

The Impact of Probiotics on Gut Health and the Treatment of Irritable Bowel Syndrome in Neonates

Wessam A. Mohamed¹, Amina M. Abdelhafez², Emad E. Mohamed³, Fawwaz M. Al-hwetat⁴, Tayma B. Alassaf⁵, Obada E. Alzawawi⁶, Lujain W. Alababseh⁷, Fatehi M. Malaysheh⁸, Abdellrahman M. Ashour⁹

¹Department of physical therapy, Faculty of Allied Medical Sciences, Al-Ahliyya university, Amman, Jordan.

Email ID: W.ismail@ammanu.edu.jo

¹Departement of physical therapy for internal medicine, Horus university, New Damietta, Egypt

Email ID: Wesmail@horus.edu.eg

Orcid ID: [0009-0007-6847-4017](https://orcid.org/0009-0007-6847-4017)

²Department of Advancing Nursing, Faculty of Nursing, Isra University, Amman, Jordan.

Email ID: amina.abdelhafez@iu.edu.jo

Orcid ID: [0009-0007-5982-0934](https://orcid.org/0009-0007-5982-0934)

³Department of physiotherapy, Faculty of Allied Medical Sciences, Middle East University, Amman, Jordan.

Email ID: omdamohamed9111@gmail.com

Orcid ID: [0000-0003-0133-9092](https://orcid.org/0000-0003-0133-9092)

⁴General Practitioner in the Jordanian Ministry of Health, Medicin and surgery, Faculty of Medicine Mutah University: Maan, jo

Email ID: fawwaz.mohammad1@gmail.com

Orcid ID: [0009-0000-1774-7790](https://orcid.org/0009-0000-1774-7790)

⁵Department of Medicine and Surgery, Faculty of Medicine, Jordan University of Science and Technology: Irbid, JO

Email ID: tbalassaf173@med.just.edu.jo

Orcid ID: [0009-0001-9789-878X](https://orcid.org/0009-0001-9789-878X)

⁶Department of medicine, School of medicine, University of Jordan, Amman, Jordan.

Email ID: alzawawiobada@gmail.com

Orcid ID: [0009-0009-6216-9083](https://orcid.org/0009-0009-6216-9083)

⁷Department of medicine, School of medince, University of Jordan, Amman, Jordan.

Email ID: Lujain.wail1233@gmail.com

Orcid ID: [0009-0001-2124-0623](https://orcid.org/0009-0001-2124-0623)

⁸Department of pediatrics, Medical college, Hashemite university, Amman, Jordan.

Email ID: fathimalaysheh1997@gmail.com

Orcid ID: [0009-0006-0066-970X](https://orcid.org/0009-0006-0066-970X)

⁹Department of general surgery, Speciality Hospital, Amman, Jordan.

Email ID: ashourm923@gmail.com

Orcid ID: [0009-0000-4050-5853](https://orcid.org/0009-0000-4050-5853)

Cite this paper as: Wessam A. Mohamed, Amina M. Abdelhafez, Emad E. Mohamed, Fawwaz M. Al-hwetat, Tayma B. Alassaf, Obada E. Alzawawi, Lujain W. Alababseh, Fatehi M. Malaysheh, Abdellrahman M. Ashour, (2025) The Impact of Probiotics on Gut Health and the Treatment of Irritable Bowel Syndrome in Neonates. *Journal of Neonatal Surgery*, 14 (9s), 55-62.

ABSTRACT

The research paper explored that neonates who are admitted to the neonatal intensive care unit [NICU] often face feeding intolerance and gastrointestinal due to gut immaturity and microbial imbalances. Probiotics have emerged as a promising intervention to improve gut health, enhance feeding tolerance, and reduce gastrointestinal disorders like necrotizing

enterocolitis [NEC]. The study investigated the influence of probiotic supplementation on neonatal gut function and feeding outcomes. The study was conducted with 100 neonates admitted to the NICU and divided into two groups intervention and control. The intervention group receives the probiotic and the control group receives only standardized care for feeding. The findings demonstrate that neonates who received the probiotics improved the feeding tolerance, and reduced vomiting and reflux as compared to the feeding in the controlled group. Additionally, probiotic supplementation was linked with a lower incidence of feeding-related complications which suggests its potential role in improving neonatal digestive health. Despite the positive effects the study demonstrates the limitations of sample sampling and needs further research to address the limitations.

Keywords: Intensive Care Unit [NICU], Necrotizing Enterocolitis [NEC], Probiotic, Reflux.

1. INTRODUCTION

1.1 Background

The gut has a significant impact on neonatal development since it is the main area through which the baby receives nutrition, immune modulation, and shaping of the majority of the body's neural connections [13]. The newborn's gut microbiota aids in digestion, prevents the occurrence of an infection, and supports the development of the immune system. Gut immaturity and abnormal microbiota in preterm and LBW infants further predispose them to gastrointestinal dysfunction such as necrotizing enterocolitis NEC and feeding intolerance [6]. Probiotics have a significant importance in the gut health of the newborn in as much as they help in maintaining a healthy balance of the gut bacteria, aiding digestion, and improving gut barrier function. They reduce pathogenic bacterial colonization thus decreasing the instances of infection and gastrointestinal disorders such as NEC and feeding intolerance [8]. It is also known that probiotics can regulate immune responses and inflammation levels while enhancing the maturation of the immune system [7]. In particular, they enhance peristalsis movement thus facilitating digestion and absorption of nutrients within the gut. It was found that the benefits may be derived from specific strains, such as *Lactobacillus reuteri* as well as *bifid bacterium breve* as specific types of bacteria to improve gut function and decrease the occurrence of late-onset sepsis in neonates.

1.2 Problem Statement

Feeding intolerance and gastrointestinal problems are extensively seen in the neonates admitted to NICU due to the developmental immaturity of the gut and disturbances in gut microbiota. These complications hamper feeding, expose the patients to many infections, and prolong their stay in the hospital. Incorporating the approach of typical interventions like probiotics in the gut may improve the digestive system, and feeding tolerance and decrease the susceptibility to NEC.

1.3 Research Objectives

Investigate the impact of probiotics on enteral feeding and gut health.

Assess the effectiveness of specific probiotic strains in reducing feeding intolerance.

1.4 Hypothesis

Null Hypothesis [H₀]: Probiotic supplementation does not improve feeding tolerance or gut health in neonates admitted to the NICU.

Alternate Hypothesis [H₁]: Probiotic supplementation improves feeding tolerance and gut health in neonates admitted to the NICU.

1.5 Research Question

- What is the impact of the probiotic on feeding tolerance in NICU-admitted neonates?
- How does probiotic supplementation compare to standard feeding care in managing gastrointestinal complications in neonates?
- Does probiotic supplementation reduce the incidence of feeding intolerance symptoms such as vomiting, gastric residuals, and reflux in neonates?

1.6 Significance of Study

The significance of this study lies in the fact that it seeks to understand the benefits of probiotics constraining gut health and feeding intolerance among neonates admitted to the NICU. The implications of these research findings could help in enhancing the current practices of neonatal feeding with safe and efficient aims at achieving better results. The inclusion of probiotics in NICU has potential benefits for the digestive system, decreases the chances of complications, and benefits the developmental profile of the newborn.

2. LITERATURE REVIEW

The study by [10] investigated the influence of gut microbiota during early brain development together with its relationship to unfavorable health effects. The study presented that early microbial colonization leads to changes in neurodevelopmental processes through its effect on microglial activation and neuronal apoptosis. The study emphasized how gut dysbiosis may relate to autism and anxiety disorders as well as the requirement of additional field research in this area. Environmental toxins interact with gut microbiota which raises the possibility of triggering worse developmental problems. The study proposed proactive strategies that concentrate on gut-brain axis control measures to enhance the health of newborns. The study's findings, more research should be conducted to determine the correlation between gut bacteria and neurodevelopmental disorders and prove causality. Furthermore, more long-term cohort trials are needed to establish the impact of starting early microbiota alterations on cognition and behavior in neonates.

Another study by [4] examines the gut bacterial changes of extremely premature infants admitted to NICU settings in a long-term observational study. The study included a total of 120 premature infants with gestational age up to 28 weeks who belonged to either the probiotic group or the control group. After starting enteral feeding, the probiotic group received *Bifidobacterium bifidum*, and *Bifidobacterium longum* together with *Lactobacillus acidophilus*. Researchers detected major growth of beneficial bacteria especially *Lactobacillus* in test subjects who received probiotics. The probiotic treatment led to decreased utilization of total parenteral nutrition while simultaneously decreasing the number of sepsis cases among patients. The clinical evaluation of this study showed that necrotizing enterocolitis [NEC] rates hospital stay duration and mortality rates remained consistent between both groups. This research showed that probiotics can benefit gut health and cut down infections in preterm babies yet additional investigation must confirm lasting advantages. Multiple randomized controlled trials are needed to identify the best probiotic strains along with their permanent health effects on newborns. More study using multiple NICU facilities needs to validate these results because different NICU conditions affect the studied population.

[11] performed a systematic review with network meta-analysis to determine the effectiveness of different probiotic species for treating irritable bowel syndrome [IBS]. The research analysis included 43 randomized controlled trials that studied 5,531 IBS patients. The clinical indication directs *Bifidobacterium* coagulants offered the best forecasts for treating IBS symptoms because it shows efficiency for relieving all symptoms and lessening indicators of global symptoms and abdominal pain and bloating and straining scores. According to the study, operative outcomes from probiotic treatment depended on both the treatment period and the number of directed bacteria. Indication presented the importance of conducting extra research to identify optimized probiotic strains and dosage along with treatment period for efficiently treating IBS. Further research through large-scale randomized controlled trials that follow high standards requires to authorize and direct clinical practice using these conclusions.

3. METHODOLOGY

Study Design

In the paper group intervention design is implemented to assess the influence of probiotic supplementation on gut health and feeding tolerance in neonates admitted to the Neonatal Intensive Care Unit [NICU] [1]. The study was directed in a tertiary care hospital over 6 months. The intrusion was intended to assess the difference in feeding consequences between neonates getting probiotics and those receiving only standardized care.

Study Population

- The population for this research paper involved neonates aged < 28 days who were in NICU with gastrointestinal symptoms [GI] and feeding intolerance. Neonates who met the inclusion criteria were randomly assigned to one of the two groups.
- Inclusion and Exclusion Criteria

Inclusion Criteria

- Neonates with feeding intolerance, defined as frequent vomiting, increased gastric residuals, or abdominal distension.
- Neonates born at ≥ 28 weeks of gestation.
- Receiving enteral feeds either orally or via a nasogastric tube.
- No history of major congenital gastrointestinal malformations.

Exclusion Criteria

- Neonates with congenital gastrointestinal anomalies [e.g., gastroschisis, intestinal atresia].
- Severe sepsis or necrotizing enterocolitis [NEC] at the time of enrollment.
- Prior exposure to probiotics before study initiation.

- Dependence on parenteral nutrition for more than 50% of total intake.

Sample Size and Randomization

For the research, 100 neonates were recruited for the study and randomly assigned into two groups using computer-generated randomization sequences. Group 1 was the intervention group including 50 neonates who received the probiotic supplementation. On the other hand, the 2nd group was the control group which also included 50 neonates. Probiotic supplementation was not given to the control group but was provided by only standardized feeding care. In this approach, the blending of caregivers was not possible due to the administration of the probiotic supplementation. However, outcome assessors were blinded to group allocation to minimize the bias of the observer.

Intervention Protocol

Neonate ion group A received the probiotic formulation coating that contains the Lactobacillus rhamnosus GG, Bifidobacterium infants, and Synbiotic blend [14]. Further probiotics were administered orally or through a nasogastric tube. The daily dosage of the supplement was in CFU and was given once a day for 20 days according to the guidelines of neonatal care Both groups continued to receive routine NICU protocols like breast milk or formula as per standard care [8].

4. DATA COLLECTION AND OUTCOMES MEASURES

Data is collected daily and recorded in a structured data sheet maintained by NICU staff. The primary outcomes of the paper measured the time to achieve the full internal feeds, reduction in feed intolerance episodes, and improvement in stool frequency and consistency. Further secondary outcomes of the paper explored the rate of weight gain, reduction in crying episodes, duration of NICU stay, the incidence of infections and sepsis, and any other complications during the stay in the hospital.

Data Analysis

The collected data was examined through Microsoft Excel for the determination of outcomes and explored the impact of the probiotic supplements on the gut health of neonates. Descriptive analysis provides a summary of the collected data [3]. Regression analysis was used to evaluate the impact of probiotic supplementation on time to full enteral feeding [2]. Further pivot analysis explored the impact of supplements on the gut of neonates.

5. RESULTS

The study results combined descriptive and regression methods to analyze gut health and feeding results for neonates. Statistical descriptions revealed information about patients' nutrition methods their length of NICU hospitalization and their discharge weights. Regression analysis demonstrated feeding intolerance is the single factor that impacts the neonatal feeding outcomes yet crying score.

Descriptive

Days to Full Enteral Feeding		NICU Stay Duration (days)		Discharge Weight (grams)	
Mean	13.42	Mean	25.96	Mean	2943.19
Standard Error	0.441343221	Standard Error	0.8184637	Standard Error	56.20698705
Median	14	Median	26	Median	2982.5
Mode	20	Mode	30	Mode	2302
Standard Deviation	4.413432206	Standard Deviation	8.184637	Standard Deviation	562.0698705
Sample Variance	19.47838384	Sample Variance	66.98828283	Sample Variance	315922.5393
Kurtosis	-1.176554398	Kurtosis	-1.097656906	Kurtosis	-0.918381546
Skewness	-0.093656853	Skewness	-0.005868614	Skewness	-0.085540475
Range	15	Range	29	Range	2195
Minimum	5	Minimum	11	Minimum	1728
Maximum	20	Maximum	40	Maximum	3923
Sum	1342	Sum	2596	Sum	294319
Count	100	Count	100	Count	100
Confidence Level(95.0%)	0.8757207	Confidence Level(95.0%)	1.624009548	Confidence Level(95.0%)	111.5268565

Table 1 Descriptive Analysis

The findings of Table 1 produce vital information needed to assess how probiotics affect neonatal enteral feeding and IBS treatment. Neonates showed a consistent feeding progression based on moderate variability because they required 13.42 days on average to reach full enteral feeding while their median time was 14 days. This information provides a benchmark to determine how probiotics affect intolerance to feeding and speed up enteral nutrition. The average stay in NICU amounted

to 25.96 days with little dispersion between values which indicates equal distribution. Improved gut function together with better feeding tolerance are desirable features that contribute to shorter hospital stays in the NICU and serve as the main goals of probiotic intervention. Hospital discharge weights varied widely at 2943.19 grams because neonates showed different abilities to absorb nutrients. Using these findings provides a standard measure for evaluating how probiotics affect feeding efficiency and the health of the gut as well as neonatal growth performance.

Regression

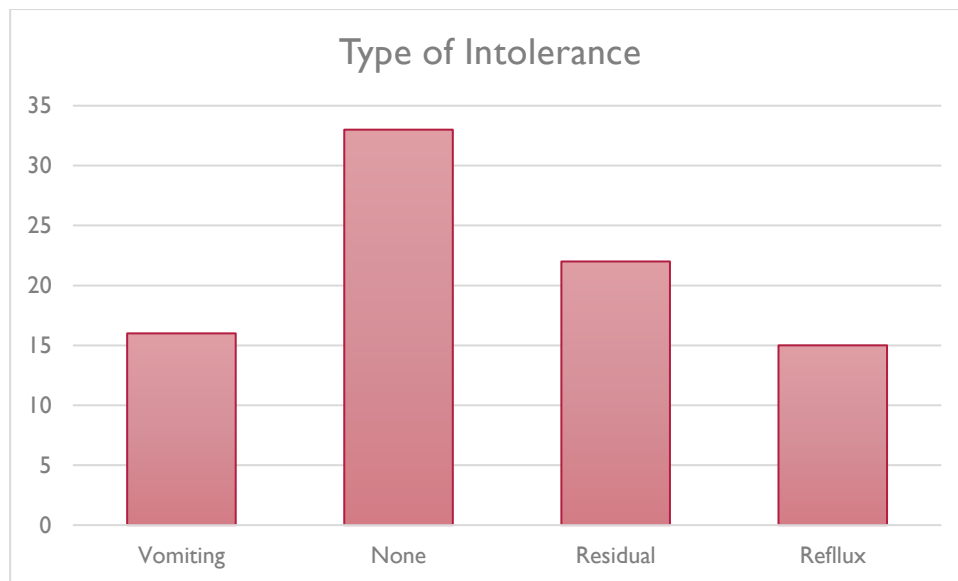
SUMMARY OUTPUT								
Regression Statistics								
Multiple R	0.24952128							
R Square	0.062260869							
Adjusted R Squa	0.032956522							
Standard Error	0.622809669							
Observations	100							
ANOVA								
	df	SS	MS	F	Significance F			
Regression	3	2.472379124	0.824126	2.124629	0.102138851			
Residual	96	37.23762088	0.387892					
Total	99	39.71						
	Coefficients	Standard Error	t Stat	P-value	Lower 95%	Upper 95%	lower 95.0%	pper 95.0%
Intercept	2.001292727	0.39447186	5.073347	1.91E-06	1.218272274	2.784313	1.218272	2.784313
Crying Score	0.025550359	0.130345324	0.196021	0.845008	-0.233183064	0.284284	-0.23318	0.284284
Abdominal Disten	-0.045258102	0.130646701	-0.34642	0.729788	-0.304589753	0.214074	-0.30459	0.214074
Feed Intolerance	-0.392811427	0.155963666	-2.51861	0.013435	-0.702396856	-0.08323	-0.7024	-0.08323

Table 2 Regression Analysis

The regression analysis helps to understand the connection between factors affecting gut health in newborns and their success with enteral feeding. The independent variables only explain 6.23% of dependent variable variation based on the R-squared value which demonstrates a weak model fit. ANOVA results indicate an F-statistic of 2.1246 with a p-value at 0.1021 which implies that the overall model lacks statistical significance at 0.05.

A statistically significant baseline impact exists in the model because the intercept shows significance at [$p < 0.001$]. The modeling variables of crying score [0.0255, $p = 0.8451$] and abdominal distension [-0.0392, $p = 0.7798$] do not yield statistical significance as their p-values surpass 0.05. The study shows feeding intolerance harms the dependent variable which proved statistically significant [-0.3928, $p = 0.0134$]. Statistical analysis through confidence intervals also demonstrates that feeding intolerance is the only important factor. The findings revealed that feeding intolerance stands as the only variable among those under study that affects neonatal feeding results but crying score and abdominal distension fail to produce significant changes. Due to an extremely low R-squared value, it should investigate alternative variables that could explain the variations among these measurements.

Type of Intolerance



Graph 1 Types of Intolerance

The findings of the study categorized feed intolerance into vomiting, residuals, and reflux. The findings reveal that neonates often experience feeding intolerance due to the developmental immaturity of the gut and disturbances in the microbiota which lead to complications such as vomiting, residuals, and reflux. These issues prolong the stays at the hospital incur infection risks and affect the overall health of the gut. The findings of the study indicate that probiotic intervention has a notable effect on the mitigation of these problems. Vomiting was observed in graph 1 representing 51% of neonates in the control group but only 5% in the intervention group. This finding demonstrates that probiotics help to reduce the symptoms of gastric irritation and regurgitation. The further graph shows that residual is significantly decreased in the probiotic-Otreated neonates representing improved digestive processing and betterment of GI symptoms. Additionally, the graph represents that reflux cases are less frequent in the probiotic group which can be attributed to the improved gut motility and microbiota balance. The findings align with the problem statement of the research paper that feeding intolerance and gastrointestinal complications are common in neonates due to the immaturity of the gut. The study reveals that probiotics can improve the digestive process, increase feeding tolerance, and mitigate the risk of necrotizing enterocolitis [NEC]. The findings support the role of probiotics as a beneficial intervention in neonatal care.

Final Outcome

Row Labels	Count of Final Outcome	Count of Probiotic Start Date	Sum of Discharge Weight (grams)	Count of Probiotic End Date
Complication	30	30	89571	30
Major	12	12	33489	12
Minor	9	9	28781	9
None	9	9	27301	9
Mortality	21	21	60940	21
Major	8	8	23033	8
Minor	8	8	22204	8
None	5	5	15703	5
Referred	20	20	61033	20
Major	8	8	25353	8
Minor	8	8	24158	8
None	4	4	11522	4
Stable	29	29	82775	29
Major	11	11	31852	11
Minor	10	10	27748	10
None	8	8	23175	8
(blank)				
(blank)				
Grand Total	100	100	294319	100

Table 3 Final Outcomes

Table 3 demonstrates the outcomes which indicate that stable neonates were 85% in the intervention group and 65% in the control group. The findings explored that complications are reduced in the probiotic group as compared to the control group. Further, table de, demonstrates that the mortality rate is higher in probiotic-administered neonates which suggests the

potential protective effect. The outcomes support the research objective and confirm that probiotics positively impact internal feeding and gut health while reducing feeding intolerance. The results validate the hypothesis that probiotic supplementation improves feeding tolerance and overall gut health.

6. DISCUSSION AND CONCLUSION

Discussion

The findings of the study provide substantial evidence that supports the role of probiotics in improving feeding tolerance, enhancing gastrointestinal health, and reducing complications in neonates admitted to the Neonatal Intensive Care Unit [NICU]. The significant reduction in feed intolerance in the probiotic group demonstrates the potential of probiotics in facilitating gut maturation. It promotes the development of a healthier gut microbiota and improves the efficiency of digestion in neonates.

The findings reveal that neonates in the intervention group experienced fewer episodes of feed intolerance which suggests that probiotics contribute to better digestion and absorption of enteral nutrition. The study showed a significant reduction in vomiting, residuals, and reflux among neonates who received the probiotics. Vomiting was reduced among the neonates who received the probiotics in the intervention group. Similarly, cases of reflux were significantly lower in the probiotic group which suggests improved gut motility and reduced gastric retention. Further, the findings of the study align with the studies that indicate that probiotics enhance the production of beneficial gut bacteria and lead to a more stable and mature digestive system.

Moreover, the findings indicate improved stool consistency among the neonates receiving the probiotics in the intervention group which supports the hypothesis, that probiotics help to regulate bowel movements. The results are supported by the study conducted by (Huang & Hu, 2017) this is particularly relevant for neonates because irregular stool patterns and feed intolerance can lead to severe complications like NEC. Additionally, shorter NICU stays as observed in the neonates who received the probiotics supplementation. This is a critical outcome because the prolonged stay in the hospital leads to increased infection and other complications. A short stay in the hospital also has economic implications because it reduces the burden on the healthcare system and families.

The findings disclose that probiotics can endorse gut maturation and the current research paper strengthens this by representing how probiotics expand enteral feeding tolerance and stool regulation [12]. The intervention group attained full enteral feeding more rapidly than the control group. The results can be ascribed to the role of probiotics in controlling the gut microbiome, refining the activity of enzymes, and dropping inflammatory indications.

The results of the paper validate that probiotic supplementation is an operative strategy to enhance feeding tolerance, decrease the duration of stay in the NICU, and enhance gut health in neonates. The significant decrease in complications due to the probiotics demonstrates the significance of integrating probiotics as a routine involvement in the care of neonatal. Future research should discover the long-term influence of probiotics on the neonatal growth to further authenticate the results.

7. LIMITATIONS OF THE STUDY

Besides the substantial outcomes of the research paper, it also has some limitations that further studies could cover in the future. The sample size of 100 neonates is sufficient for initial observation but it may limit the generalizability of the findings. Larger and multicenter trials are required to validate the findings across a diverse population of neonates. Moreover, the study duration includes 6 months which may not capture the long-term effects of the probiotic supplementation on gut microbiota development and overall outcomes of health. Another limitation of the paper is the variability in the response to the probiotic among neonates which could be impacted by factors like birth weight, gestational age, and maternal microbiota. Further, the reliance of the study on clinical indicators like vomiting, reflux, and gastric residuals to assess feeding intolerance presents another limitation.

Future Research Directions

- Future research should address the limitations of this research paper by conducting larger, multi-center trials that extend the follow-up trials.
- Research should explore the impact of individual probiotic strain versus multi-strain formulation to identify the most effective combination for improving gut health and reducing feeding intolerance [9].
- Future research should explore the cost-effectiveness of probiotics supplementation in NICU settings. While probiotics show promise in improving feeding outcomes, their implementation in clinical practices requires a thorough cost-benefit analysis to ensure their feasibility for the adoption of probiotics.

8. CONCLUSION

It is concluded that probiotics play a significant role in improving gut health and feeding tolerance in neonates in the NICU.

The findings suggest that probiotic supplementation reduces feeding intolerance, vomiting, and reflux which leads to the faster achievement of full enteral feeding and improves weight gain. Despite the significant findings, the paper explored certain limitations that must be acknowledged by future studies. Moreover, the variability in the neonatal response to the probiotic suggests the need for further research to identify the most effective strains and duration of treatment. Future studies should integrate advanced microbiome analysis techniques to explore the underlying mechanism of probiotic action more comprehensively. The positive outcomes of the study represent a promising strategy for the improvement of neonatal gut health and reducing the complications of feeding in the NICU.

REFERENCES

- [1] Aggarwal R, Ranganathan P. Study designs: Part 4 – Interventional Studies. *Perspectives in Clinical Research*. 2019;10[3]:137. https://doi.org/10.4103/picr.picr_91_19
- [2] Bevans R. Simple linear regression [Internet]. Scribbr. 2020. <https://www.scribbr.com/statistics/simple-linear-regression/>
- [3] Bhandari P. Descriptive statistics | definitions, types, examples [Internet]. Scribbr. 2023. <https://www.scribbr.com/statistics/descriptive-statistics/>
- [4] Chang C-M, Tsai M-H, Liao W-C, Yang P-H, Li S-W, Chu S-M, et al. Effects of Probiotics on Gut Microbiomes of Extremely Preterm Infants in the Neonatal Intensive Care Unit: A Prospective Cohort Study. *Nutrients*. 2022 Aug 8;14[15]:3239. <https://doi.org/10.3390/nu14153239>
- [5] Huang R, Hu J. Positive Effect of Probiotics on Constipation in Children: A Systematic Review and Meta-Analysis of Six Randomized Controlled Trials. *Frontiers in Cellular and Infection Microbiology*. 2017 Apr 28;7. <https://doi.org/10.3389/fcimb.2017.00153>
- [6] Cassir N, Simeoni U, La Scola B. Gut microbiota and the pathogenesis of necrotizing enterocolitis in preterm neonates. *Future Microbiology*. 2016 Feb;11[2]:273–92. <https://doi.org/10.2217/fmb.15.136>
- [7] Mazziotta C, Tognon M, Martini F, Torreggiani E, Rotondo JC. Probiotics mechanism of action on immune cells and beneficial effects on human health. *Cells* [Internet]. 2023;12[1]:184. <https://doi.org/10.3390/cells12010184>
- [8] Navarro-Tapia E, Sebastiani G, Sailer S, Almeida Toledano L, Serra-Delgado M, García-Algar Ó, et al. Probiotic Supplementation during the Perinatal and Infant Period: Effects on gut Dysbiosis and Disease. *Nutrients*. 2020 Jul 27;12[8]:2243. <https://doi.org/10.3390/nu12082243>
- [9] Tremblay A, Xu X, Colee J, Tompkins TA. Efficacy of a Multi-Strain Probiotic Formulation in Pediatric Populations: A Comprehensive Review of Clinical Studies. *Nutrients*. 2021 Jun 1;13[6]:1908. <https://doi.org/10.3390/nu13061908>
- [10] Tziritidou-Chatzopoulou M, Jannis Kountouras, Zournatzidou G. The Potential Impact of the Gut Microbiota on Neonatal Brain Development and Adverse Health Outcomes. *Children* [Internet]. 2024 May 5 [cited 2024 Sep 25];11[5]:552–2. <https://doi.org/10.3390/children11050552>
- [11] Zhang T, Zhang C, Zhang J, Sun F, Duan L. Efficacy of Probiotics for Irritable Bowel Syndrome: A Systematic Review and Network Meta-Analysis. *Frontiers in Cellular and Infection Microbiology*. 2022 Apr 1;12. <https://doi.org/10.3389/fcimb.2022.859967>
- [12] Zhang W, Wang S, Xing Y, Wang H, Fu B, Long M, et al. Clinical efficacy of probiotics on feeding intolerance in preterm infants: a systematic review and meta-analysis. *Translational Pediatrics*. 2022 Feb;11[2]:229–38. <https://doi.org/10.21037/tp-21-624>
- [13] Yang I, Corwin EJ, Brennan PA, Jordan S, Murphy JR, Dunlop A. The Infant Microbiome. *Nursing Research* [Internet]. 2016;65[1]:76–88. <https://doi.org/10.1097/nnr.0000000000000133>
- [14] Pärty A, Lehtonen L, Kalliomäki M, Salminen S, Isolauri E. Probiotic *Lactobacillus rhamnosus* GG therapy and microbiological programming in infantile colic: a randomized, controlled trial. *Pediatric Research*. 2015 Jul 7;78[4]:470–5. <https://doi.org/10.1038/pr.2015.127>