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# BENEFITS OF COLOSTRUM THERAPY FOR PREMATURE INFANTS ADMITTED TO NEONATAL UNITS: AN INTEGRATIVE LITERATURE REVIEW

# BENEFÍCIOS DA COLOSTROTERAPIA PARA BEBÉS PREMATUROS INTERNADOS EM UNIDADES NEONATAIS: UMA REVISÃO INTEGRATIVA DA LITERATURA

# BENEFICIOS DE LA COLOSTROTERAPIA PARA NEONATOS PREMATUROS INGRESADOS EN UNIDADES NEONATALES: UNA REVISIÓN INTEGRATIVA DE LA LITERATURA

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# ABSTRACT

**Introduction:** Oropharyngeal administration of colostrum in preterm infants can have a positive impact on the immune system and overall health, reducing the incidence of necrotizing enterocolitis (NEC) and late-onset sepsis, as well as improving short-term outcomes. With colostrum therapy being a minimally invasive technique that can enhance immunological and anti-inflammatory benefits.

**Objective:** To synthesize the available scientific literature on the benefits of colostrum therapy for preterm infants admitted to Neonatal Intensive Care Units (NICU).

**Methods:** A systematic literature review was conducted using the PICO methodology to refine the research question. The article search was carried out on the PubMed and Ebsco/Medline platforms, published between January 2009 and April 2023. Five articles were carefully selected, following the guidelines outlined in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) method throughout the process.

**Results:** The main findings reported in the selected articles suggest that colostrum therapy offers significant benefits for preterm infants, including shorter time to achieve enteral feeding, improvement in the immune system, reduced risk of necrotizing enterocolitis and late-onset sepsis, and lower incidence of intraventricular hemorrhage. It was also observed that colostrum therapy promotes mother-infant bonding and facilitates breastfeeding.

**Conclusion:** Based on the analyzed studies, the benefits of colostrum therapy are evident. However, a weak level of evidence was found in the selected articles due to methodological issues, highlighting the need to improve the methodological quality of future studies to support the widespread implementation of this practice in Neonatal Units, both nationally and internationally.


**Keywords:** Colostrum; Neonatal Intensive Care Units; Premature Newborn.

# RESUMO

**Introdução:** A administração orofaríngea de colostro em recém-nascidos prematuros pode ter um impacto positivo no sistema imunológico e na saúde geral, reduzindo a incidência de enterocolite necrosante (EN) e sépsis tardia, além de melhorar os resultados a curto prazo. A colostroterapia é uma técnica minimamente invasiva que pode potencializar os benefícios imunológicos e anti-inflamatórios.

**Objetivo:** Fazer uma síntese da literatura científica disponível sobre os benefícios da colostroterapia para bebés prematuros internados em Unidades de Cuidados Intensivos Neonatais (UCIN).

**Métodos:** Foi realizada uma revisão sistemática da literatura utilizando a metodologia PICO para refinar a questão de investigação. A pesquisa de artigos foi realizada nas plataformas PubMed e Ebsco/Medline, publicados entre janeiro de 2009 e abril de 2023. Cinco artigos foram cuidadosamente selecionados, seguindo as diretrizes delineadas no método PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analysis*) durante todo o processo.

**Resultados:** Os principais resultados relatados nos artigos selecionados sugerem que a colostroterapia oferece benefícios significativos para os recém-nascidos prematuros, incluindo menor tempo para atingir a via entérica, melhoria no sistema imunológico, redução do risco de enterocolite necrosante e sépsis tardia, e menor incidência de hemorragia intraventricular. Observou-se também que a colostroterapia promove o vínculo mãe-bebé e facilita a amamentação.

**Conclusão:** Com base nos estudos analisados, os benefícios da colostroterapia são evidentes. No entanto, foi encontrado um nível de evidência fraco nos artigos selecionados devido a questões metodológicas, destacando a necessidade de aumentar a qualidade metodológica dos estudos futuros para apoiar a implementação generalizada desta prática nas Unidades Neonatais, tanto a nível nacional como internacional.


**Palavras-chave:** Colostro; Recém-Nascido Prematuro; Unidade de Cuidados Intensivos Neonatais.

# RESUMEN

**Introducción:** La administración orofaríngea de calostro en recién nacidos prematuros puede tener un impacto positivo en el sistema inmunológico y la salud general, reduciendo la incidencia de enterocolitis necrotizante (EN) y sepsis tardía, además de mejorar los resultados a corto plazo. A calostroterapia una técnica mínimamente invasiva que puede potenciar los beneficios inmunológicos y antiinflamatorios.

**Objetivo:** Hacer una síntesis de la literatura científica disponible sobre los beneficios de la calostroterapia para los bebés prematuros ingresados en Unidades de Cuidados Intensivos Neonatales (UCIN).

**Métodos:** Se realizó una revisión sistemática de la literatura utilizando la metodología PICO para refinar la cuestión de investigación. La búsqueda de artículos se realizó en las plataformas PubMed y Ebsco/Medline, publicados entre enero de 2009 y abril de 2023. Se seleccionaron cuidadosamente cinco artículos, siguiendo las directrices delineadas en el método PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analysis*) durante todo el proceso.

**Resultados:** Los principales resultados reportados en los artículos seleccionados sugieren que la calostroterapia ofrece beneficios significativos para los recién nacidos prematuros, incluyendo un menor tiempo para alcanzar la alimentación enteral, mejora del sistema inmunológico, reducción del riesgo de enterocolitis necrotizante y sepsis tardía, y menor incidencia de hemorragia intraventricular. También se observó que la calostroterapia promueve el vínculo madre-bebé y facilita la lactancia.

**Conclusión:** Con base en los estudios analizados, los beneficios de la calostroterapia son evidentes. Sin embargo, se encontró un nivel de evidencia débil en los artículos seleccionados debido a problemas metodológicos, lo que destaca la necesidad de mejorar la calidad metodológica de los estudios futuros para apoyar la implementación generalizada de esta práctica en las Unidades Neonatales, tanto a nivel nacional como internacional.

**Descriptores:** Calostro; Recien Nacido Prematuro; Unidades de Cuidados Intensivos Neonatales.

# INTRODUCTION

Preterm births are considered a global public health issue, affecting approximately fifteen million babies annually, of which about 1 million do not survive due to prematurity-related complications[1]. Estimates indicate that around 30% of preterm newborns (NB) face complications arising from an immature immune response and underdeveloped digestive tract, resulting in significant long-term sequelae such as growth deficits, delayed neurodevelopment, vision and hearing impairments, causing irreparable damage to child health[2].

In Portugal, the prematurity rate has been increasing, accounting for about 8% of annual births[3]. Preterm newborns present deficiencies in both innate and adaptive immunity, increasing the risk of infections. In this context, late-onset sepsis and necrotizing enterocolitis (NEC) are significant causes of morbidity and mortality, especially in very low birth weight (VLBW) newborns[4]. Abnormal gut flora is a risk factor for NEC and sepsis in preterm NB[5]. Multifactorial mechanisms for NEC and late-onset sepsis require the presence of an immature immune system and triggers that disturb the normal gut microbiome, resulting in an increase in potentially pathogenic bacteria and an exaggerated inflammatory response[6].

In addition to the increased infection risk due to immunological immaturity, many preterm NB lack the protection provided by breast milk, particularly colostrum, which can act as a protective factor and ensure better recovery for babies admitted to a Neonatal Intensive Care Unit (NICU)[2]. The oropharynx and intestinal tract of a fetus are continuously exposed to immunological factors present in the amniotic fluid until 40 weeks of gestation, stimulating the fetal immune system and accelerating intestinal maturation[6]. After birth, breast milk replaces the functions of amniotic fluid, containing a wide variety of microbiomes and biologically active components, including growth factors, immunoglobulin A, platelet-activating factor (PAF), lactoferrin, and oligosaccharides[6].

Exclusive breastfeeding has been shown to reduce infection rates in preterm NB[4] and is associated with better neurodevelopmental outcomes[7]. The immunoactive factors in breast milk provide specific benefits through oropharyngeal contact, promoting immunocompetence via immunomodulation mechanisms[6].

Some VLBW babies frequently present unstable clinical symptoms at birth, such as irregular breathing, weak sucking, and poor gastrointestinal function. Fasting or slow progression to enteral feeding is common in preterm babies, preventing them from receiving all the protective biological factors provided by human milk[7]. Most preterm NB under 32 weeks of gestation are fed through a tube, increasing the risk of NEC and sepsis due to the absence of oropharyngeal exposure to immunoactive factors during this critical period[6].

One way to provide the advantages of breast milk to preterm NB is through oropharyngeal administration of colostrum, known as colostrum therapy[4]. Colostrum, defined as the breast milk produced during the first five days after birth, is rich in immunological and growth factors, with high concentrations of proteins and minerals and low concentrations of fats and lactose. Its most important characteristic is the presence of large quantities of protective factors, actively influencing the development of the immune system in preterm NB[8].

Colostrum therapy does not involve swallowing movements by the NB. During this intervention, a small amount of colostrum is placed directly on the oropharyngeal mucosa, inside the oral cavity, for absorption. According to Lopes J *et al*[2], colostrum therapy involves using maternal colostrum as an immune, rather than nutritional, therapy. The technique involves administering 0.2 ml of colostrum (0.1 ml on each side of the cheek) every 3 hours for five consecutive days, starting between 24-96 hours after birth[2]. Colostrum contains secretory immunoglobulin A, growth factors, lactoferrin, and cytokines. When in contact with the oral mucosa, colostrum interacts with the local lymphoid tissue, modulating the inflammatory response in the NB, stimulating the immune system, and promoting gastrointestinal maturation[7]. The intervention is safe and well-tolerated, even for smaller and sicker VLBW preterm NB[4].

The objective of this literature review is to understand the benefits that colostrum therapy can offer preterm newborns (NB) admitted to Neonatal Intensive Care Units (NICU). This study was motivated by the observation that preterm NB, often lacking breast milk, could potentially benefit from colostrum therapy regarding their health condition. Thus, this study aims to explore, through a review of the available international literature, the possible positive effects of colostrum therapy in preterm NB, particularly in the context of NICU admission.

The purpose of this study is to provide a comprehensive view of colostrum therapy, highlighting its potential efficacy in reducing the incidence of necrotizing enterocolitis and late-onset sepsis, as well as improving the immunological development and overall recovery of preterm NB. Additionally, the study aims to identify gaps in the existing literature and areas for future research, to support the widespread implementation of this practice in neonatal units at both national and international levels.

# METHODS

## *Ethical Considerations*

It was not necessary to request approval from the Ethics Committee, as this work constitutes secondary research. During the formulation of the problem, principles of clarity, objectivity, and precision were respected. The research path was designed to ensure that the results obtained would be relevant to nursing care interventions and/or practices. In the specific case of the chosen theme, the goal was to identify the benefits of colostrum therapy for premature babies admitted to Neonatal Intensive Care Units (NICU). The data obtained from the selected studies were analyzed while strictly respecting the results of these investigations. The citation of authors followed academic and scientific best practice standards.

## *Study Type*

A Clinical nursing practice is based on the most current scientific evidence, which translates into high-quality nursing care. This practice, known as evidence-based nursing, involves the collection, interpretation, evaluation, and implementation of clinical data essential for professional decision-making[9].

This study is an Integrative Literature Review, motivated by the need to implement high-quality care based on the most recent scientific evidence. This method allows for the inclusion of studies with different methodological designs (quantitative and qualitative), providing a more comprehensive understanding of the phenomenon studied.

## *Methodological Procedures*

This integrative literature review synthesized and analyzed research studies on the use of colostrum therapy as an intervention to improve clinical outcomes for preterm newborns in Neonatal Intensive Care Units (NICU). The following methodological steps were followed, as proposed by Mota de Sousa[10]: (i) identification of the research question; (ii) definition of the inclusion and exclusion criteria for the studies; (iii) definition of the information to be extracted from the studies; (iv) analysis of the included articles; (v) presentation and discussion of the results; and (vi) synthesis of the conclusions.

As the first methodological step, the following research question was formulated: "What are the benefits of colostrum therapy for a preterm baby admitted to a NICU?". The research question was reformulated using the PICO methodology[11], which includes categories to be addressed in this integrative literature review. "P" corresponds to Population, "I" to Intervention, "C" to Comparison/Control, and "O" to Outcomes. Based on this, the following research question was formulated: "What are the benefits (Outcomes) of colostrum therapy (Intervention) for preterm infants (Population) admitted to a NICU (Comparison)?".

In the second methodological step, the following inclusion and exclusion criteria were established: the inclusion criteria were as follows: articles published between January 2018 and March 2024; full text available online; written in Portuguese and English; studies conducted with preterm newborns using maternal colostrum as therapy. The exclusion criteria included all duplicate articles, articles whose titles were not relevant to the PICO question, articles in languages other than Portuguese and English, articles that were not free or not available online, and articles do not present in the databases included in this integrative review methodology.

After formulating the PICO research question, data collection was conducted in March 2024 in the PubMed and EBSCO/Medline databases. The keywords used were: "Colostrum", "Infant", "Premature", and "Neonatal Intensive Care". These descriptors were organized using the boolean operators OR and AND as follows: ("Colostrum" AND "Infant" AND "Premature" AND "Neonatal Intensive Care").

For the article selection task, a first reading of the title and abstract was conducted to verify consensus regarding their inclusion and/or exclusion, following the predefined criteria. If the title and abstract were of interest or inconclusive, the entire document was read to minimize the loss of valuable information for the study. If the article was deemed relevant to the study, it was included. After this initial screening, ten articles were identified. Of these, one was removed due to duplication, resulting in nine articles. After reading the title, one article was excluded. Subsequently, reading the abstracts led to the exclusion of four more articles, resulting in five articles selected for full reading. All five articles were retrieved and included in the final review.

The PRISMA flowchart[12] details the article selection process, illustrating the steps of identification, screening, eligibility, and inclusion of the studies in the review (Figure 1↗).

# RESULTS

In order to address the proposed objectives, several articles were reviewed, and their content was analyzed. The characteristics and main results obtained are summarized in Chart 1↗, listed in chronological order of publication.

# DISCUSSION

Colostrum therapy has shown promising benefits for preterm newborns (NB) in Neonatal Intensive Care Units (NICU). According to the study by Moreno-Fernandez *et al*[4], preterm NB who received colostrum therapy reached enteral nutrition sooner than those who did not receive the intervention. This finding suggests a significant metabolic advantage for the underdeveloped gastrointestinal tract of preterm NB, potentially reducing the presence of morbidities associated with prematurity. Early enteral feeding is crucial to prevent intestinal atrophy, which can increase the risk of localized inflammation, feeding intolerance, necrotizing enterocolitis (NEC), and hospital-acquired infections. Therefore, colostrum therapy may play a vital role in promoting gastrointestinal health and preventing severe complications.

Additionally, Moreno-Fernandez *et al*[4] observed that preterm NB who received oropharyngeal colostrum exhibited significantly higher IgA levels, particularly after fifteen to thirty days of administration. IgA is a crucial immunoglobulin for protecting mucous membranes from pathogens. The elevation of IgA levels indicates an improvement in the neonates' immune profile, suggesting that colostrum therapy may strengthen the immune system of preterm NB, making them less susceptible to infections.

On the other hand, the longitudinal study by Wang *et al*[7], expected to be completed in 2024, has not yet fully clarified the effects of oropharyngeal colostrum administration on the intestinal microbiome and metabolites. Previous studies suggest that the gut microbiome plays a critical role in the immune and brain development of newborns. Wang *et al*[7] hypothesized that colostrum therapy could increase intestinal bacterial diversity, promote the abundance of bifidobacteria and other dominant microbiota, and enhance the production of short-chain fatty acids. These fatty acids are essential for reducing vascular damage caused by oxidative stress, protecting the integrity of the intestinal barrier, and preventing prematurity-related diseases through modulation of the gut-brain axis. Although the final results are not yet available, the raised hypothesis suggests that colostrum therapy may significantly impact intestinal health and immune development in preterm NB.

The results of the study by OuYang *et al*[6] indicated a potential lower incidence of necrotizing enterocolitis and late-onset sepsis in preterm infants with gestational age ≤ 32 weeks who received oropharyngeal colostrum therapy. Additionally, these NB showed a lower incidence of intraventricular hemorrhage and a shorter time to reach full enteral feeding. These findings are particularly important because NEC and late-onset sepsis are two of the leading causes of morbidity and mortality in preterm NB. The reduction in the incidence of these conditions suggests that colostrum therapy could significantly improve clinical outcomes in these babies. The reduced time to achieve full enteral feeding also indicates a quicker and more efficient recovery of the gastrointestinal tract.

Moreover, OuYang *et al*[6] reported a lower incidence of severe intraventricular hemorrhage in the group that received oropharyngeal colostrum therapy. Intraventricular hemorrhage is a severe complication that can result in long-term neurological damage. The reduction of this condition reinforces the potential of colostrum therapy to improve not only immediate outcomes but also the long-term outcomes of preterm NB. These authors further emphasize the importance of conducting large, multicenter, and well-designed studies to confirm the effects of oropharyngeal colostrum administration.

Lopes *et al*[2] highlight the importance of colostrum therapy in strengthening the mother-infant bond. Active participation of the mother in the treatment of her preterm baby can promote breastfeeding and emotional bonding, which is crucial for the healthy development of the NB. This psychosocial aspect is often underestimated, but it is essential for the overall well-being of both the baby and the mother.

Despite the promising results, some authors suggest the need for more robust evidence before implementing colostrum therapy as a standard practice in NICUs. Wang *et al*[7] emphasize the need for additional studies to fully understand the mechanisms by which colostrum therapy affects the gut microbiome and metabolites. Furthermore, OuYang *et al*[6] recommend conducting multicenter and well-designed studies to validate the benefits observed in their preliminary findings.

Considering the results of the reviewed studies, it is evident that colostrum therapy offers multiple benefits for preterm NB. However, it is important to recognize the limitations of the existing studies. Most of the studies have relatively small sample sizes and are conducted in single centers. Large, multicenter, and well-designed studies are needed to confirm the beneficial effects of colostrum therapy and to establish clear guidelines for its clinical implementation.

Colostrum therapy shows promise as an intervention to improve the health and clinical outcomes of preterm NB. Its implementation has the potential to reduce the incidence of severe complications associated with prematurity, strengthen the immune system, and promote faster and more efficient recovery. However, more research is needed to consolidate this evidence and optimize treatment protocols.

### *Study Limitations*

This study presents some limitations that should be considered when interpreting the results. First, the integrative review is based on secondary studies, which may introduce biases related to the methodologies used in the original studies. Additionally, the research was limited to articles published in Portuguese and English and available in the PubMed and Ebsco/Medline databases, which may have excluded relevant studies published in other languages or other databases. Another limitation is the relatively small number of studies included in the review, which may not provide a comprehensive view of all aspects related to colostrum therapy in preterm newborns. The methodological quality of the selected studies also varied which could affect the robustness of the conclusions. Finally, the lack of multicenter and well-designed studies on the subject limits the generalization of the results.

### *Contributions to Nursing*

Despite the limitations, this study offers important contributions to nursing practice. Colostrum therapy, as a minimally invasive intervention, shows promise in improving clinical outcomes for preterm newborns admitted to Neonatal Intensive Care Units (NICU). The results suggest that colostrum therapy can accelerate enteral feeding, strengthen the immune system, reduce the incidence of necrotizing enterocolitis and late-onset sepsis, and promote the mother-infant bond. This information can guide nurses in the implementation of evidence-based practices that improve the quality of neonatal care. Furthermore, by highlighting the need for more robust and well-designed research, this study contributes to the advancement of scientific knowledge in the field of nursing, encouraging future studies that may provide stronger evidence for clinical practice. The adoption of colostrum therapy in neonatal units, based on scientific evidence, can lead to significant improvements in the health and development of preterm newborns, directly reflecting on the quality of nursing care.

# FINAL CONSIDERATIONS

This integrative literature review has shown that, although the scientific evidence on the clinical impact of colostrum therapy in preterm newborns admitted to Neonatal Intensive Care Units (NICU) is still limited, the potential benefits of this intervention are promising. Several reviewed studies demonstrated that colostrum therapy can accelerate the time required to achieve full enteral feeding, improve immune response, reduce the incidence of necrotizing enterocolitis (NEC) and late-onset sepsis, and decrease the occurrence of intraventricular hemorrhage. Additionally, colostrum therapy fosters valuable bonding between the mother and newborn, strengthening breastfeeding and emotional attachment.

The results indicate that colostrum therapy provides a significant metabolic advantage to the underdeveloped gastrointestinal tract of preterm NB. The observed elevation of IgA levels suggests a strengthening of the immune system, increasing resistance to infections. Studies have also raised important hypotheses about the impact of colostrum therapy on the intestinal microbiome and the production of beneficial metabolites, though more evidence is needed to confirm these effects.

However, despite the promising results, there is a clear need for additional, large, multicenter studies to confirm these findings and establish robust clinical guidelines for the implementation of colostrum therapy. Most of the reviewed studies present limitations such as small sample sizes and being conducted in single centers, which may influence the generalization of the results.

In conclusion, colostrum therapy is a safe and potentially beneficial intervention for preterm newborns in NICUs. To consolidate this evidence and support the widespread implementation of this practice, further research is needed to assess the impact of colostrum therapy on major clinical outcomes in preterm babies. The adoption of this practice in neonatal units at both national and international levels could significantly contribute to improving neonatal care and clinical outcomes for these vulnerable infants.

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CR: Study design, data analysis, review and discussion of results.
AM: Study design, data analysis, review and discussion of results.
IB: Study design, data analysis, review and discussion of results.
MG: Study design, data analysis, review and discussion of results.
AD: Study coordination, study design, data collection, storage and analysis, review and discussion of the results.
All authors have read and agreed with the published version of the manuscript.

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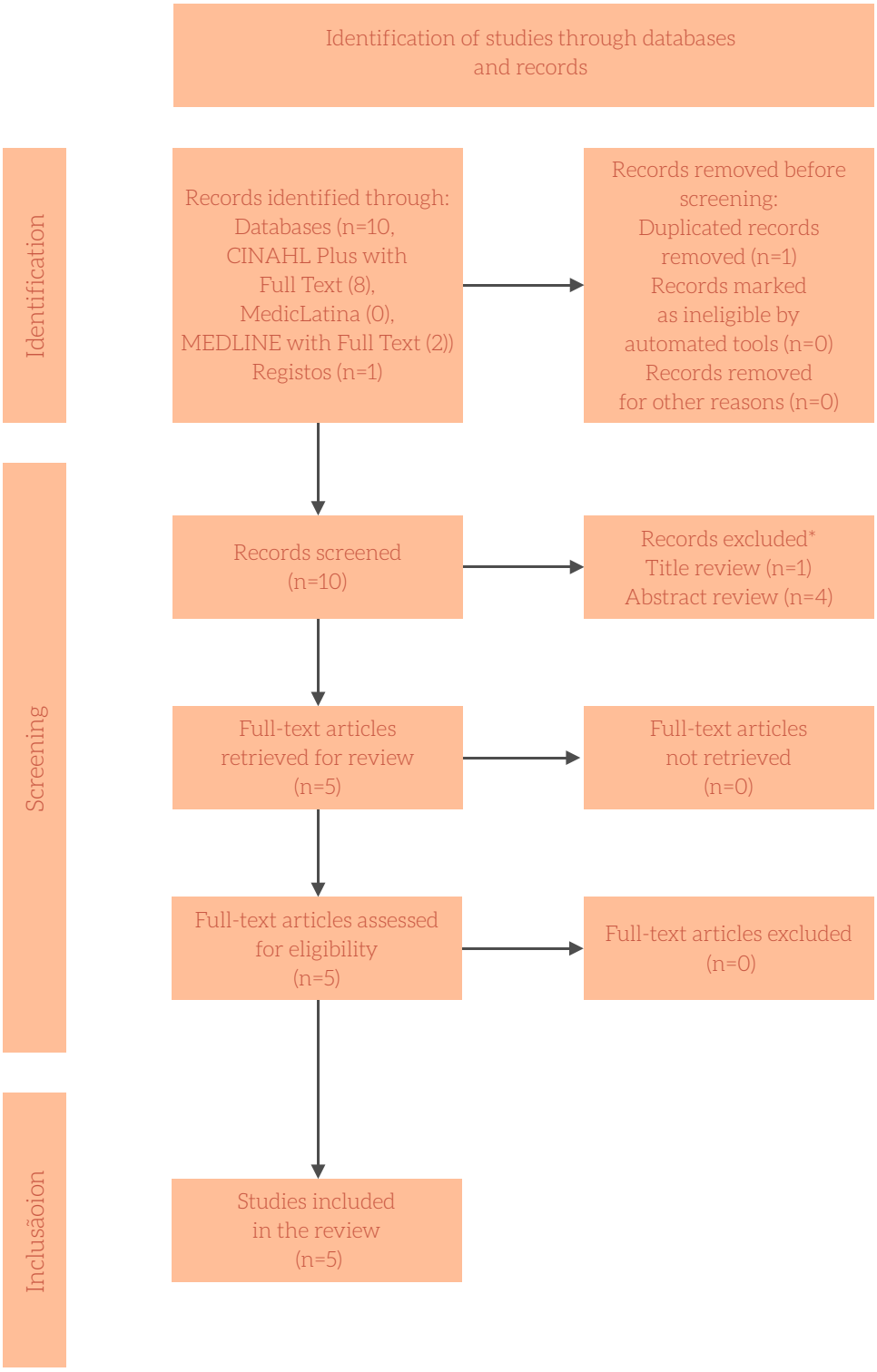


Figure 1 – PRISMA flow diagram representing the research process.

Chart 1 – Results of studies supporting the benefits of colostrum therapy.

| Title, Authors, (Year), Reference, and Study Design | Objectives | Interventions/ Phenomena of Interest | Results and Conclusions |
|---|---|---|---|
| Oropharyngeal Administration of Maternal Colostrum: A Literature Review, Lopes J. *et al* (2018)[2]. Literature Review. | Review the benefits of oropharyngeal administration of colostrum in preterm infants. | Review of existing studies on colostrum therapy. | Colostrum therapy provides immunological benefits and strengthens mother-infant bonding. |
| Improvement of Immunological Response Mediated by Oropharyngeal Administration of Colostrum in Preterm Neonates, Moreno-Fernandez *et al* (2019)[4]. Cohort Study. | Assess the impact of oropharyngeal administration of colostrum on the immune system of preterm newborns. | Oropharyngeal administration of colostrum in preterm newborns. | Longer time to reach enteral nutrition; increased IgA levels after 15-30 days; improved immune profile. |
| Exploratory Study on the Use of Colostrum Therapy in a Neonatal Unit in a Brazilian Maternity, Nascimento *et al* (2020)[8]. Exploratory Study. | Explore the effects of colostrum therapy in preterm infants in a neonatal unit. | Oropharyngeal administration of colostrum in preterm newborns. | Benefits in reducing hospital infections; improvement in gastrointestinal development. |
| Oropharyngeal Administration of Colostrum to Prevent Necrotizing Enterocolitis and Late-Onset Sepsis in Preterm Infants with Gestational Age ≤ 32 Weeks: A Single-Center Randomized Controlled Pilot Trial, OuYang *et al* (2021)[6]. Randomized Controlled Trial. | Evaluate the efficacy of oropharyngeal colostrum administration in preventing necrotizing enterocolitis and late-onset sepsis in preterm infants with gestational age ≤ 32 weeks. | Oropharyngeal administration of colostrum in preterm infants with gestational age ≤ 32 weeks. | Lower incidence of necrotizing enterocolitis and late-onset sepsis; lower incidence of intraventricular hemorrhage; shorter time to achieve full enteral feeding. |
| Oropharyngeal Administration of Colostrum Targeting Gut Microbiota and Metabolites in Very Preterm Infants: Protocol for a Multicenter Randomized Controlled Trial, Wang *et al* (2023)[7]. Multicenter Randomized Controlled Trial Protocol | Investigate the impact of colostrum therapy on gut microbiota and metabolites in very preterm infants. | Oropharyngeal administration of colostrum in preterm newborns. | Hypothesis of increased intestinal bacterial diversity; promotion of bifidobacteria abundance; short-chain fatty acid production; protection of intestinal barrier integrity. |