tachypnea of the newborn. *Cochrane Database of Systematic Reviews* **2**, CD011466.

Heuvel, M.P. van den, Kersbergen, K.J., Reus, M.A. de, Keunen, K. & Kahn, R.S. *et al.* (2014) Neonatal connectome during preterm brain development. *Cerebral Cortex* **25**, 3000–3013.

Hochreiter, S. (1997) *Long Short-term Memory*, *Neural Computation*. MIT Press, Cambridge, MA.

Hodson, W.A. (2018) 29 - Temperature Regulation. In, C.A. Gleason and S.E. Juul (eds) *Avery's Diseases of the Newborn (Tenth Edition)*. Philadelphia: Elsevier, pp. 361-367.e1.

Hong, J. & Rha, D. (2023) The long-term outcome and rehabilitative approach of intraventricular hemorrhage at preterm birth. *Journal of Korean Neurosurgical Society* **66**, 289–297.

Honnorat, M., Plaisant, F., Serret-Larmande, A., Claris, O. & Butin, M. (2023) Neurodevelopmental outcome at two years for preterm infants with Intraventricular hemorrhage: A case-control study. *Pediatric Neurology* **141**,52–57.

Hudson, F.D. (2022) How can we trust in IoT? The role of engineers in ensuring trust in the clinical IoT ecosystem. In, *Women Securing the Future with TIPPSS for Connected Healthcare*. Florence D. Hudson (Ed.) Springer, Cham, Switzerland.

Islam, S.M.R., Kwak, D., Kabir, M.D.H., Hossain, M. & Kwak, K.-S. (2015) The Internet of Things for health care: a comprehensive survey. *IEEE Access* **3**, 678–708.

Jameel, H.F., Shaalan, H.T., Munghr, A.S., Hamzah, M.M. & Oleiwi, F.M. (2024) Investigation smart infant incubator with multi-sensors control system. *Journal of Biomedical Engineering and Technology* **11,** 1-7.

Jenkinson, A.C., Dassios, T. & Greenough, A. (2024) Artificial intelligence in the NICU to predict extubation success in prematurely born infants. *Journal of Perinatal Medicine*, **52**, 119–125.

Jobe, A.H. & Ikegami, M. (2000) Lung development and function in preterm infants in the surfactant treatment era. *Annual Review of Physiology* **62**, 825–846.

Jois, R.S. (2019) Understanding long-term neurodevelopmental outcomes of very and extremely preterm infants: A clinical review. *Australian Journal of General Practice* **48**, 26-32.

Joshi, R. (2019) *Towards automated solutions for predictive monitoring of neonates*. Phd Thesis 1 (Research TU/e / Graduation TU/e). Technische Universiteit Eindhoven, The Netherlands.

Jothi, C.S., Starlin, M.A., Kiruba, R.R., Surya, E. & Jeevanasree, P. *et al.* (2025) Revolutionizing healthcare through robotics and AI integration: a comprehensive approach. In, *Exploring the Micro World of Robotics Through Insect Robots*. IGI Global Scientific Publishing, Hershey, PA.

K, A., Vincent, P.M.D.R., Srinivasan, K., Chang, C.-Y. (2021) Deep learning assisted neonatal cry classification via support vector machine models. *Frontiers in Public Health* **9**, 670352.

Kamleh, M., Williamson, J.M., Casas, K., Mohamed, M. (2021) Reduction in newborn screening false positive results following a new collection protocol: a quality improvement project. *The Journal of Pediatric Pharmacology and Therapeutics* **26**, 723–727.

Karnati, S., Kollikonda, S. & Abu-Shaweesh, J. (2020) Late preterm infants – changing trends and continuing challenges - ClinicalKey **7**, 36–44.

Khanam, F.-T.-Z., Perera, A.G., Al-Naji, A., Gibson, K., Chahl, J. (2021) Non-contact automatic vital signs monitoring of infants in a neonatal intensive care unit based on neural networks. *Journal of Imaging* **7**, 122.

Kharrat, A. & Jain, A. (2022) Hemodynamic dysfunction in neonatal sepsis. *Pediatric Research* **91**, 413–424.

Khazaei, H., McGregor, C., Eklund, J.M., El-Khatib, K. (2015) Real-time and retrospective health-analytics-as-a-service: a novel framework. *JMIR Medical Informatics* **3**, e4640.

Kronn, D. (2019) Navigating newborn screening in the NICU: A User's Guide. *NeoReviews* **20**, e280–e291.

Kusuda, S. (2025) Chapter 2 - Physiology of extremely preterm infants. In, S. Kusuda, H. Nakanishi & T. Isayama (eds) *Neonatal Intensive Care for Extremely Preterm Infants*. Academic Press, San Diego.

Lawn, J.E., Cousens, S. & Zupan, J. (2005) 4 million neonatal deaths: When? Where? Why? *The Lancet*, 365, 891–900.

LeBlanc, S., Haushalter, J., Seashore, C., Wood, K.S., Steiner, M.J. *et al.* (2018) A quality-improvement initiative to reduce NICU transfers for neonates at risk for hypoglycemia. *Pediatrics* **141**, e20171143.

Linsell, L., Johnson, S., Wolke, D., Morris, J., Kurinczuk, J.J. *et al.* (2018) Trajectories of behavior, attention, social and emotional problems from childhood to early adulthood following extremely preterm birth: a prospective cohort study. *European Child & Adolescent Psychiatry* **28**, 531–542.

Litjens, G., Kooi, T., Bejnordi, B.E., Setio, A.A.A., Ciompi, F. *et al.* (2017) A survey on deep learning in medical image analysis - ScienceDirect. *Medical Image Analysis* **42**, 60–88.

Lundberg, S.M. & Lee, S.I. (2017) A unified approach to interpreting model predictions. *Advances in Neural Information Processing Systems* **2017**, 4766–4775.

Madhusudhan, R. & Pravisha, P. (2023) A blockchain-enabled IoT framework for NICU infant health monitoring system. In, *2023 7th Cyber Security in Networking Conference (CSNet)*. *2023 7th Cyber Security in Networking Conference (CSNet)*, pp. 199–203.

Mahdi, M.A., Gittaffa, S.A. & Issa, A.H. (2022) Multiple fault detection and smart monitoring system based on machine learning classifiers for infant incubators using raspberry Pi 4. *IIETA*, 771–778.

Makris, G., Eleftheriades, A. & Pervanidou, P. (2023) Early life stress, hormones, and neurodevelopmental disorders. *Hormone Research in Paediatrics* **96**, 17–24.

Mally, P.V., Bailey, S. & Hendricks-Muñoz, K.D. (2010) Clinical issues in the management of late preterm infants. *Current Problems in Pediatric and Adolescent Health Care* **40**, 218–233.

Manworren, R.C.B., Horner, S., Joseph, R., Dadar, P., Kaduwela, N. (2024) Performance evaluation of a supervised machine learning pain classification model developed by neonatal nurses. *Advances in Neonatal Care* **24**, 301.

Martinez-Biarge, M., Groenendaal, F., Kersbergen, K.J., Benders, M.J.N.L., Foti, F. *et al.* (2019) Neurodevelopmental outcomes in preterm infants with white matter injury using a new MRI classification. *Neonatology* **116**, 227–235.

Martini, S. & Corvaglia, L. (2023) Premature Infants. In, M. Lima and M.C. Mondardini (eds) *Frailty in Children: From the Perioperative Management to the Multidisciplinary Approach*. Cham: Springer International Publishing, Switzerland.

Maurya, L., Kaur, P., Chawla, D., Mahapatra, P. (2021) Non-contact breathing rate monitoring in newborns: A review. *Computers in Biology and Medicine* **132**, 104321.

Mitra, U. & Rehman, S.U. (2025) Leveraging AI and machine learning for next-generation clinical decision support systems (CDSS). In, *AI-Driven Innovation in Healthcare Data Analytics*. IGI Global Scientific Publishing, Hershey, PA.

Mohammad, K. (2025) Cyber shield: advances in detection, isolation, and containment mechanisms. In, *AIAA SCITECH 2025 Forum*. American Institute of Aeronautics and Astronautics.

Molnár, Z., Luhmann, H.J. & Kanold, P.O. (2020) Transient cortical circuits match spontaneous and sensory-driven activity during development. *Science* **370**, eabb2153.

Moster, D., Lie, R.T. & Markestad, T. (2008) Long-term medical and social consequences of preterm birth. *New England Journal of Medicine* **359**, 262–273.

Mukai, Y., Morita, K., Shirai, N.C., Wakabayashi, T., Shinkoda, H. *et al.* (2021) Automatic classification of neonatal sleep-wake states based on facial video analysis. *IEEE Xplore*, 1–6.

Nabetani, M., Mukai, T. & Shintaku, H. (2021) Preventing brain damage from hypoxic–ischemic encephalopathy in neonates: update on mesenchymal stromal cells and umbilical cord blood cells. *American Journal of Perinatology* **39**, 1754–1763.

Nan, J. & Xu, L.-Q. (2023) Designing interoperable health care services based on fast healthcare interoperability resources: literature review. *Journal of Medical Internet Research* **11**, e44842.

Obermeyer, Z. & Emanuel, E.J. (2016) Predicting the future — big data, machine learning, and clinical medicine. *The New England Journal of Medicine*, **375**, 1216-1219.

Olmi, B., Frassineti, L., Lanata, A., Manfredi, C. (2021) Automatic detection of epileptic seizures in neonatal intensive care units through EEG, ECG and video recordings: a survey. *IEEE Access* **9**, 138174–138191.

Pace, E. & Yanowitz, T. (2022) Infections in the NICU: neonatal sepsis. *Seminars in Pediatric Surgery* 31, 151200.

Paneth, N. (2018) Hypoxia-ischemia and brain injury in infants born preterm. *Developmental Medicine & Child Neurology* **60**, 115.

Pani, N. & Panda, C.K. (2012) Anaesthetic consideration for neonatal surgical emergencies', *Indian Journal of Anaesthesia* **56**, 463–469.

Périsset, A., Natalucci, G., Adams, M., Karen, T., Bassler, D. *et al.* (2023) Impact of low-grade intraventricular hemorrhage on neurodevelopmental outcome in very preterm infants at two years of age. *Early Human Development*, **177–178**, 105721.

Petanjek, Z., Banovac, I., Sedmak, D., Hladnik, A. (2023) Dendritic spines: synaptogenesis and synaptic pruning for the developmental organization of brain circuits. In, *Dendritic Spines Structure, Function, and Plasticity*. 1st Edn. Springer.

Petri, S. & Tinelli, F. (2023) Visual impairment and periventricular leukomalacia in children: A systematic review. *Research in Developmental Disabilities* **135**, 104439.

Pigueiras-del-Real, J., Ruiz-Zafra, A., Benavente-Fernández, I., Lubián-López, S.P., Shah, S.A.H. *et al.* (2024) NeoVault: empowering neonatal research through a neonate data hub. *BMC Pediatrics* **24**, 787.

Pigueiras-del-Real, J., Gontard, L.C., Benavente-Fernández, I., Lubián-López, S.P., Gallero-Rebollo, E. *et al.* (2024) NRP: a multi-source, heterogeneous, automatic data collection system for infants in neonatal intensive care units. *IEEE Journal of Biomedical and Health Informatics* **28**, 678–689.

Pulver, L.S., Denney, J.M., Silver, R.M., Young, P.C. (2010) Morbidity and discharge timing of late preterm newborns. *Clinical Pediatrics* **49**, 1061–1067.

Qureshi, S.A., Aziz-ul-Rehman, Hussain, L., Sadiq, T., Shah, S.T.H. *et al.* (2024) Breast cancer detection using mammography: image processing to deep learning. *IEEE Access* **4**,1-26.

Racine, N., Chow, C., Hamwi, L., Bucsea, O., Cheng, C. *et al.* (2024) Health care professionals' and parents' perspectives on the use of AI for pain monitoring in the neonatal intensive care unit: multisite qualitative study. *JMIR Advancing Digital Health & Open Science* **3**, e51535.

Rahman, J., Brankovic, A., Tracy, M., Khanna, S. (2024) Exploring computational techniques in preprocessing neonatal physiological signals for detecting adverse outcomes: scoping review. *Interactive Journal of Medical Research*, **13**, e46946.

Rahmani, A.M., Gia, T.N., Negash, B., Anzanpour, A., Azimi, I. *et al.* (2018) Exploiting smart e-Health gateways at the edge of healthcare Internet-of-Things: A fog computing approach. *Future Generation Computer Systems* **78**, 641–658.

Ratta, R., Sodhi, J. & Saxana, U. (2025) The relevance of trust in the implementation of AI-driven clinical decision support systems by healthcare professionals: An extended UTAUT model. *Electronic Journal of Knowledge Management* **23,** 47–66.

Ribeiro, M.T., Singh, S. & Guestrin, C. (2016) "Why should I trust you?": explaining the predictions of any classifier. *NAACL-HLT 2016 - 2016 Conference of the North American Chapter of the Association for Computational Linguistics: Human Language Technologies, Proceedings of the Demonstrations Session*.

Rozé, J.-C. *et al.* (2020) Assessment of neonatal intensive care unit practices and preterm newborn gut microbiota and 2-Year neurodevelopmental outcomes. *JAMA Network Open* **3**, e2018119.

Rubin, I.L., Coles, C.D. & Barnhill, J. (2023) Behavioral and mental health disorders (including attentional disorders). In, D.D. Eisenstat et al. (eds) *Neurodevelopmental Pediatrics: Genetic and Environmental Influences*. Cham: Springer International Publishing, Switzerland.

Rumbold, J.M.M. & Pierscionek, B. (2017) The effect of the general data protection regulation on medical research. *Journal of Medical Internet Research* **19**, e47.

Russ, J.C. (2016) *The Image Processing Handbook*. CRC Press, Baco Raton.

Sahni, R. & Polin, R.A. (2013) Physiologic underpinnings for clinical problems in moderately preterm and late preterm infants. *Clinics in Perinatology* **40**, 645–663.

Sashi-Kumar, V., Paul, V.K. & Sathasivam, K. (2016) Innovating affordable neonatal care equipment for use at scale. *Journal of Perinatology* **36**, S32–S36.

Scheuer, T., dem Brinke, E. auf, Grosser, S., Wolf, S.A., Mattei, D. *et al.* (2021) Reduction of cortical parvalbumin-expressing GABAergic interneurons in a rodent hyperoxia model of preterm birth brain injury with deficits in social behavior and cognition. *Development*, **148**, dev198390.

Selvaraju, R.R., Cogswell, M., Das, A., Vedantam, R., Parikh, D. *et al.* (2020) Grad-CAM: visual explanations from deep networks via gradient-based localization. *International Journal of Computer Vision* **128**, 336–359.

Shah, S.A.H., di Terlizzi, A.& Deriu, M.A. (2022a) Intelligent system development to monitor the neonatal behaviour: A review. In, DETERMINED 2022: Neurodevelopmental Impairments in Preterm Children — Computational Advancements, August 26, 2022, Ljubljana, Slovenia.CEUR Workshop Proceedings

Shah, S.A.H., Shah, S.T.H., Khaled, R., Buccoliero, A., Shah, S.B.H. *et al.* (2024a) Explainable AI-based skin cancer detection using CNN, particle swarm optimization and machine learning. *Journal of Imaging* **10**, 332.

Shah, S.T.H., Qureshi, S.A., Rehman, A. ul, Shah, S.A.H., Amjad, A. *et al.* (2021) A novel hybrid learning system using modified breaking ties algorithm and multinomial logistic regression for classification and segmentation of hyperspectral images. *Applied Sciences* **11**, 7614.

Shah, S.T.H., Calati, V., Bizzarri, A., Deriu, M.A. (2022b) Medical imaging and artificial intelligence to investigate neuro-cardiac pathologies and discover hidden relationships: a state of the art review. In, DETERMINED 2022: Neurodevelopmental Impairments in Preterm Children — Computational Advancements, August 26, 2022, Ljubljana, Slovenia. CEUR Workshop Proceedings

Shah, S.T.H., Shah, S.A.H., Qureshi, S.A., Di Terlizzi, A., Deriu, M.A. (2023) Automated facial characterization and image retrieval by convolutional neural networks. *Frontiers in Artificial Intelligence* **6**, 1230383.

Shah, S.T.H., Shah, S.A.H., Khan, I.I., Imran, A., Shah, S.B.H. *et al.* (2024b) Data-driven classification and explainable-AI in the field of lung imaging. *Frontiers in Big Data* **7**, 1393758.

Sharma, D., Vara Padmavathi, I., Tabatabaii, S.A., Farahbakhsh, N. (2019) Late preterm: a new high risk group in neonatology: The Journal of Maternal-Fetal. *Journal of Maternal-Fetal* **34**, 2717–2730.

Sharma, R. & Meena, H.K. (2024) Emerging trends in EEG signal processing: a systematic review | SN Computer Science. *Springer Nature Computer Science* **5**, 415.

Shayegh, S.V. & Tadj, C. (2025) Deep audio features and self-supervised learning for early diagnosis of neonatal diseases: sepsis and respiratory distress syndrome classification from infant cry signals. *Electronics* **14,** 248.

Singh, A.K. *et al.* (2023) Incubator for home-based baby care using IoT. *Journal of Biomedical Engineering and Technology* **10**, 1–7.

Sweeney, K.T., Ward, T.E. & McLoone, S.F. (2012) Artifact removal in physiological signals—practices and possibilities. *IEEE Transactions on Information Technology in Biomedicine* **16**, 488–500.

Tan, X., Zhang, X., Chai, J., Ji, W., Ru, J. *et al.* (2024) Constructing a predictive model for early-onset sepsis in neonatal intensive care unit newborns based on

SHapley Additive exPlanations explainable machine learning. *Translational Pediatrics* **13**, 1933946–1931946.

Tana, M., Tirone, C., Aurilia, C., Lio, A., Paladini, A. *et al.* (2023) Respiratory management of the preterm infant: supporting evidence-based practice at the bedside. *Children (Basel)* **10**, 535.

Tashakkori, R., Mozdgir, A., Karimi, A., Bozorgzadeh Vosta Kolaei, S. *et al.* (2024) The prediction of NICU admission and identifying influential factors in four different categories leveraging machine learning approaches. *Biomedical Signal Processing and Control* **90**, 105844.

Tetorou,K. Sisa,C. Iqbal,A. Dhillon,K. & Hristova,M.(2021) Current therapies for neonatal hypoxic–ischaemic and infection-sensitised hypoxic–ischaemic brain damage. *Frontiers in Synaptic Neuroscience* **13**, 709301.

Topol, E.J. (2019a) *Deep Medicine: How Artificial Intelligence Can Make Healthcare Human Again*. Basic Books, New York.

Topol, E.J. (2019b) High-performance medicine: the convergence of human and artificial intelligence. *Nature Medicine* **25**, 44–56.

Tresp, V., Overhage, J.M., Bundschus, M., Rabizadeh, S., Fasching, P.A. *et al.* (2016) Going digital: a survey on digitalization and large-scale data analytics in healthcare. *Proceedings of the IEEE* **104**, 2180–2206.

Vaishnavi, V., Braveen, M., Muthukumaran, N., Poonkodi, P. (2024) Premature infant cry classification via elephant herding optimized convolutional gated recurrent neural network. *Circuits, Systems, and Signal Processing* **43**, 6592–6619.

Vandormael, C., Schoenhals, L., Hüppi, P.S., Filippa, M., Tolsa, C.B. (2019) Language in preterm born children: atypical development and effects of early interventions on Neuroplasticity. *Neural Plasticity* **2019**, 6873270.

Variane, G.F.T., Camargo, J.P.V., Rodrigues, D.P., Magalhães, M., Mimica, M.J. (2022) Current status and future directions of neuromonitoring with emerging technologies in neonatal care. *Frontiers in Pediatrics* **9**, 755144.

Varisco, G. (2023) *Monitoring the critical newborn: Towards a safe and more silent neonatal intensive care unit*. Phd Thesis 1 (Research TU/e / Graduation TU/e). Eindhoven University of Technology, The Netherlands.

Villarroel, M., Chaichulee, S., Jorge, J., Davis, S., Green, G. *et al.* (2019) Non-contact physiological monitoring of preterm infants in the neonatal intensive care unit. *NPJ Digital Medicine* **2**, 128.

Vitale, F.M., Chirico, G. & Lentini, C. (2021) Sensory stimulation in the NICU environment: devices, systems, and procedures to protect and stimulate premature babies. *Children* **8**, 334.

Vrancken, S.L., van Heijst, A.F. & de Boode, W.P. (2018) Neonatal hemodynamics: from developmental physiology to comprehensive monitoring. *Frontiers in Pediatrics* **6**, 87.

Vuppu, D.K. & Iragamreddy, V.R. (2023) Clinical profile of late preterm neonates admitted to a tertiary care NICU. *PriMera Scientific Medicine and Public Health* **3**, 16.

Wallois, F., Routier, L. & Bourel-Ponchel, E. (2020) Chapter 25 - Impact of prematurity on neurodevelopment. In, A. Gallagher et al. (eds) *Handbook of Clinical Neurology*. Elsevier, Amsterdam.

Wang, M., Ma, Z., Wang, Y., Liu, J., Guo, J. (2023) A multi-view convolutional neural network method combining attention mechanism for diagnosing autism spectrum disorder. *PLOS ONE* **18**, e0295621.

Wilgocka, K., Skrzetuska, E., Krucińska, I., Sujka, W. (2023) Textronic solutions used for premature babies: a review. *AUTEX Research Journal*, **23**, 18–28.

Xiao, W. & Luo, X. (2024) Observations on the clinical effects of music therapy on premature infants in neonatal intensive care units. *Noise and Health* **26**, 436.

Xu, Y., Jabeen, F., Treur, J., Taal, H.R., Roelofsma, P.H.M.P. (2024) Supporting medical team decision in the neonatal domain: how safety and security risk management through cyberspace can be supported by adaptive agent network models with internal mental models. In, P.H.M.P. Roelofsma et al. (eds) *Using Shared Mental Models and Organisational Learning to Support Safety and Security Through Cyberspace: A Computational Analysis Approach*. Cham: Springer Nature Switzerland.

Yan, Z. & Rein, B. (2022) Mechanisms of synaptic transmission dysregulation in the prefrontal cortex:

pathophysiological implications. *Molecular Psychiatry* **27**, 445–465.

You, J., Yang, H., Hao, M., Zheng, J. (2019) Late preterm infants' social competence, motor development, and cognition. *Frontiers in Psychiatry* **10**, 69.

Zaguir, N.A., de Magalhães, G.H. & de Mesquita Spinola, M. (2024) Challenges and enablers for GDPR compliance: systematic literature review and future research directions. *IEEE Access* **12**, 81608–81630.

Zeng, Y., Yu, D., Song, X., Wang, Q., Pan, L. *et al.* (2024) Camera-based cardiorespiratory monitoring of preterm infants in NICU. *IEEE Transactions on Instrumentation and Measurement* **73**, 5019813.

Zhao, Y., Zhu, H., Shu, Q., Huan, R., Chen, S. *et al.* (2024) Towards a deeper insight into face detection in neonatal wards. In, M.G. Linguraru et al. (eds) *Medical Image Computing and Computer Assisted Intervention – MICCAI 2024*. Cham: Springer Nature Switzerland.

Zhou, H., Zhou, F., Zhao, C., Xu, Y., Luo, L. (2024a) Multimodal data integration for precision oncology: challenges and future directions. *arXiv. Preprint*

Zhou, L., Guess, M., Kim, K.R., Yeo, W.-H. (2024b) Skin-interfacing wearable biosensors for smart health monitoring of infants and neonates. *Communications Materials* **5**, 72.