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Analysis of Risk Factors for Necrotizing Enterocolitis (NEC) in Newborns: A Systematic Literature Review

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A B S T R A C T

Necrotizing enterocolitis (NEC) is a serious condition in newborns involving inflammation and intestinal necrosis. A number of risk factors have been identified, which complexly interact and contribute to the development of this condition. An in-depth understanding of these risk factors has major implications for the prevention, diagnosis and management of NEC in newborns. Babies born prematurely, especially before 32 weeks' gestation, have a higher risk of developing NEC. Low birth weight, regardless of prematurity status, remains a significant independent risk factor. Imbalances in blood circulation, especially in the intestines, can increase the risk of NEC. Hypotension and other medical conditions that affect blood flow to the intestines can be potential triggers. Infection and inflammation, both systemic and local, play a central role in the development of NEC. Bacterial contamination in the digestive tract can trigger an inflammatory response that contributes to the pathophysiological process of NEC. Formula feeding, especially in premature infants, is associated with an increased risk of NEC. The importance of providing exclusive breastfeeding and introducing foods slowly to protect the newborn's intestinal health. Excessive use of antibiotics or without clear indications can change the balance of intestinal microflora and increase the risk of NEC. The importance of judicious selection and use of antibiotics to minimize negative impacts on gut health.

1. Introduction

Necrotizing enterocolitis (NEC) is a serious condition that often affects newborn babies, especially those born prematurely. NEC is defined as intestinal inflammation and necrosis and has a high mortality rate in the neonatal population. Although developments in pediatric medicine have made significant progress in understanding and treating this condition, the risk factors that cause NEC remain the focus of in-depth study. Investigation of risk factors for NEC in newborns has been an important subject in the medical literature. As the incidence of NEC increases, an in-depth understanding of the factors influencing the development of this condition becomes crucial for the design of effective prevention strategies.[1-3]

This study aims to detail and evaluate the current literature, discussing various risk factors for NEC in newborns and providing comprehensive insight for pediatric healthcare practitioners. It is important to recognize that the multifactorial nature of NEC makes it challenging to establish a single cause, and therefore, careful study of the interaction of these factors is necessary. In order to further understand the causes and development of NEC, this literature review will detail the role of various elements such as prematurity, low birth weight, blood circulation conditions, infectious factors, early feeding, use of antibiotics, and genetic factors that can influence the risk of NEC in babies. Newborn. Through a thorough search of the literature, this study hopes to provide a

more in-depth picture of the risk factors for NEC, support better understanding in clinical practice, and ultimately lead to more effective prevention efforts and improved quality of newborn care.[4-6]

2. Methods

The literature search process was carried out on various databases (PubMed, Web of Sciences, EMBASE, Cochrane Libraries, and Google Scholar) regarding the analysis of risk factors for necrotizing enterocolitis in newborns. The search was performed using the terms: (1) "analysis" OR "factor" OR "risk" OR" necrotizing enterocolitis" AND (2) "NEC" OR "newborn." The literature is limited to clinical studies and published in English. The literature selection criteria are articles published in the form of original articles, a study about risk factor analysis of necrotizing enterocolitis in newborns, studies were conducted in a timeframe from 2013-2023, and the main outcome was an analysis of risk factors for necrotizing enterocolitis in the newborn. Meanwhile, the exclusion criteria were studies that were not related to the analysis of risk factors for necrotizing enterocolitis in newborns, the absence of a control group, and duplication of publications. This study follows the preferred reporting items for systematic reviews and meta-analysis (PRISMA) recommendations.

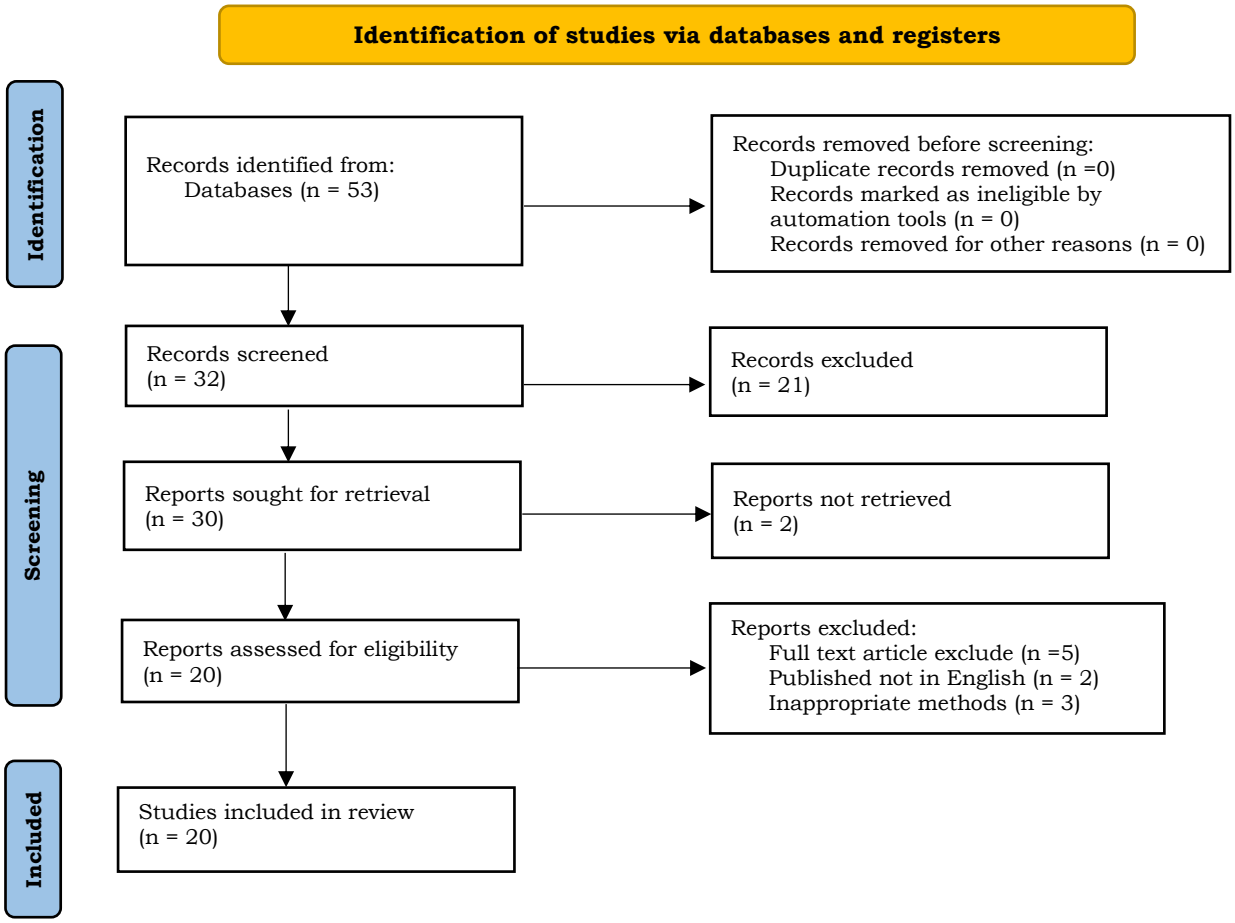

Figure 1. PRISMA flowchart.

3. Results and Discussion

Prematurity

Necrotizing enterocolitis (NEC) is a serious condition in newborn babies that is closely related to prematurity. Babies born before reaching 32 weeks' gestation have a higher risk of developing NEC compared with babies born at a longer gestational age. In-depth scientific research has revealed this association and highlighted various biological mechanisms that strengthen the association between

prematurity and NEC risk. One factor that strengthens the link between prematurity and NEC is the imperfect function of the digestive tract in premature babies. In the early stages of development, the digestive tract of premature babies is not yet fully mature, including the availability of digestive enzymes and optimal absorption of nutrients. This condition creates an environment that is susceptible to disruption and inflammation. The immune system in premature babies is also still in the developing stage. Weaknesses in the body's immune defenses make premature babies more susceptible to infection and inflammation. NEC is often preceded by an inflammatory reaction in the digestive tract, and a weakened immune system can accelerate the development of this condition in premature babies. Premature babies tend to have a more ineffective intestinal barrier, increasing the risk of penetration of bacteria and toxins into the intestinal wall. This dysfunction can trigger detrimental inflammatory responses and is ultimately associated with the development of NEC. An in-depth review of the scientific literature notes that prematurity is not only a major risk factor for NEC but also creates a biological basis that exacerbates the consequences of the condition. Therefore, intensive care and special preventive strategies are needed for premature babies to reduce the risk and serious impact of NEC on their development and survival. A deeper understanding of the relationship between prematurity and NEC opens the door to further research and innovation in clinical approaches to the population of newborns most vulnerable to this condition.[7-9]

Low birth weight

Necrotizing enterocolitis (NEC) continues to be a serious concern in neonatal care, and its association with low birth weight (LBW) provides an additional dimension to the complexity of risk factors. Although LBW frequently occurs in premature infants, studies have shown that even in term infants, low birth weight remains an independent risk factor for the development of NEC. LBW and prematurity often go hand in hand, creating an environment that is vulnerable to neonatal health problems. Prematurity has direct consequences in terms of lack of time for the development of organs and body systems, including the digestive tract, which can increase the risk of NEC. Interestingly, despite the strong association between LBW and prematurity, recent studies show that low birth weight remains an independent risk factor for NEC, even in term-born infants. This suggests that there are specific biological and pathophysiological mechanisms involved in LBW that can trigger the development of NEC, independent of prematurity factors. LBW can reflect prenatal conditions that influence the growth and development of blood vessels, creating ischemic conditions in the intestine. Vascular and oxygenation dysfunction associated with LBW may increase intestinal susceptibility to inflammation, contributing to the risk of NEC. LBW infants often experience challenges in feeding and nutrient absorption, which can lead to oxidative stress and changes in gut microflora, factors known to contribute to the development of NEC. Understanding that LBW itself may be an independent risk factor for NEC, it is important for healthcare practitioners to pay special attention to infants with this condition, regardless of prematurity status. Careful care and a more intensive preventive approach may be necessary to reduce the risk of NEC in LBW babies, whether born prematurely or at term. Integration of this knowledge into clinical practice can support efforts to optimize care and health outcomes in newborns.[10-12]

Blood circulation disorders

The balance of blood circulation in newborn babies plays a central role in maintaining the health of organs and body systems, including the digestive tract. Blood circulation imbalance, especially in the intestine, has been identified as a significant risk factor that can increase the likelihood of necrotizing enterocolitis (NEC). Elucidating the relationship between medical conditions that affect blood flow and the risk of NEC is important in efforts to better prevent and manage this condition. Babies who have hypotension or low blood pressure have a higher risk of developing NEC. Hypotension can result in decreased blood flow to vital organs, including the intestines, and cause disruption

of oxygenation and nutrition, which can trigger inflammation and necrosis in the intestines. Certain medical conditions, such as blood circulation disorders that affect blood flow to the intestines, can be direct triggers for the development of NEC. This imbalance can be caused by various factors, including vascular abnormalities or systemic circulation disorders that lead to uneven blood distribution throughout the body. Medical conditions that cause ischemia, namely a lack of blood and oxygen supply to tissues, can worsen the risk of NEC. Intestinal ischemia can create an environment that supports the growth of pathogenic bacteria, inflammation, and, ultimately, intestinal tissue necrosis. Systemic medical conditions such as septic shock or generalized inflammatory conditions can affect blood circulation and increase the risk of NEC. The body's response to infection or inflammation can lead to adverse vascular changes at local and systemic levels. Careful monitoring of blood pressure and circulatory function in newborns, especially those with risk factors such as prematurity or low birth weight, may be key in preventing NEC. Early intervention to correct circulatory disorders and treat hypotension may help reduce the risk of developing NEC. Through a deeper understanding of the role of blood circulation imbalances in NEC risk, healthcare practitioners can direct more proactive and timely care. Efforts to identify and treat medical conditions that may affect intestinal blood flow may be a critical step in reducing the disease burden of NEC in the newborn population.[13-15]

Infection and inflammation

Infection and inflammation play a central role in the pathophysiology of necrotizing enterocolitis (NEC), a serious and potentially lethal condition in newborns. A deeper understanding of how bacterial contamination in the gastrointestinal tract can trigger an inflammatory response leading to the development of NEC has major implications for the development of effective prevention and management strategies for this condition. NEC often begins with bacterial contamination in the digestive tract. Newborn babies, especially those who are premature, have a digestive tract that is susceptible to colonization by pathogenic bacteria. This contamination can stimulate an inflammatory response and cause an imbalance in the intestinal microflora, factors that are closely related to the development of NEC. Infection can involve local areas around the intestines or can be systemic, influencing the whole body. Local inflammatory responses in the intestine can develop into detrimental inflammation and can lead to tissue necrosis. Meanwhile, systemic inflammatory responses can worsen the condition and increase the severity of NEC. Dysbiosis, or an imbalance of normal gut microflora, can occur as a result of infection and inflammation. A decrease in the diversity of good bacteria (probiotics) and an increase in pathogenic bacteria can create an environment that supports the development of NEC. Some bacteria, especially certain types such as *Clostridium difficile*, can produce toxins that are detrimental to the intestines. These toxins can damage the intestinal lining and trigger an inflammatory reaction, serving as a potential trigger for the development of NEC. Babies with predisposing factors such as prematurity or low birth weight may be more susceptible to infection and inflammation. These factors may create conditions that favor the development of NEC in infants who are already in a more fragile health situation. Prevention of infection and inflammation, particularly through hygiene practices and food intake management, maybe a key step in reducing the risk of NEC. Careful monitoring for signs of infection and inflammation in newborns is also important for early detection and timely intervention. Through this understanding, research and treatments focused on managing gut microflora, preventing infection, and controlling inflammation can become an integral part of clinical efforts to reduce the incidence and impact of NEC in the newborn population.[16-18]

Feeding

Formula feeding of newborns, especially premature babies, has been the focus of research in the context of the risk of necrotizing enterocolitis (NEC). The association between early formula feeding and increased risk of NEC highlights the importance of

exclusive breastfeeding practices and slow introduction of foods in protecting the gut health of preterm infants. Premature babies have digestive tracts that are not yet fully mature, and formula feeding can put extra stress on a still-vulnerable digestive system. Epidemiological studies show that premature babies who are fed formula have a higher risk of developing NEC compared to those who are breastfed. Breast milk has a unique composition and contains many immune factors, digestive enzymes, and essential nutrients that support gut health. Exclusive breastfeeding has been associated with a reduced risk of NEC, and breast milk is known to have protective properties against infection and inflammation. Apart from the type of food given, the way food is introduced also has an important role. The gradual introduction of food gives the baby's body the opportunity to adapt to changes in nutrition and prevents excessive stress on the digestive system. Exclusive breastfeeding for the first six months of life, in accordance with global health organization recommendations, has been shown to provide significant protection against the risk of NEC in premature infants. The immunological and nutritional components in breast milk provide optimal support for the growth and development of the baby's intestines. The choice of type and management of nutrition in premature babies requires a careful approach. Formula feeding may be necessary in some cases, but this decision should be carefully considered and carried out under close supervision. Feeding premature babies should be discussed with the healthcare team, and medical consultation should be undertaken to adjust the nutritional plan according to the baby's individual needs. By understanding the link between formula feeding and the risk of NEC in premature infants, healthcare practitioners can focus on more thoughtful nutritional approaches to reduce the risk of this serious complication. Parental education and interdisciplinary support are also important to promote understanding of the benefits of exclusive breastfeeding and the introduction of carefully managed feedings in premature infants.[18,19]

Use of antibiotics

Giving antibiotics to newborns, especially if done excessively or without clear indications, is a critical issue that can impact intestinal health and increase the risk of necrotizing enterocolitis (NEC). Understanding how antibiotics can alter the balance of intestinal microflora opens a window for increased awareness and wiser management of antibiotic use in newborns. Healthy intestinal microflora play an important role in digestive function, immunity, and protection against invasion by pathogenic bacteria. The use of antibiotics can bother this balance by reducing the number and diversity of good bacteria in the intestine. Antibiotics not only target pathogenic bacteria but can also damage the good bacteria that are essential for gut health. This can create an environment that favors the growth of pathogenic bacteria and increases the risk of intestinal inflammation, an early step in the development of NEC. Excessive use of antibiotics can increase the risk of overgrowth of Candida-type yeast in the intestine. Candida overgrowth can significantly alter the intestinal microflora and cause intestinal inflammation. The balance of intestinal microflora plays a role in modulating the immune system. Drastic changes in microflora composition can affect the body's immune response, increasing the risk of inflammation and intestinal damage. The importance of administering antibiotics based on clear indications and accurate diagnosis is becoming increasingly crucial. Inappropriate administration of antibiotics can lead to negative impacts that far outweigh the benefits. In situations where administration of antibiotics is necessary, careful monitoring and careful management should be implemented. The choice of antibiotic, duration of use, and monitoring of intestinal microflora are important factors to minimize negative impacts. Efforts to restore the balance of intestinal microflora after antibiotic use may involve administering probiotics and other strategies that support the growth of good bacteria. Through awareness of the impact of antibiotic use on intestinal microflora and the associated risks of NEC, healthcare practitioners can be more cautious in the use of antibiotics in newborns. A judicious approach to

antibiotic selection and use, as well as effective preventive measures, can help maintain gut health and reduce the risk of developing NEC in this more vulnerable population.[19,20]

4. Conclusion

Necrotizing enterocolitis (NEC) is a serious condition in newborns involving inflammation and intestinal necrosis. A number of complex risk factors that interact and contribute to the development of this condition have been identified. An in-depth understanding of these risk factors has major implications for the prevention, diagnosis, and management of NEC in newborns. Babies born prematurely, especially before 32 weeks gestation, have a higher risk of developing NEC. Low birth weight, regardless of prematurity status, remains a significant independent risk factor. Imbalances in blood circulation, especially in the intestines, can increase the risk of NEC. Hypotension and other medical conditions that affect blood flow to the intestines can be potential triggers. Infection and inflammation, both systemic and local, play a central role in the development of NEC. Bacterial contamination in the digestive tract can trigger an inflammatory response that contributes to the pathophysiological process of NEC. Formula feeding, especially in premature infants, is associated with an increased risk of NEC. The importance of providing exclusive breastfeeding and introducing foods slowly to protect the newborn's intestinal health. Excessive use of antibiotics or without clear indications can change the balance of intestinal microflora and increase the risk of NEC. The importance of judicious selection and use of antibiotics to minimize negative impacts on gut health.

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