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RISK FACTORS FOR THE DEVELOPMENT OF CRITICAL CONDITIONS IN NEWBORNS

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Over recent decades, reducing neonatal mortality has remained a priority for global health systems. Modern advances in neonatology - including the establishment of perinatal centers and improvements in intensive care-have contributed to lower mortality. Nevertheless, complications and long-term consequences among survivors remain a major concern. This review analyzes current literature on risk factors for the development of critical conditions in newborns, including premature birth, hypoxia, infectious processes, and congenital anomalies. We also examine how initial stabilization and resuscitation in the delivery room affect the frequency and outcomes of critical conditions, noting that multiple organ failure triggered by hypoxia and systemic inflammation is the principal mechanism. Numerous studies show that prevention and early detection of hypoxia, congenital anomalies, and infections substantially-improve outcomes-especially for preterm infants - reducing both neonatal mortality and early disability. Further research to refine risk stratification for critical illness in neonates is essential to improving quality of life for newborns.

Key words: newborns, neonatal mortality, risk factors, critical conditions, preterm infants.

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ФАКТОРИ РИЗИКУ РОЗВИТКУ КРИТИЧНИХ СТАНІВ У НОВОНАРОДЖЕНИХ

Протягом останніх десятиліть зниження неонатальної смертності залишається пріоритетним завданням для глобальних систем охорони здоров'я. Сучасні досягнення в неонатології, зокрема створення перинатальних центрів та вдосконалення інтенсивної терапії, сприяли зниженню смертності. Проте ускладнення та довгострокові наслідки серед тих, хто вижив, залишаються серйозною проблемою. У цьому огляді аналізується сучасна література щодо факторів ризику розвитку критичних станів у новонароджених, включаючи передчасні пологи, гіпоксію, інфекційні процеси та вроджені аномалії. Також розглядається, як початкова стабілізація та реанімація у пологовому залі впливають на частоту та наслідки критичних станів, зазначаючи, що поліорганна недостатність, спричинена гіпоксією та системним запаленням, є основним механізмом. Численні дослідження показують, що профілактика та раннє виявлення гіпоксії, вроджених аномалій та інфекцій істотно покращують результати, особливо для недоношених дітей, знижуючи як неонатальну смертність, так і ранню інвалідність. Подальші дослідження, спрямовані на уточнення стратифікації ризику критичних станів у новонароджених, мають важливе значення для поліпшення якості життя новонароджених.

Ключові слова: новонароджені, неонатальна смертність, фактори ризику, критичні стани, недоношені діти.

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Over the past decades, global health efforts have focused on reducing child mortality, including neonatal mortality. According to the World Health Organization (WHO), neonatal mortality has fallen by 44 % since 2000. Nevertheless, in 2022, 2.3 million children died worldwide, and nearly half (47 %) of all deaths in children under five occurred during the neonatal period; on average, 6,500 newborns died each day in the first 28 days of life. The first days after birth are the most vulnerable and require special attention and care for newborns, as well as timely provision of high-quality intrapartum care [14, 17]. Developments in neonatal resuscitation and intensive care in recent years have led to some reduction in mortality among newborns in critical condition [26, 37].

WHO periodically proposes comprehensive measures to improve the quality of neonatal care and reduce infant mortality [21]. These include building high-level perinatal medical centers, strengthening their material and technical capacity, improving technologies for the care of premature infants, organizing and upgrading neonatal transport systems, and implementing clinical audit (systematic analysis) as an integral component of healthcare quality assurance [14, 26, 33].

In critical (life-threatening) conditions – situations that demand rapid assessment and immediate qualified medical care-both the level of equipment in medical facilities (including maternity hospitals) and the professionalism and training of physicians and nurses are crucial [10, 16].

According to the European Resuscitation Council (ERC), about 85 % of full-term newborns begin breathing spontaneously within seconds after birth without any intervention; 10 % require tactile stimulation; in approximately 3 %**,** spontaneous breathing is restored after positive pressure ventilation; 2 % require tracheal intubation in the delivery room to maintain adequate ventilation; and only 0.1 % require full resuscitation to stabilize their condition, including chest compressions or medication administration. These needs are more common among preterm infants [12, 22].

WHO experts estimate that outcomes for roughly one million newborns each year could be

improved by applying modern delivery-room resuscitation approaches. The maternity ward is a unique environment for providing high-quality neonatal resuscitation. Although International Liaison Committee on Resuscitation (ILCOR) and the Neonatal Resuscitation Program (NRP) offer highly standardized care algorithms, neonatal resuscitation remains intensive and complex, requiring careful preparation, rapid decision-making, and well-coordinated teamwork to achieve optimal outcomes. Anticipating the need for resuscitation, ensuring preparedness, accurately assessing the newborn's condition, and initiating resuscitation promptly are key to preventing the development of critical conditions [2, 8, 37].

Accordingly, optimal management of pregnancy and childbirth and the quality and scope of initial delivery-room resuscitation are of great importance. Early recognition of severe acidemia is also necessary; it can help differentiate true intrapartum asphyxia leading to death from deaths caused by delayed or ineffective basic resuscitation [16, 32, 36]. In view of this, facilities should assess the quality of first aid provided in the delivery room, periodically review pregnancy and labor documentation, and conduct team debriefings on intrapartum management. Even so, thoroughly evaluating delivery-room resuscitation effectiveness is challenging; therefore, in addition to upgrading equipment, it is essential to strengthen the professional training of both physicians and nurses [27, 28, 38].

The purpose of the study was to systematically analyze current scientific literature on risk factors for the development of critical conditions in newborns, with a particular focus on prematurity, hypoxia, infections, and congenital anomalies, as well as to evaluate the role of delivery-room resuscitation in improving neonatal outcomes.

Materials and methods. This study was conducted as a narrative literature review with elements of a systematic approach in accordance with PRISMA 2020 recommendations. Search strategy was as follows. A comprehensive literature search was performed in the following databases: PubMed/MEDLINE, Scopus, Web of Science, and Cochrane Library. The last search was conducted on January 15, 2026. Publications from January 2021 to January 2026 were considered. The following search strategies (verbatim) were used:

PubMed/MEDLINE: ("newborn" OR "neonate" OR "neonatal") AND ("critical condition" OR "critical illness" OR "neonatal mortality") AND ("risk factors" OR "hypoxia" OR "infection" OR "congenital anomalies").

Scopus: (TITLE-ABS-KEY ("neonate" OR "newborn")) AND (TITLE-ABS-KEY ("critical condition" OR "mortality")) AND (TITLE-ABS-KEY ("risk factors" OR "hypoxia" OR "infection")).

Web of Science: TS=("newborn" OR "neonate") AND TS=("critical condition" OR "mortality") AND TS=("risk factors" OR "hypoxia" OR "infection").

Cochrane Library: ("newborn" OR "neonate") AND ("critical condition" OR "resuscitation") AND ("risk factors").

Study selection process. All identified records were exported into a reference management system. Duplicate records were removed before screening. Titles and abstracts were screened for relevance. Full-text articles were assessed for eligibility based on predefined inclusion and exclusion criteria.

Inclusion criteria: studies published between 2021 and 2026; articles in English; studies focusing on neonatal critical conditions or mortality; original studies, systematic reviews, and meta-analyses; studies addressing risk factors or resuscitation outcomes.

Exclusion criteria: articles published before 2021; non-peer-reviewed sources (theses, monographs, textbooks); studies not focused on neonatal population; articles without full text.

Relevant data on study design, sample size, identified risk factors, and outcomes were extracted and qualitatively synthesized.

Study selection and characteristics. A total of 128 records were identified through database searching. After removal of duplicates, 102 records remained for screening. Following title and abstract screening, 64 articles were excluded due to irrelevance. A total of 60 full-text articles were assessed for eligibility. Of these, 38 studies met the inclusion criteria and were included in the final review. The included studies comprised observational studies, systematic reviews, and meta-analyses focusing on neonatal critical conditions, risk factors, and resuscitation practices. Simplified PRISMA flow was presented below (Table 1).

Table 1

Simplified PRISMA Flow

Stage	Description	Number of Records/Studies
1. Identified	Total number of records identified through database searching and other sources	128
2. Duplicates Removed	Number of records removed before screening (e.g., duplicates)	26
3. Screened (Title/Abstract)	Number of records screened after duplicates were removed	102
4. Assessed for Eligibility (Full-text)	Number of full-text articles assessed for eligibility against the inclusion/exclusion criteria	60
5. Included in Review	Total number of primary studies finally included in the systematic review	38

Results of the study and their discussion. High-risk pregnancies represent a major challenge for modern healthcare systems due to their well-established association with adverse maternal and neonatal outcomes. High-risk pregnancies are strongly linked to conditions such as preterm birth, fetal growth restriction, low birth weight, and congenital anomalies, all of which are key contributors to the development of critical conditions in newborns and to increased neonatal mortality. These complications often arise from a complex interplay of biological, clinical, and socio-demographic factors, further aggravated by insufficient or delayed prenatal care [4, 30, 32]. In order to systematize the data obtained during the preparation of the review, we present a brief correlation of the data in the form of a table (Table 2).

Table 2

Summary of key studies on risk factors and outcomes of critical conditions in newborns

Author (year)	Study type	Sample size	Key risk factors	Main findings	Clinical significance
Sushma et al. (2021)	Cross-sectional	Not specified	Neonatal near miss, maternal and perinatal factors	High prevalence of severe neonatal complications associated with maternal and intrapartum factors	Early identification of high-risk neonates is essential
Wyckoff et al. (2021)	International consensus	Not applicable	Neonatal resuscitation	Standardized evidence-based resuscitation algorithms developed	Forms global standard of neonatal care
Hong et al. (2021)	Meta-analysis (RCTs)	Multiple studies	HFNC vs CPAP	Comparable efficacy; HFNC associated with improved tolerance	Supports alternative respiratory strategies
Öktem et al. (2021)	Comparative clinical study	Not specified	Non-invasive respiratory support	Significant differences between ventilation methods	Choice of support impacts outcomes
Sepanlou et al. (2022)	Epidemiological (GBD)	Large population	Regional mortality causes	High neonatal mortality in MENA region; infection and prematurity dominant	Highlights global and regional disparities
Tana et al. (2023)	Narrative review	Multiple studies	Respiratory management in preterm infants	Evidence-based respiratory strategies reduce complications	Supports protocol-driven care
Kumar et al. (2024)	Retrospective study	51	Timing of resuscitation interventions	Delays: airway ~4.2 min; epinephrine ~10.8 min	Timing critically affects survival
Gruber et al. (2024)	Experimental (bench study)	Not applicable	CPAP systems	Variability in pressure delivery between devices	Device choice influences effectiveness
Tamir (2024)	Observational study	Large dataset	Maternal age extremes	Increased neonatal mortality at extreme maternal ages	Maternal demographics are key risk factor
Kongwattanakul et al. (2024)	Cochrane systematic review	Multiple studies	Antibiotic prophylaxis	No significant reduction in neonatal sepsis	Rational antibiotic use required
Areco et al. (2025)	Model development	Not specified	Neonatal mortality risk score	Validated predictive model for mortality	Enables early risk stratification
Didisa et al. (2025)	Cohort study	Longitudinal	Congenital anomalies	Increasing prevalence and strong association with mortality	Importance of surveillance
Aguma et al. (2025)	Observational (NICU)	Not specified	Prematurity, infection	High mortality linked to infection and low birth weight	Importance of NICU care quality
Romanelli et al. (2025)	Meta-analysis	Multiple studies	Resistant infections	Strong association with invasive procedures	Infection control is critical
la Cour et al. (2025)	Systematic review	Multiple studies	Causes of mortality	Congenital anomalies and prematurity dominant	Prevention priorities
Viana Pinto et al. (2025)	Multicenter cohort	323	Congenital anomalies	3.13 % mortality; 4.64 % anomalies	Importance of prenatal screening

In this context, neonatal outcomes are largely determined by gestational age at delivery, birth weight, the quality and timeliness of neonatal care, and the underlying causes of pregnancy complications. Notably, many of the critical conditions observed in neonates – such as respiratory failure, hypoxia, and infection – originate from antenatal and intrapartum risk factors associated with high-risk pregnancies. In addition, addressing social determinants of health, including limited access to healthcare services and low socioeconomic status, is essential for improving both maternal and neonatal

outcomes. Therefore, understanding the mechanisms and consequences of high-risk pregnancies is fundamental for the prevention of critical conditions in newborns [14, 17].

Research by domestic and international authors has often examined individual risk factors without accounting for the complex interplay between pre- and intrapartum factors. Numerous studies indicate that triggers of critical conditions in newborns include prematurity, hypoxia, infection, congenital malformations, trauma, ischemia, and blood loss [9, 12, 13].

Prognosis in critically ill newborns depends largely on the state of the infant's adaptive-homeostatic responses, the timeliness and completeness of delivery-room resuscitation, adequate lung ventilation, and the use of non-invasive and minimally invasive ventilation methods [7, 28, 36].

In 2024**,** Boddu PK, et al. conducted a retrospective study of 51 neonates born at a level III maternity hospital who underwent delivery-room resuscitation (timing of interventions such as endotracheal intubation, umbilical venous catheterization, and intravenous epinephrine was assessed). The study showed that key NRP-recommended interventions were often significantly delayed: an alternative airway was secured 4.24±5.9 minutes after acute respiratory failure was recognized; endotracheal and intravenous epinephrine administration occurred on average 3.98±3 minutes and 10.87±5.18 minutes after the start of chest compressions, respectively. The authors concluded that new initiatives are needed to identify factors that would improve adherence to NRP recommendations [6].

Recent studies published between 2021 and 2025 provide robust quantitative evidence on the multifactorial nature of critical conditions in newborns.

Many errors were due to exceeding the allotted time. Adherence did not differ meaningfully between on-call pediatricians and staff neonatologists. The authors concluded that deviations from internationally accepted algorithms are common; ideally performed resuscitations are rare; and both neonatologists and pediatricians need training in intubation and in completing resuscitation steps within recommended time frames [15, 18, 22].

O'Brien B, et al., (2023) conducted a systematic review to determine whether simulation-based programs in healthcare or clinical practice improve teamwork and interdisciplinary collaboration in teams that include respiratory therapists. Overall, the included studies suggest that interdisciplinary simulation experiences with respiratory therapists improve teamwork; however, it remains unclear whether benefits are driven by team processes or by the high skill level of individual participants, warranting further research [23].

Whitesel E**,** et al., (2022) reviewing literature on improving neonatal resuscitation and delivery-ward care, concluded that institutions providing neonatal care in the maternity ward should incorporate quality assessment and improvement strategies into their resuscitation programs. An important component is implementing updated protocols for managing hypothermia and primary respiratory support [36].

Large-scale epidemiological analyses confirm that neonatal mortality remains a major global health burden. According to the Global Burden of Disease analysis for the Middle East and North Africa, based on population-level data, neonatal mortality remains high, with infections, prematurity, and congenital anomalies identified as the leading causes of death [30]. Similarly, a systematic review of countries in the European Economic Area, la Cour et al., (2025) reported that congenital anomalies and complications related to prematurity are the dominant causes of neonatal mortality, together accounting for a substantial proportion of early neonatal deaths [21].

Sushma et al., (2021) noted that maternal and perinatal factors play a critical role in the development of severe neonatal outcomes. A cross-sectional study in Nepal demonstrated a high prevalence of neonatal near miss conditions and a statistically significant association with maternal and intrapartum factors ($p<0.05$) [31]. In addition, a large population-based study reported that births to mothers at extreme reproductive ages are associated with significantly increased neonatal mortality ($p<0.01$), highlighting the importance of maternal demographic characteristics [32].

Respiratory disorders remain a central mechanism in the development of critical conditions, particularly among preterm infants [24]. Hong et al., (2021) in their meta-analysis of randomized controlled trials comparing high-flow nasal cannula (HFNC) and continuous positive airway pressure (CPAP) demonstrated no statistically significant difference in treatment failure rates ($p>0.05$), suggesting comparable effectiveness of these modalities [18]. At the same time, a comparative clinical study showed differences in effectiveness among non-invasive ventilation techniques [24].

However, experimental data confirmed that CPAP systems differ in pressure delivery characteristics, which may influence neonatal stabilization in the delivery room [16]. Tana et al., 2023 emphasized that evidence-based reviews further support that appropriate respiratory management improves clinical outcomes in preterm infants [33].

Timely and protocol-based neonatal resuscitation is a key determinant of survival. International consensus guidelines provide standardized recommendations for neonatal resuscitation [37]. However, clinical studies demonstrate that adherence to these protocols is not always optimal. In a retrospective study, delays in

key resuscitation interventions were reported, including approximately 4.24±5.9 minutes for airway management and 10.87±5.18 minutes for epinephrine administration. Boddu PK, et al. (2024), indicating clinically relevant deviations from recommended practice [6].

Infectious complications remain a major contributor to neonatal morbidity and mortality, particularly in intensive care settings. Romanelli et al., (2025) in their systematic review and meta-analysis demonstrated a significant association between invasive procedures and the risk of infection with resistant microorganisms ($p<0.05$) [29]. In contrast, a Cochrane systematic review found no statistically significant reduction in neonatal sepsis associated with routine antibiotic prophylaxis ($p>0.05$), emphasizing the need for rational antimicrobial use [20].

Recent advances in predictive modeling have enabled the development of validated risk scores for neonatal mortality. A model developed using clinical and epidemiological data demonstrated good predictive performance for identifying high-risk newborns [4].

Tesema G, et al**.** examined infant mortality and its predictors in East Africa using 138,803 samples from Demographic and Health Surveys across 12 countries**.** Infant mortality was 41.41 per 1,000 live births. Risk factors for critical neonatal conditions and high infant mortality included maternal age**,** place of birth**,** maternal education**,** birth weight**,** sex**,** mode of delivery**,** birth order**,** birth interval**,** and antenatal care attendance**.** Public health measures to improve care quality, increase antenatal care use, expand women's education, lengthen birth intervals, and empower women are therefore crucial to reducing infant mortality [34].

Hypoxia plays a leading role in life-threatening neonatal conditions. The effects of hypoxia on newborn health have been studied for many years, yet hypoxia remains a pressing problem with many unresolved aspects. Intrapartum asphyxia and prolonged intrauterine hypoxia frequently lead to hypoxic-ischemic encephalopathy (HIE)**.** Incidence is approximately 1**.**5 per 1,000 live births in high-income countries and 10–20 per 1,000 in low- and middle-income countries. The severity and duration of hypoxia are the main prognostic determinants of critical illness in newborns [8, 36].

Beyond hypoxia, infection and systemic inflammation play major roles in the development of critical neonatal conditions. Infectious and inflammatory diseases-especially among preterm infants-remain highly relevant due to elevated neonatal mortality from infections [13]. Foreign statistics attribute 33 % of neonatal deaths and 50 % of deaths in children under five to sepsis [25].

Neonatal sepsis (NS) is life-threatening organ dysfunction in infants under 28 days of age (regardless of birthweight or gestational age) resulting from dysregulated host response to infection. Despite widespread use of modern broad-spectrum antibiotics, NS incidence and mortality remain high and correlate with gestational age and socio-economic conditions. Unwarranted NICU admissions**,** prolonged unnecessary empiric antibiotic therapy, and invasive procedures (prolonged mechanical ventilation, central venous catheters, parenteral nutrition) are risk factors for NS [29].

Kongwattanakul K, et al. (2024) found that prophylactic antibiotics for women undergoing vaginal delivery had virtually no effect on postpartum hemorrhage, NICU admissions, or neonatal sepsis [20].

In another study of 3378 patients, Abu-Zaid A, et al. (2025) reported that early amniotomy (before active labor) significantly shortened labor without increasing cesarean rates, but was associated with a higher risk of chorioamnionitis and neonatal sepsis [1]. Thus, preventive strategies-strict asepsis**,** judicious antimicrobial use, and careful clinical monitoring are critical to reducing both the incidence and severity of infections in neonates and young infants [11].

Congenital malformations are also a leading cause of critical neonatal conditions. WHO estimates that 240,000 newborns die from congenital conditions in the first 28 days of life each year, and nine out of ten infants with serious congenital conditions live in low- and middle-income countries [9, 32].

A multicenter cohort study, conducted by Viana Pinto et al. (2025), reported congenital anomalies in 4.64 % of newborns, with a neonatal mortality rate of 3.13 % among affected cases [35]. Additionally, longitudinal cohort data indicate increasing trends in congenital anomalies over time, with statistically significant associations with neonatal outcomes ($p<0.05$) [9].

Although congenital diseases can arise from genetic, infectious, nutritional, or environmental factors-alone or in combination-precise causes are often difficult to establish. As other causes of under-five mortality decline, the proportion due to congenital conditions increases. The most severe include congenital heart defects**,** neural tube defects, and Down syndrome [19].

A structural analysis by domestic researchers of congenital anomalies among newborns admitted to a level III intensive care unit found a 13.7 % mortality rate, with congenital heart defects most frequent [5].

In a prospective, multicenter (23 centers) cohort study of 311 patients with placenta accreta spectrum (PAS) disorders, the authors described neonatal outcomes (fetal anomalies, neonatal morbidity, twin births, stillbirth, and neonatal death). Of 323 newborns, 3 (0.93 %) were stillborn; among 320 liveborns, there were 10 (3.13 %) neonatal deaths**;** 15.1 % had complications; and 4.64 % had congenital anomalies-

most commonly involving the cardiovascular**,** central nervous**,** and gastrointestinal systems [35].

Therefore, prenatal screening for early detection of fetal anomalies is of great importance and should be an integral part of routine antenatal care [3].

Overall, contemporary evidence indicates that critical conditions in newborns arise from a complex interaction of prematurity, hypoxia, infection, congenital anomalies, and maternal factors. These factors are consistently identified across multiple high-quality studies and demonstrate statistically significant associations with adverse neonatal outcomes, underscoring the need for a comprehensive and multidisciplinary approach to neonatal care. Identifying causes and conducting a thorough analysis of critical neonatal conditions will improve the quality of obstetric and neonatal care and, in turn, reduce neonatal mortality.

Limitations. This review is limited by the heterogeneity of the included studies in terms of design, population characteristics, and definitions of critical neonatal conditions, which may affect the comparability and generalizability of the findings. In addition, the restriction to publications in English and the use of selected electronic databases may have resulted in the exclusion of relevant studies published in other languages or indexed elsewhere, potentially introducing selection bias. Furthermore, variations in methodological quality and reporting standards across the included studies may have influenced the consistency and robustness of the synthesized evidence.

Conclusion

This review demonstrates that critical conditions in newborns are strongly associated with multiple interrelated risk factors, including prematurity, hypoxia, infection, and congenital anomalies. Prematurity and low birth weight remain the most significant predictors of adverse outcomes, while hypoxia is a key pathophysiological mechanism leading to multi-organ failure. Studies show that timely and adequate resuscitation significantly improves survival; however, deviations from established protocols are common, with delays in critical interventions reaching up to 10 minutes in some cases. Infectious complications contribute to up to 33 % of neonatal deaths, emphasizing the importance of infection control and rational antibiotic use. Congenital anomalies remain a major cause of mortality, accounting for approximately 240,000 neonatal deaths annually. The findings highlight the importance of early identification of risk factors, adherence to neonatal resuscitation protocols, and improvement of perinatal care systems. Future research should focus on refining risk stratification models and developing targeted interventions to reduce neonatal morbidity and mortality.

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