- ***Basic Research***

Effect of Early Oral Colostrum Administration on Prevention of Late Onset Sepsis among Preterm Infants

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Abstract

Background and aim: Late-onset sepsis remains a major contributor to death among preterm infants. Early oral administration of maternal colostrum has emerged as a promising immunomodulatory intervention to reduce infection risk in preterm infants. The study aimed to evaluate the effect of early oral colostrum administration on prevention of late onset sepsis among preterm infants. **Research design**: A quasi-experimental research design was utilized to achieve the aim of the study. **Setting**: The study was conducted at neonatal intensive care unit in El Manial University Hospital. **Sample**: A purposive sample of eighty preterm infants were allocated into two groups: the study group received 2 ml of mother's colostrum administered to the oral mucosa every three hours for the first 72 hours of life, while the control group received standard care. Clinical monitoring for signs of sepsis was conducted up to NICU discharge. Neonatal characteristics were collected by using a structured questionnaire and Sepsis Prediction Score were used for both groups four times. Data was analyzed using SPSS version 29, with p-values <0.05 considered statistically significant. **Results:** The incidence of late-onset sepsis was significantly lower in the study group compared to the control group ($p = 0.00$). Additionally, infants in the study group demonstrated more achievement of breastfeeding, shorter NICU stay and reduced inflammatory markers. **Conclusion:** Early oral colostrum administration is a safe, low-cost, and effective intervention for reducing the risk of late-onset sepsis in preterm infants. **Recommendation**: Implementation of EOCA protocols in NICU settings is recommended to improve neonatal outcomes and also educating pregnant women and mothers about the importance and benefits of early colostrum feeding is crucial for newborn health.

Keywords: Colostrum, Oral administration, Late-onset sepsis, Preterm infants.

Introduction

Premature infants often have multiple complications after birth, such as necrotizing enterocolitis, late-onset sepsis, bronchopulmonary dysplasia, and retinopathy of prematurity (Fu, et al, 2023). Late-onset sepsis (LOS) is a significant cause of morbidity and mortality among preterm infants. Infants who develop late-onset sepsis are at higher risk of in-hospital morbidities, death, and poor neurodevelopmental outcomes among survivors. Nearly 18% of neonatal mortality across the world has occurred due to neonatal sepsis infections (Flannery, et al., 2022).

Late-onset sepsis was defined as the isolation of a pathogenic species from a normally sterile body fluid such as blood or cerebrospinal fluid, beyond 72 hours after birth. Culture-positive LOS was defined by positive blood or cerebral spinal fluid culture after 3 days of age. These infections can be caused by bacteria such as coagulase-negative Staphylococci and Staphylococcus aureus, fungi such as Candida species, and viruses including herpes simplex virus and cytomegalovirus. Overall, LOS is a major contributor to morbidity and mortality in both term and preterm newborn infants, particularly in those receiving care in neonatal intensive care units (Flannery& Puopolo, 2024).

Neonatal sepsis is a clinical syndrome caused by pathogenic bacteria, and can invade the blood circulation, affect the growth, and attack the reproduction system of neonates during the 1st month of life, which is characterized by hemodynamic changes and other systemic symptoms of infection. It also can lead to the failure of body organs and thereby causing damage to the tissues resulting in death of the neonates (Balayan, et al, 2020). Colostrum is a deep, yellow or orange color, this is because it contains high levels of beta carotene. It is rich in immune, growth and tissue repair factors. Colostrum is a complex biological fluid which helps in the development of immunity in the newborn. It contains significant quantities of complement components that act as natural anti-microbial agents to actively stimulate the maturation of an infant’s immune system (Carr, et al., 2021).

Mother's colostrum is an infant’s first immunological protective agent because it contains immunomodulating bio-factors such as lactoferrin, oligosaccharide, and immunoglobulin (Ig). Lactoferrin is a glycoprotein containing rich anti-microbial, anti-inflammatory, antioxidant, and immunomodulating functions. Lactoferrin is relatively high in concentration in colostrum and specifically promotes a healthy microbiome, protects the intestine against injuries due to oxidative stress and inflammation, and prevents pathogenic translocation into the bloodstream, which prevents LOS (Slouha, et al.,2023 & Martín-Álvarez et al., 2020).

Nurses had an important role in administration of colostrum safely to provide the benefits of colostrum to all sick and preterm infants who cannot access oral breast feeds and can be used even in the critically ill, ventilated, fragile infants. Nurses can use a syringe or sterile cotton swab to drop or apply a small amount of colostrum in a newborn's mouth. When in contact with the oral mucosa, colostrum interacts with local lymphoid tissue and can modulate an inflammatory response in newborns (Romero-Maldonado, et al,2022). Nurses also can place colostrum in the buccal cavity by a syringe or gloved finger. Colostrum is not swallowed by the infant, but it is absorbed locally by the buccal mucosa (Salve, et al, 2023).

Significance of study:

According to a report from the World Health Organization (WHO) (2024), approximately 15 million babies are born premature worldwide every year and declared that sepsis is a global health priority. Despite effective treatment strategies, including appropriate antimicrobial treatment, it remains a leading cause of neonatal death and a significant contributor to

neonatal morbidities in neonatal intensive care units and the community. It is therefore imperative to identify the preventive measures that reduce the risk of sepsis in the neonatal period.

Late onset sepsis that can lead to death, increased morbidities, prolonged hospital stay, increased cost of care, and worse long-term outcomes among survivors (Coggins, & Glaser, 2022). Studies have shown that colostrum administration is a safe and simple procedure that reduces the incidence of necrotizing enterocolitis, late-onset sepsis, severe intraventricular hemorrhage, feeding intolerance, shortens the time to full enteral feeding, hospitalization time in preterm infants, cost-effective and easily implementable practice that may improve overall preterm outcomes (Fu, et al, 2023, OuYang et al., 2021 & Sharma et al., 2020).Without early exposure to maternal colostrum, preterm infants are more susceptible to morbidities; hence, the importance of medical advances for administration of colostrum (Slouha, et al, 2023). Hereafter the current study will undertake to early feeding with colostrum on minimizing the late-onset sepsis among preterm infants. Hopefully, the results will set standard care that can be followed to administer colostrum to preterm infants in NICU and provide guidance and recommendations that should be reflected in pediatric nursing education and providing evidence-based data that can develop nursing practice and research in the field of pediatric surgery nursing.

Aim of the study

This study aimed to evaluate the effect of early oral colostrum administration on prevention of late onset sepsis among preterm infants.

Research Hypotheses

H_1: Preterm infants who were administered early oral colostrum had less chances of developing late onset sepsis than in the control group.

H_2: Preterm infants who were fed early oral colostrum had lower sepsis prediction score than in the control group.

H_3: Preterm infants who were given early oral colostrum had a shorter hospital stay than in the control group.

Research design

A Quasi experimental research design was utilized in the current study. Aquasi-experimental design is one type of experimental design that is very similar to the true experimental design except an absence of randomization or control. A non-equivalent group design is the most prevalent sort of quasi-experimental design and will be used to achieve the aim of the current study. In non-equivalent group design, the researcher picks two groups that look comparable and feasible, but only one group (study) receives the intervention while the other (control) will receive the standard care (American Psychological Association, 2024).

Setting

The current study was conducted at the neonatal intensive care unit in the El Manial University Hospital (Kasr El Aini Hospital) which affiliated to Cairo University Hospitals. It consists of two units; provide secondary and tertiary level of care for high-risk neonates. Each one of the two units consists of four parts (2 ICUs, one isolation room for infected cases and a growing room). The study will be conducted in ICU and in the growing room. The capacity of the two units is 50 incubators. The two units well equipped and provide care for free to neonates all over Egypt.

Sample

A purposive sample of 80 preterm infants who fulfill the inclusion criteria were equally divided into control group and study group. Each group included 40 preterm infants. The

number of admissions in NICU was 480 preterm infants in 2022. The inclusion criteria for preterm infants will be both genders, newly admitted within 24 hours after birth, NPO, their gestational age between 32 to 36 weeks or their birth weight > 2500gm, free from sepsis, have sepsis prediction score less than (1) and those who need only secondarily level of care. The exclusion criteria of preterm infants; preterm infants of infected mothers and whose mother was exposed to premature rupture of membrane.

The determination of sample size was based upon the following calculation formula (http://www.ifad.org/gender/tools/hfs/ anthropometry).

$$n = \frac{T^2 \times p(1-p)}{m^2}$$

Description:

n = required sample size.

t = confidence level at 95% (standard value of 1.96).

p = estimated prevalence of preterm infants in 2022 at the NICU (0.048).

m = margin of error at 5% (standard value of 0.05).

$$n = \frac{(1.96)^2 \times 0.048(1-0.048)}{(0.05)^2} = 72.2$$

Tools of data collection:

Two tools were used for data collection:

Tool (1). A structured questionnaire: It was constructed by the researchers after extensive reviewing of the related literature, and it includes three parts:

Part I: preterm infants' data: It includes questions about demographic and clinical data of the preterm infants such as gender, weight, gestational age, age on admission, medical diagnosis, connections, length of hospital stay, type of feeding on discharge and type of milk.

Part II: physiological parameters of preterm infants: It involves temperature, heart rate, respiratory rate and oxygen saturation.

Part III: laboratory inflammatory biomarkers: it comprises WBCs, CRP, and blood culture.

Tool (2). Sepsis Prediction Score: this tool was adopted from Sofouli (2023). This tool comprises clinical and physiological parameters that have been identified as early indicators of neonatal sepsis. The score is applied at specific time intervals to support early identification and timely intervention. It includes 8 items: temperature, feeding volume, platelet count, blood glucose level, CRP, circulatory changes (capillary refill time (CRT) > 5 s, hypotension), increase of oxygen requirement and deterioration of respiratory function (apneas or need for mechanical ventilation). Each scored (1) point with total points of items is (8) the minimum point is (0) which indicates no sepsis while the maximum point is (8) which proves late onset sepsis. The higher the score, the higher the possibility of LOS. A score of 0-<3 indicated Low possibility of sepsis, 3-<5 indicated Very strong suspicion of sepsis and 5-8 indicated that Sepsis is definite.

Tool Validity and reliability:

Data collection tools were submitted to three experts in the field of pediatric nursing to test the content and face validity. Modifications of the tools have been done according to the experts' judgment on clarity of sentences, appropriateness of content and sequence of items. The Sepsis Prediction Score demonstrated strong content validity, as it was developed based on a comprehensive review of current literature and evaluated by a panel of experts in neonatology, nursing, and infectious diseases. The tool also showed criterion-related validity, as its predictive ability was assessed against confirmed clinical diagnoses and laboratory markers of sepsis. These validation steps ensured the tool's relevance and accuracy in

identifying neonates at risk for late-onset sepsis (Sofouli, 2023). In the current study, the score was applied consistently by trained healthcare professionals to maintain inter-rater reliability and enhance the objectivity of sepsis risk assessment across participants. The reliability of the tool using Cronbach alpha was 0.85.

Ethical consideration:

Primary approval obtained from research ethical committee at the faculty of nursing, Cairo University. Mothers of preterm infants (or family members who attend with the infant) who participated in the study were informed about the aim, procedure, benefits, and nature of the study and a written consent was obtained by the researcher from them. The researcher emphasized that participation in the study was voluntary, and participant can refuse to participate in the study without any reason and obtained data will be only used for the research purpose. The anonymity and confidentiality issues of information were assured, and they have the right to withdraw from the study at any time during the study without any effect on the care provided to their children.

Procedure:

Official permissions obtained from the director of the Obstetrics and Gynecology Hospital and from the head of NICU. In the first visit a written formal consent was obtained from the mothers after explanation of the aim, and nature of the study. After getting acceptance from mothers to participate in the study, one mother was assigned to the study group and another on to control group and so on until completing the number of samples. Firstly, the researcher had been taught the mother the appropriate techniques to express breast milk by hand or with an electric or manual pump using demonstration pictures and videos. Mothers asked to bring her personal breast pump. If the mothers have no pump, the researcher brought breast pumps to each mother to be used personally.

Also, the researchers told the mother that freshly expressed breast milk can be stored at room temperature for up to 4 hours, in the refrigerator for up to 4 days, in the ice compartment of the fridge for up to 2 weeks or in the freezer for about 6 months. The mother requested to attend the NICU for 3 consecutive days to express her breast milk and giving it to the researchers. If the mothers unable to express her breast milk in the hospital, she recommended to express it at home and store the milk in fridge then bring it the next day to the NICU.

In the first day, the researchers got the permission from the physician that the preterm infant has been administered 1-2 ml of colostrum in oral cavity immediately within 24 hours after birth, every 3 hours, for 72 hours. The researchers filled in the preterm infants' data sheet and LOS prediction score from the study and control group. Data about neonates for both the control and study groups were obtained by the researchers by checking the preterm infants' medical records on individual bases (tool1). Also, sepsis prediction score (tool II) was filled 24 hours after birth prior to the intervention which was taken about 20-25 minutes.

Next, the researchers introduced themselves to the mothers and the nurses of the unit and gave each mother of preterm infants of the study group a sterile cup and asked to perform the expression of breast milk on it after proper hand and breast washing. Also, the researchers selected a two skillful nurse one of them is working day duty and the other nurse is working on night duty and discussed with them the aim of the study and data collection method. Also, the researchers demonstrated to the nurses how to give the colostrum in the infant's mouth with appropriate amount (2ml) and the researchers told the nurses about frequency of colostrum administration. The researcher started to give the preterm infant the first dose of colostrum at 10 am and the 2nd dose at 1pm. Then the researchers asked the nurses to help

them complete the remaining 6 doses (4 pm, 7 pm, 10 pm, 1 am, 4 am and 7 am) and help the researchers to complete the data collections. After the intervention at 72 hours, at one week and on discharge; the researchers filled the physiological parameter (too 1, part II), the laboratory inflammatory markers (tool 1, part III) and LOS prediction score (tool 2) from the study and control group. The researchers visited the NICU 3 days weekly (Sunday, Tuesday and Thursday) until finishing the total sample of preterm infants and all of them discharged from NICU.

Statistical design

The collected data were scored, tabulated, and analyzed by computer using statistical package for the social sciences (SPSS) program, version 29. A two-way MANOVA was used to test for the overall differences between the two groups. Also, the t-test was used for comparison between the two groups at each time. Pearson correlation coefficient was used to study correlations between variables. The level of significance for all tests was set at $p<0.05$. The reliability of the tool using Cronbach alpha was 0.85.

Results:

Table (1) shows that the demographic and clinical characteristics of the study and control groups were largely comparable. No statistically significant differences were observed between groups regarding gender distribution ($p = 0.49$), gestational age ($p = 0.74$), weight on admission ($p = 0.11$), mode of delivery ($p = 0.50$), primary diagnosis on admission ($p = 0.82$), or method of oxygen support ($p = 0.59$), indicating a balanced baseline across groups. However, a significant difference was noted in age at admission, with the study group admitted significantly earlier than the control group (mean ± SD: 2.08 ± 1.37 vs. 5.65 ± 2.20 hours, $p = 0.00$). The same table also shows that feeding practices on discharge showed marked differences between the two groups. The study group had a significantly higher proportion of newborns discharged on breastfeeding (42.5% vs. 12.5%, $p = 0.00$), and among those receiving bottle feeding, expressed breast milk was more commonly used in the study group compared to the control group (39.1% vs. 2.9%, $p = 0.00$). Although the length of NICU stay was shorter in the study group (mean ± SD: 25.70 ± 17.17 vs. 33.83 ± 20.52 days), with no statistical significance difference ($p = 0.06$).

Table (2) detects that there was a statistically significant difference in respiration rate between the study and control groups over time ($p = .049$). Both groups demonstrated a general decline in respiration rate from baseline to discharge; however, the reduction was more marked in the study group, from 64.02 ± 9.56 breaths/min at baseline to 48.6 ± 4.71 at discharge, compared to a decline from 66.03 ± 10.51 to 44.05 ± 2.43 in the control group. For pulse rate, the study group demonstrated a consistent and substantial reduction from baseline (148.40 ± 22.24) to discharge (118 ± 12.8), while the control group exhibited an increase at 72 hours (173.30 ± 8.70) before a slight decline at discharge (119.90 ± 11.13). This parameter showed a highly significant difference between groups ($p = .000$). Body temperature also differed significantly between groups over time ($p = .000$). The study group maintained relatively stable temperature readings, the mean increasing slightly from 36.02 ± 1.01 to 37.0 ± 0.11by discharge. whereas, the control group exhibited a more pronounced rise, peaking at 37.97 ± 0.47 at one-week post-intervention before slightly decreasing to 37.01 ± 0.12 at discharge. In contrast, there was no significant difference in oxygen saturation was found between the two groups across the measured time points ($p = .626$). Both groups showed an overall mean improvement, with the study group increasing from 82.4 ± 2.44 to 96.50 ± 2.41 and the control group from 83.80 ± 2.53 96.85 ± 2.14.

Table (3) reveals that the analysis of laboratory biomarkers revealed statistically significant differences between the study and control groups over time in white blood cell (WBC) counts and C-reactive protein (CRP) levels (p = .0000). The mean of WBC counts in the study group increased from baseline 4.96 ± 1.02 to a peak at 72 hours 7.85 ± 2.09, followed by a decline to near-baseline levels at discharge 5.65 ± 1.69. While, the control group exhibited a markedly higher and more variable response, rising from 5.41 ± 1.06 at baseline to 17.1 ± 12.7 at one week, before slightly decreasing to 6.41 ± 1.06 at discharge. Also, CRP mean levels differed notably between groups. In the study group, the mean CRP increased modestly from 0.35 ± 0.02 mg/L at baseline to 3.19 ± 3.26 mg/L at one week, then decreased to 1.15 ± 0.77 mg/L at discharge. Conversely, the control group showed a pronounced increase from 0.48 ± 0.03 mg/L to a peak of 9.29 ± 7.58 mg/L at one week, followed by a modest decline to 1.08 ± 0.48 mg/L at discharge.

Figure (1) illustrates that the blood culture results across the four time points demonstrated a statistically significant difference between the study and control groups (p = 0.00). At baseline, all participants in the study and control groups had negative blood cultures. By 72 hours after the intervention, all neonates in both groups remained culture-negative, except for a single positive result in the control group. However, by one-week post-intervention, the proportion of negative cultures in the study group declined modestly to 87.5%, while a marked reduction was observed in the control group, where only 35.0% remained negative. Positive culture rates were notably higher in the control group (65.0%) compared to the study group (12.5%). At discharge, all participants in the study group had negative blood cultures (100%), compared to 95.0% in the control group, where two neonates (5.0%) still tested positive.

Table (4) indicates that significant differences between the study and control groups were observed across the means of all sepsis prediction score variables. The study group demonstrated significantly lower incidence rates for fever (>38°C) (p=.001), decreases in feeding volume (p=.020), platelet count <150,000/mm³ (p=.009), and blood glucose fluctuations >50% (p=.010). Additionally, CRP >1 mg/dL (p=.016), circulatory changes (p=.049), increased oxygen requirements (p=.001), and respiratory function deterioration (p=.006) were all significantly lower in the study group over time. The same table also shows that there was a statistically significant difference between the study and control groups regarding the total sepsis predictionscore over time (p = .000).

Table (5) reveals that there was no statistically significant difference between preterm neonates in both groups regarding sepsis prediction score total means prior to intervention (p = 0.13) and on discharge (p = 0.15), but there was a statistical significant difference between preterm neonates in both groups regarding their sepsis prediction score total mean at 72 hours and one week post intervention (P=0.04 & 0.00) respectively.

Table (6) proves that at baseline prior to intervention, both study and control groups demonstrated a 100% rate of low possibility of sepsis with no statistically significant difference (p = 1.0). However, at 72 hours post-intervention, the preterm neonates with a low possibility of sepsis remained higher in the study group (85.0%) compared to the control group (45.0%), at one week, 75.0% of the study group versus only 20.0% of the control group exhibiting low sepsis suspicion and on discharge, 95.0% of the study group retained a low sepsis probability compared to 72.5% in the control group. The same table also reveals there were statistically significant differences between the study and group at 72 hours post intervention, one week after intervention and by discharge (p = 0.037, 0.001 and 0.01) respectively.

Table (7) highlights that in the study group there was a negative significant correlation between preterm neonates' gestational age with the sepsis prediction score (r = -0.22, p = .01). No significant associations were found with current age or weight in either group. However, the length of NICU stay was positively correlated with the sepsis prediction score in both the study (r = 0.51, p = 0.00) and control groups (r = 0.44, p = 0.00). Regarding gender and mode of delivery, it showed no significant relation with the sepsis prediction score in either group. In contrast, oxygen support was significantly associated with higher sepsis prediction scores in both the study (F = 5.1, p = 0.00) and control groups (F = 5.3, p = 0.00). Additionally, the method of feeding on discharge was significantly related to sepsis risk in both groups (study: F = 5.5, p = .005; control: F = 11.7, p

Table (1) Preterm infants' demographic and clinical characteristics of both groups (n=80).

Newborn characteristics	Study group (n=40)		Control group (n=40)		X2 / T	p
	No.	%	No.	%		
Gender Male Female	 21 19	 52.5 47.5	 24 16	 60 40	0.45	0.49
Gestational age(weeks) Mean ± SD	34.35 ± 1.78		34.23 ± 1.58		0.33	0.74
age on admission (hours) Mean ± SD	2.08 ± 1.37		5.65 ± 2.20		8.7	0.00*
Weight on admission (gm) Mean ± SD	1744.25 ± 375.31		1642.25± 161.88		1.5	0.11
Mode of delivery NVD CS	 23 17	 57.5 42.5	 20 20	 50 50	0.45	0.50
Diagnosis on admission RDSI Preterm	 19 21	 47.5 52.5	 20 20	 50 50	0.05	0.82
Method of Oxygen support CPAP Blinder Nasal Head box Incubator None	 12 10 3 4 2 9	 30 25 7.5 10 5 22.5	 17 8 6 3 1 5	 42.5 20 15 7.5 2.5 12.5	3.7	0.59
Method of feeding on discharge Breast Bottle	 17 23	 42.5 57.5	 5 35	 12.5 87.5	29.1	0.00*
Type of bottle-feeding milk on discharge EBM Formula	 9 14	 39.1 60.9	 1 34	 2.9 97.1	76.1	0.00*
Length of NICU stay(days) Mean ± SD	25.70 ± 17.17		33.83 ± 20.52		1.9	0.06

*Significant at p-value<0.05

Table (2): Comparison of mean preterm infants' physiological parameters between both the study and control groups

Physiological parameters	Prior to intervention		72 hours post intervention		One week post intervention		On discharge		Between groups difference	
	Mean ± SD		Mean ± SD		Mean ± SD		Mean ± SD			
	Study group	Control group	Study group	Control group	Study group	Control group	Study group	Control group	F	p
Respiration	64.02 ± 9.56	66.03 ± 10.51	62.08 ± 8.75	65.10 ± 4.81	57.00 ± 6.61	57.48 ± 10.6	48.6 ± 4.71	44.05 ± 2.43	3.927	.049*
Pulse	148.40 ± 22.24	141.40 ± 20.23	136.40 ± 16.12	173.30 ± 8.70	130.83 ± 15.34	168.78 ± 9.81	118 ± 12.8	119.90 ± 11.13	127.69	.000*
Temperature	36.02 ± 1.01	36.49 ± 1.21	36.42 ± 1.11	37.71 ± 0.33	37.10 ± 0.76	37.97 ± 0.47	37.0 ± 0.11	37.01 ± 0.12	49.08	.000*
Oxygen saturation	82.4 ± 2.44	83.80 ± 2.53	88.80 ± 3.33	89.00 ± 2.36	92.33 ± 2.12	91.25 ± 2.05	96.5 ± 2.41	96.85 ± 2.14	.238	.626

Table (3): Comparison of mean preterm neonates' laboratory biomarkers (WBC & CRP) between study and control groups

Lab biomarkers	Prior to intervention		72 hours post intervention		One week post intervention		On discharge		Between groups difference	
	Mean ± SD		Mean ± SD		Mean ± SD		Mean ± SD		F	p
	Study group	Control group	Study group	Control group	Study group	Control group	Study group	Control group		
WBC	4.96 ± 1.02	5.41 ± 1.06	7.85 ± 2.09	11.21 ± 14.4	7.95 ± 1.94	17.1 ± 12.7	5.65 ± 1.69	6.41 ± 1.06	13.373	.000*
CRP	0.35 ± 0.02	0.48 ± 0.03	0.81 ± 0.05	3.07 ± 1.66	3.19 ± 3.26	9.29 ± 7.58	1.15 ± 0.77	1.08 ± 0.48	15.757	.000*

*Significant at p-value<0.05

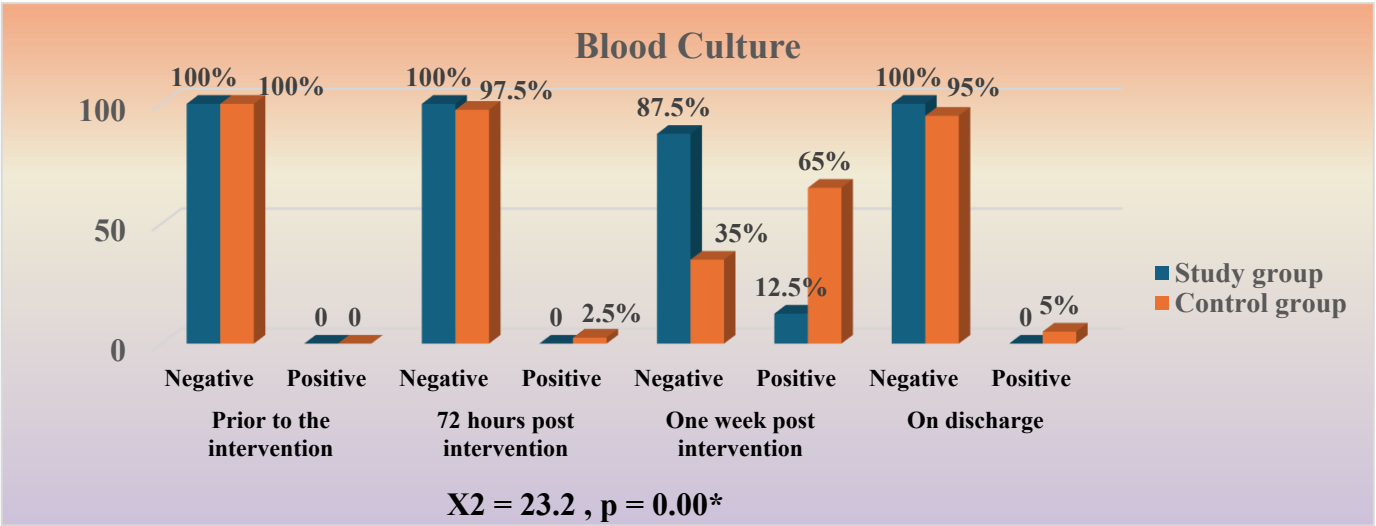

Figure (1): Percentage distribution of preterm neonates' blood culture of study and control groups

Table (4): Preterm neonates mean Sepsis Prediction Score variables of both groups prior to intervention, at 72 hours post intervention, one week post intervention and on discharge

Variables	Prior to the intervention		72 hours post intervention		One week post intervention		On discharge		Between groups difference	
	Mean ± SD		Mean ± SD		Mean ± SD		Mean ± SD			
	Study	Control	Study	Control	Study	Control	Study	Control	F	p
Body temperature (fever) > 38 ◦C	0.00 ± 0.00	0.00 ± 0.00	0.03 ± 0.16	0.15 ± 0.36	0.13 ± 0.33	0.50 ± 0.51	0.00 ± 0.00	0.05 ± 0.22	11.957	.001*
Decrease in feeding volume or residuals > 20%	0.00 ± 0.00	0.00 ± 0.00	0.43 ± 0.50	0.48 ± 0.51	0.33 ± 0.47	0.65 ± 0.48	0.10 ± 0.30	0.23 ± 0.42	5.470	.020*
Platelet counts < 150,000/mm3	0.13 ± 0.22	0.09 ± 0.16	0.25 ± 0.44	0.23 ± 0.42	0.23 ± 0.42	0.60 ± 0.50	0.08 ± 0.27	0.23 ± 0.42	6.895	.009*
Blood glucose changes > 50%	0.00 ± 0.00	0.00 ± 0.00	0.13 ± 0.33	0.20 ± 0.41	0.23 ± 0.42	0.55 ± 0.50	0.03 ± 0.16	0.05 ± 0.22	6.745	.010*
CRP > 1 mg/dL	0.48 ± 0.03	0.35 ± 0.02	0.03 ± 0.16	0.00 ± 0.00	0.35 ± 0.48	0.75 ± 0.44	0.23 ± 0.42	0.33 ± 0.47	5.953	.016*
Circulatory changes	0.00 ± 0.00	0.00 ± 0.00	0.18 ± 0.38	0.40 ± 0.50	0.25 ± 0.44	0.50 ± 0.51	0.08 ± 0.27	0.00 ± 0.00	3.925	.049*
Increase of oxygen requirement	0.76 ± 0.34	0.64 ± 0.50	0.40 ± 0.50	0.63 ± 0.49	0.23 ± 0.42	0.58 ± 0.50	0.00 ± 0.00	0.00 ± 0.00	10.693	.001*
Deterioration of respiratory function	0.30 ± 0.16	0.26 ± 0.18	0.18 ± 0.38	0.39± 0.42	0.05 ± 0.22	0.35 ± 0.48	0.00 ± 0.00	0.00 ± 0.00	7.777	.006*
Total score	1.67 ± 0.75	1.34 ± 0.86	1.60 ± 1.89	2.38 ± 2.07	1.78 ± 2.36	4.48 ± 2.75	0.50 ± 1.04	0.88 ± 0.99	7.42	0.00*

*Significant at p-value<0.05

Table (5): Comparison of the total mean sepsis prediction score of both groups prior to intervention at 72 hours post intervention, one week post intervention and on discharge.

Time	Sepsis Prediction Score		t- test	P
	Mean ± SD			
	Study	Control		
Prior to intervention	1.67 ± 0.75	1.34 ± 0.86	1.5	0.13
72 hours post intervention	1.60 ± 1.89	2.38 ± 2.07	2.6	0.04*
One week after intervention	1.78 ± 2.36	4.48 ± 2.75	4.1	0.00*
On discharge	0.50 ± 1.04	0.88 ± 0.99	1.4	0.15

Table (6): Percentage distribution of preterm neonates' sepsis level of study and control groups

*Significant at p-value<0.05	Prior to the intervention						72 hours post intervention						One week post intervention						On discharge					
	Study group (n=40)		Control group (n=40)		X^2	p	Study group (n=40)		Control group (n=40)		X^2	p	Study group (n=40)		Control group (n=40)		X^2	p	Study group (n=40)		Control group (n=40)		X^2	p
Sepsis level	No.	%	No.	%			No.	%	No.	%			No.	%	No.	%			No.	%	No.	%		
Low sepsis possibility	40	100	40	100	0.0	1.0	34	85.0	18	45.0	13.1	.037*	30	75.0	8	20.0	16.4	0.001*	38	95.0	29	72.5	8.9	0.01*
Very strong suspicious of sepsis	0	0.0	0	0.0			5	12.5	19	47.5			7	17.5	15	37.5			2	5.0	11	27.5		
Sepsis is definite	0	0.0	0	0.0			1	2.5	3	7.5			3	7.5	17	42.5			0	0.0	0	0.0		

*Significant at p-value<0.05

Table (7): Correlation between preterm neonates selected characteristics and sepsis prediction score

Preterm neonates' characteristics	sepsis prediction score			
	Study		Control	
	R	P	r	p
Gestational age (weeks)	-0.22	0.01*	-0.05	0.52
Current age (hours)	0.04	0.63	0.09	0.28
Weight (gm) on admission	-0.14	0.11	-0.1	0.23
Length of NICU stay(days)	0.51	0.00*	0.44	0.00*
Gender	T=0.99	0.32	T=1.4	0.15
Delivery mode	F=0.04	0.83	F=2.6	0.1
Oxygen support	F=5.1	0.00*	F=5.3	0.00*
Method of feeding on discharge	F=5.5	0.005*	F=11.7	0.00*

*Significant at p-value<0.05

Discussion

Colostrum is rich in immunoglobulins, lactoferrin, lysozyme, leukocytes, and growth factors, all of which contribute to the maturation of the mucosal immune system and offer antimicrobial protection. The practice of oropharyngeal administration of colostrum (OAC) takes advantage of these bioactive components even when enteral feeding is not yet established. This study investigated the effect of early oral colostrum administration on the prevention of late-onset sepsis among preterm infants.

The current study demonstrated that the demographic and clinical characteristics of the study and control groups (table 1) were largely comparable, with no statistically significant differences in gender, gestational age, birth weight, mode of delivery, primary diagnosis, or oxygen support, thereby reinforcing the internal validity of the outcome measures. The only significant baseline difference was the age at admission, with the intervention group being admitted earlier (mean 2.08 vs. 5.65 hours, $p = 0.00$), potentially facilitating earlier initiation of supportive interventions, including oral colostrum administration (OAC), which has been associated with improved immunological and nutritional outcomes in preterm infants (Li et al., 2021).

Feeding practices at discharge differed significantly between groups. The study group exhibited a higher rate of exclusive breastfeeding (42.5% vs. 12.5%, $p = 0.00$) and greater use of expressed breast milk among those discharged on bottle feeds (39.1% vs. 2.9%, $p = 0.00$), suggesting that practices implemented in this group potentially including positively influenced feeding outcomes. Existing literature supports the role of OAC in enhancing mucosal immunity, improving feeding tolerance, and facilitating earlier progression to full enteral feeding (Zhou et al., 2023).

Although the length of NICU stay was shorter in the study group (25.70 vs. 33.83 days), the difference was not statistically significant ($p = 0.06$). Nonetheless, when considered alongside improved feeding metrics, this is of clinical importance and may reflect the beneficial impact of early colostrum administration. Systematic reviews have suggested that OAC can reduce the incidence of late-onset sepsis and support earlier NICU discharge, though findings vary in statistical significance across studies (Wu et al., 2024; Patel et al., 2023). Despite, most baseline characteristics were balanced, significant differences in age at admission and feeding outcomes indicate that early NICU admission and colostrum therapy may positively shape neonatal trajectories. These findings contribute to the growing evidence base supporting OAC as a safe, feasible, and effective intervention for improving outcomes in preterm neonates.

The present study revealed significant differences in key physiological parameters between the study and control groups over time (table 2), most notably in respiration rate, pulse rate, and body temperature. These findings suggest that early interventions, such as

the administration of oral colostrum, may have contributed to enhanced physiological stabilization in preterm infants.

Respiration rate significantly differed between the groups ($p = .049$), with both exhibiting a downward trend from baseline to discharge. The decline was more prominent in the study group, potentially indicating more efficient respiratory adaptation. Similar findings have been reported in studies where early colostrum therapy was associated with improved respiratory outcomes, possibly due to the immunomodulatory properties of colostrum components like lactoferrin and secretory IgA, which may reduce pulmonary inflammation and infection risk (Zhou et al., 2023; Lee et al., 2022).

Pulse rate trends further underscored the benefit of early intervention. The study group showed a consistent and significant reduction in pulse rate from baseline to discharge, while the control group exhibited an initial increase followed by a modest decline. The observed group differences were highly significant ($p = .000$). These findings are consistent with previous studies suggesting that early colostrum exposure may promote autonomic stability and reduce systemic inflammatory stress, reflected in more normalized heart rates (Patel et al., 2023; Wu et al., 2024). In addition, early colostrum may attenuate the hypothalamic–pituitary–adrenal axis response, facilitating cardiovascular regulation in fragile preterm neonates (Li et al., 2021).

Significant differences were also observed in body temperature regulation over time ($p = .000$). The study group maintained relatively stable temperatures, whereas the control group experienced more fluctuation, peaking one-week post-intervention. Stability in thermoregulation in the study group may again be linked to the protective bioactive factors in colostrum that support gut integrity and immune modulation, leading to better homeostatic control (Zhou et al., 2023). Colostrum's role in promoting gut colonization with beneficial microbiota might also play a part in enhancing systemic resilience (Zhang et al., 2020).

Conversely, no statistically significant difference was observed in oxygen saturation between groups over time ($p = .626$), despite both showing improvement from baseline to discharge. This may suggest that while early colostrum administration improves systemic inflammatory and autonomic markers, it does not directly alter oxygen saturation trajectories, which may be more influenced by other clinical interventions such as ventilatory support. Collectively, these results align with growing evidence that early oropharyngeal administration of colostrum can positively influence the physiological adaptation of preterm infants. Several recent meta-analyses and trials confirm that this simple, low-cost intervention contributes to better cardiovascular and immune homeostasis, lowers the incidence of sepsis, and promotes overall neonatal stability (Zhou et al., 2023; Wu et al., 2024; Li et al., 2021).

This study identified statistically significant differences in key inflammatory biomarkers; WBC counts and CRP levels between the study and control groups over time ($p = .000$) (table 3). These findings provide compelling evidence of the potential immunomodulatory benefits of early oral colostrum administration in preterm neonates. In the study group, WBC counts exhibited a controlled, physiological response, increasing from 4.96 ± 1.02 to a peak at 72 hours (7.85 ± 2.09) before returning close to baseline levels by discharge (5.65 ± 1.69). Conversely, the control group displayed a highly elevated and variable leukocyte response, rising sharply to 17.1 ± 12.7 at one week and only partially resolving to 6.41 ± 1.06 at discharge. This pronounced leukocytosis in the control group may reflect a heightened inflammatory or infectious response, suggesting a lack of early immunologic modulation. These findings support evidence from Romero-Maldonado et al. (2022), who demonstrated that early oral colostrum primes the mucosal immune system, resulting in improved regulation of inflammatory markers and reduced infection rates.

The CRP patterns further reinforce this immunological effect. While both groups showed a postnatal rise, the increase was substantially lower and more stable in the study group. Peak CRP levels in the study group reached only 3.19 ± 3.26 mg/L, compared to 9.29 ± 7.58 mg/L in the control group at one week. By discharge, both groups had CRP levels returning toward normal, but the study group had achieved lower peak inflammatory activation. Previous research highlights the anti-inflammatory potential of colostrum due to its high content of anti-infective agents such as lactoferrin, lysozyme, and transforming growth factor-beta (TGF-β), which can attenuate systemic inflammation and potentially reduce the risk of late-onset sepsis (Wu et al., 2024; Patel et al., 2023). These results also are aligned with findings from Colonetti et al. (2022), who reported that the bioactive components of colostrum—such as lactoferrin, lysozyme, and TGF-β—modulate inflammatory pathways and contribute to reduced systemic inflammation in preterm infants.

Moreover, studies have suggested that early administration of colostrum may contribute to gut barrier integrity and microbial colonization with beneficial bacteria, reducing translocation of pathogens and thus systemic inflammatory markers such as CRP (Zhou et al., 2023; Zhang et al., 2020). This mechanism could explain the more controlled biomarker profiles observed in the study group. Furthermore, early oral colostrum appears to enhance gut barrier integrity and promote beneficial microbial colonization, reducing the translocation of pathogens and systemic inflammatory responses. This protective mechanism, discussed by Slouha et al. (2023), may underlie the more controlled biomarker trends observed in the study group. The role of early colostrum in strengthening mucosal immunity is well-documented, with Zhang et al. (2021) demonstrating its efficacy in lowering both CRP and sepsis rates in neonates ≤32 weeks' gestation.

Meta-analytic findings by Tao et al. (2023) further support the present study's conclusion, confirming that early oral colostrum significantly improves clinical outcomes, including

inflammatory markers, in preterm populations. These cumulative data suggest that EOC not only mitigates excessive inflammatory responses but may also serve as an accessible and cost-effective strategy to enhance neonatal immune defense mechanisms. The significantly lower and more stable WBC and CRP levels in the colostrum group support the hypothesis that the preterm infants who will be administered early oral colostrum will have less chances of developing late onset sepsis than in the control group. These findings, corroborated by a growing body of recent literature, advocate for the integration of EOC into routine NICU practice to modulate immune responses and reduce infection-related complications.

The present study demonstrated statistically significant differences in blood culture results across four time points between the study and control groups ($p = .000$) (figure 1), suggesting a protective role of early oral colostrum administration in preterm infants and further underscoring the immunoprotective benefits of early oral colostrum administration. Initially, all participants in both groups had negative blood cultures, indicating a comparable baseline. However, differences began to emerge as the intervention progressed. A notable divergence was observed by one-week post-intervention, with only 35.0% of the control group maintaining negative cultures compared to 87.5% in the study group. This trend supports prior findings that highlight the immunoprotective benefits of colostrum when administered early in life.

The antimicrobial and immunomodulatory properties of colostrum are well-documented. It is rich in secretory immunoglobulin A, lactoferrin, cytokines, and growth factors, which play critical roles in immune development and gut mucosal defense in neonates (Martín-Álvarez et al., 2020). Several randomized controlled trials have reported that oral administration of colostrum significantly reduces the incidence of late-onset sepsis and other infections in very low birth weight infants (Aggarwal et al., 2021; Ferreira et al., 2019). These outcomes are consistent with our findings, where the study group experienced markedly fewer positive blood cultures and faster clearance of infection markers like CRP and WBC counts.

Furthermore, the immunologic benefits appear to extend beyond acute infection control. Studies have shown that early colostrum exposure positively modulates inflammatory cytokine expression, promotes gut barrier function, and reduces systemic inflammatory responses (Romero-Maldonado et al., 2022; Martins et al., 2024). Our results mirrored these mechanisms, with the study group showing more stable inflammatory markers and lower peak CRP and WBC values compared to the control group.

Notably, the sustained blood culture negativity in the study group at discharge (100%) suggests long-term benefits from early colostrum administration. This aligns with findings from Fazli et al. (2024), who observed improved nutritional outcomes and reduced infection rates in preterm neonates receiving oropharyngeal mother’s milk. Similarly,

Zhang et al. (2021) reported a reduction in necrotizing enterocolitis and sepsis rates in infants who received early colostrum therapy. The implications for NICU protocols are significant. Routine early oral colostrum administration could serve as a simple, cost-effective intervention to reduce neonatal morbidity and mortality. As recommended by current clinical evidence, including the findings of Li et al. (2021) and Wu et al. (2024), this practice should be considered as part of standard supportive care for preterm infants.

By 72 hours post-intervention, the appearance of a single positive blood culture in the control group marked the first divergence. This disparity became more pronounced one-week post-intervention, with only 35.0% of the control group maintaining negative cultures, compared to 87.5% in the study group. The significantly higher rate of positive cultures in the control group (65.0%) suggests an increased susceptibility to systemic infections, potentially due to the absence of early immunological priming provided by colostrum. These findings are consistent with a growing body of evidence supporting the antimicrobial and immunomodulatory effects of colostrum in neonates, particularly among preterm infants who are at heightened risk for late-onset sepsis (LOS). Colostrum contains a rich concentration of bioactive molecules such as lactoferrin, secretory IgA, lysozyme, cytokines, and oligosaccharides, which collectively contribute to enhanced mucosal immunity and reduced bacterial translocation from the gut (Li et al., 2021; Zhou et al., 2023). Previous randomized controlled trials and meta-analyses have shown that oropharyngeal administration of colostrum significantly reduces the incidence of culture-positive sepsis in very low birth weight infants by promoting gut barrier function and modulating the neonatal immune response (Wu et al., 2024; Patel et al., 2023). The markedly lower sepsis rate in the study group at one week supports this mechanism and reinforces the therapeutic role of colostrum in reducing neonatal infections.

By discharge, all infants in the study group had reverted to negative cultures (100%), while two neonates in the control group (5.0%) still exhibited positive results, further highlighting the potential for sustained immunologic benefits of early colostrum exposure. This final observation reinforces the hypothesis that the early immunologic advantages conferred by colostrum can persist through the neonatal intensive care unit (NICU) stay, offering protection against nosocomial infections and contributing to improved clinical outcomes. The significant difference in blood culture profiles between the two groups illustrates the potential of early colostrum administration as a non-invasive, low-cost strategy to reduce late-onset sepsis in preterm neonates. These findings are in line with emerging clinical guidelines advocating for the routine implementation of oropharyngeal colostrum therapy in NICUs as part of comprehensive infection prevention protocols.

This study demonstrated statistically significant differences across multiple variables of a sepsis prediction score between the study and control groups (table 4). with the study group receiving early oral colostrum showing markedly lower scores and reduced incidence of key clinical indicators of sepsis. Specifically, the study group exhibited

significantly reduced rates of fever (>38°C), decreased feeding volume, thrombocytopenia, and fluctuations in blood glucose parameters that are closely associated with early signs of systemic infection in neonates. Additionally, significant reductions in CRP >1 mg/dL, circulatory changes, respiratory deterioration, and increased oxygen requirements were observed in the study group compared to controls. These findings suggest a clear protective effect of early colostrum exposure in modulating immune and systemic responses.

These results align with the literature demonstrating that early oral colostrum administration can positively influence the immunological and clinical course of preterm infants. Colonetti et al. (2022) and Romero-Maldonado et al. (2022) highlighted that colostrum is rich in bioactive agents including immunoglobulins, lactoferrin, lysozyme, and cytokines—that enhance mucosal immunity and reduce systemic inflammatory responses. Such immune modulation may explain the significantly lower CRP levels and reduced incidence of circulatory and respiratory deterioration observed in the colostrum group. As well as these results are consistent with a growing body of evidence indicating the immunological benefits of colostrum when administered oropharyngeally to preterm infants. Colostrum contains high concentrations of immunoglobulins (particularly IgA), lactoferrin, cytokines, and growth factors such as TGF-β, which contribute to enhanced mucosal immunity, reduced systemic inflammation, and improved intestinal barrier function (Arslanoglu et al., 2021; Rao et al., 2021). These bioactive components may account for the reduced inflammatory responses and lower sepsis scores observed in the present study.

In addition, early colostrum exposure has been linked to improved gut barrier function and colonization by beneficial microbiota, reducing bacterial translocation and the risk of bloodstream infection, a key driver of elevated sepsis scores (Slouha et al., 2023; Zhang et al., 2021). These effects may underlie the lower incidence of metabolic and hematologic disturbances, including glucose instability and thrombocytopenia, found in the colostrum group. Recent clinical trials and systematic reviews have further substantiated these findings. For example, Aydemir et al. (2023) reported significantly lower CRP levels and reduced sepsis-related complications in preterm infants who received early oral colostrum administration within the first 48 hours of life. Similarly, Cacho et al. (2020) demonstrated improved immune regulation and fewer episodes of late-onset sepsis following early colostrum administration, emphasizing its potential role as an adjunctive immune-priming strategy in NICU protocols.

Moreover, a meta-analysis by Wang et al. (2021) found that early oral colostrum significantly decreased the incidence of late-onset sepsis, shortened hospital stays, and improved feeding tolerance in neonates born <32 weeks of gestation. The current study's results—particularly the lower total sepsis prediction scores in the intervention group—are in line with these reported benefits and underscore the need for standardized

implementation of colostrum therapy in neonatal care settings. Tao et al. (2023) further support these findings in their meta-analysis, reporting that early oral colostrum significantly reduces the incidence of late-onset sepsis, respiratory complications, and other morbidities among preterm infants. The present study's results strengthen this evidence by demonstrating consistent reductions across a validated sepsis prediction scoring system.

The observed reduction in respiratory and circulatory deterioration may also be attributed to colostrum's antimicrobial and anti-inflammatory properties, which enhance immune surveillance and mitigate the systemic impact of early microbial colonization (Nguyen et al., 2023). This supports the hypothesis that early oral colostrum not only prevents infection but also stabilizes the overall physiological status of preterm infants and reduce the preterm infants' hospital stay. Collectively, the lower frequency of clinical and laboratory indicators of sepsis in the colostrum group underscores the therapeutic potential of early oral colostrum administration. By mitigating the early physiological signs of infection and reducing the cumulative sepsis score, early oral colostrum administration appears to confer both immunological and systemic stabilization benefits in this vulnerable population. These findings provide further justification for incorporating early colostrum therapy into routine neonatal intensive care protocols to proactively manage sepsis risk among preterm infants. This study reinforces existing literature by providing further evidence of the benefits of early colostrum administration in reducing the clinical signs of sepsis and lowering cumulative sepsis risk scores in preterm neonates.

The findings from this study (tale 5) indicate that while there were no statistically significant differences in sepsis prediction scores between the study and control groups prior to intervention ($p = 0.13$) or at discharge ($p = 0.15$), significant differences emerged at 72 hours and one-week post-intervention ($p = 0.04$ and $p = 0.00$, respectively). These time points correspond to the early critical period during which the neonatal immune system is particularly susceptible to LOS. The lower sepsis scores in the colostrum group reflect a probable immunomodulatory effect of early oral colostrum exposure, which appears to dampen systemic inflammatory responses and reduce clinical indicators of sepsis.

The early administration of colostrum, rich in immunomodulatory components such as secretory IgA, lactoferrin, lysozyme, and cytokines, appears to support enhanced mucosal and systemic immunity. The lower sepsis prediction scores at 72 hours and one week in the study group suggest a more regulated immune response, potentially attributed to the priming effects of early oral colostrum on oropharyngeal-associated lymphoid tissue (OALT), as supported by prior studies (Rao et al., 2021; Wang et al., 2021). These mechanisms can lead to improved immune regulation and resistance to infection, as seen in the significant reduction in sepsis-related symptoms (e.g., fever, abnormal glucose levels, respiratory deterioration) in the study group.

Previous research has shown that the innate immune stimulation via early colostrum exposure contributes to a reduction in sepsis incidence and severity. For example, a randomized controlled trial by Aydemir et al. (2023) reported significantly reduced inflammatory markers and clinical signs of sepsis in neonates receiving early oral colostrum compared to controls. Similarly, Cacho et al. (2020) observed enhanced immune readiness and a lower incidence of LOS following early colostrum administration in very low birth weight infants. Recent clinical trials and systematic reviews support the benefits of early oral colostrum in modulating inflammatory biomarkers and clinical sepsis scores. For instance, Shoji et al. (2023) demonstrated that EOC reduced both CRP levels and clinical sepsis scores in very low birth weight infants, likely by modulating the neonatal inflammatory cascade. Similarly, Basu et al. (2022) reported that early colostrum therapy was associated with lower sepsis severity and a decreased need for respiratory support.

Additional evidence by Munblit et al. (2020) and Yang et al. (2021) emphasizes colostrum's role in enhancing immune maturity through its impact on cytokine signalling and leukocyte activation. These effects were reflected in our findings, where the study group demonstrated significantly fewer abnormal platelet counts, circulatory instability, and oxygen requirement increases common early signs of LOS. The transient absence of statistical difference at discharge may reflect the overall improvement in both groups with standard NICU care; however, the marked reduction in sepsis scores during the critical early postnatal period in the intervention group reinforces the timing-sensitive benefits of colostrum therapy. These findings align with the conclusions drawn in recent meta-analyses and clinical trials highlighting that early oral colostrum is most effective when initiated within the first hours of life and maintained consistently (Arslanoglu et al., 2021; Wang et al., 2021).

Furthermore, studies suggest that early oral colostrum administration contributes to gut microbial homeostasis and barrier integrity, reducing translocation of pathogenic bacteria and associated systemic inflammation, which are central mechanisms in LOS pathogenesis (Nguyen et al., 2023; Zhang et al., 2020). These biological mechanisms could explain the significant reduction in sepsis risk indicators by 72 hours and their persistence through the first week, as demonstrated in our findings. The lack of difference at discharge may be attributed to standardized NICU care protocols or the late resolution of inflammatory responses in the control group. However, the significant early divergence in scores reinforces the importance of the timing of early oral colostrum initiation. The integration of early oral colostrum into neonatal protocols could serve as a preventive strategy against LOS, especially in settings with high sepsis prevalence and limited access to advanced immunotherapies.

Overall, these results support the growing evidence that oral colostrum administration is an effective, safe, and low-cost intervention that can reduce early inflammatory responses

and sepsis risk in preterm neonates, particularly when initiated promptly after birth. This underscores the need for integrating colostrum administration protocols into routine NICU practice, especially for high-risk infants.

This study demonstrates that at baseline, both the study and control groups showed an equal and favourable profile regarding sepsis risk, with a 100% classification under low sepsis probability and no statistically significant difference ($p = 1.0$) (table 6). However, significant divergence was observed following the intervention. At 72 hours post-intervention, a markedly higher proportion of neonates in the study group retained a low probability of sepsis (85.0%) compared to the control group (45.0%) ($p = 0.037$). This gap widened at one week, with only 20.0% of control infants maintaining a low sepsis prediction score, versus 75.0% in the study group ($p = 0.001$). By discharge, the colostrum group continued to exhibit a protective trend (95.0% vs. 72.5%, $p = 0.01$).

These findings suggest that early oral administration of colostrum contributes to improved immunological outcomes and contributes to improved immunological outcomes and may significantly reduce the risk of LOS in preterm neonates, supporting existing literature that highlights its immunomodulatory and protective roles. These components can inhibit pathogen colonization, modulate inflammatory responses, and enhance mucosal immunity during the critical early days of life. Colostrum contains a rich supply of immunoprotective agents, including immunoglobulins (notably sIgA), lactoferrin, cytokines, and growth factors, which act synergistically to bolster mucosal immunity and limit pathogen translocation (Zhou et al., 2023; Shoji et al., 2023). This is particularly vital in preterm infants, whose immune systems and gut barriers are underdeveloped.

In alignment with the current results, Studies by Ochoa et al. (2021) and Kusumaningrum et al. (2022) reported similar improvements in clinical sepsis outcomes and reduced infection markers following early colostrum therapy. Their findings align with the current results, particularly in showing how EOC decreases systemic inflammation and supports stable immune function. Basu et al. (2022) and Shoji et al. (2023) found that preterm neonates receiving EOC therapy exhibited significantly lower sepsis prediction scores and reduced incidence of clinical sepsis. Yang et al. (2021) also demonstrated that early colostrum exposure accelerated immune system maturation and was associated with reduced inflammatory biomarker levels, leading to fewer infections and complications.

The substantial reduction in sepsis prediction scores by one-week post-intervention in the study group reflects the immunomodulatory impact of colostrum exposure. This aligns with work by Chen et al. (2023), who demonstrated that preterm neonates receiving EOC exhibited lower rates of bloodstream infections and reduced clinical signs of sepsis, attributed to early mucosal immune priming. The current study findings further substantiate the protective role of colostrum in reducing systemic inflammation and clinical markers of sepsis. The sustained higher rates of preterm infants with low sepsis

suspicion in the study group across all follow-up points underscore the long-lasting impact of early immunological priming provided by colostrum. Additionally, the observed trends align with the notion that colostrum not only reduces inflammatory responses but also promotes a favourable microbial environment and gut homeostasis, both essential for lowering systemic infection risks (Munblit et al., 2020; Shoji et al., 2023).

Furthermore, recent evidence suggests that early oral colostrum administration may also play a role in promoting beneficial microbiota colonization and reducing pro-inflammatory responses, contributing to a lower sepsis burden (Pérez et al., 2020; Zhang et al., 2021). These mechanisms help explain the consistently higher percentage of neonates in the colostrum group who remained in the low-risk sepsis category across all time points. Collectively, the significantly better sepsis prediction outcomes in the study group support the routine use of early oropharyngeal colostrum as a non-invasive, low-cost intervention to enhance immunity and mitigate the burden of LOS among preterm infants in NICU settings. Taken together, these results support the incorporation of early colostrum therapy as a proactive strategy in NICU settings, not only to reduce the risk of late-onset sepsis but also to promote early immune system development in preterm infants.

Correlation analysis in the current study (table 7) revealed meaningful relationships between several clinical variables and sepsis prediction scores in preterm infants. In the study group, a significant negative correlation between gestational age and sepsis prediction scores was observed ($r = –0.22$, $p = .01$), suggesting that infants born at earlier gestational ages had a higher risk of developing sepsis. This finding aligns with established knowledge that lower gestational age is a major determinant of neonatal immune immaturity and vulnerability to systemic infections (Zhou et al., 2023; Shoji et al., 2023).

While no significant associations were observed between sepsis prediction scores and current age or weight in either group, the length of NICU stay demonstrated a strong positive correlation with sepsis prediction scores in both the study ($r = 0.51$, $p = .00$) and control groups ($r = 0.44$, $p = .00$). This correlation supports existing literature indicating that prolonged hospitalization increases the risk of nosocomial infections and inflammatory complications in preterm neonates (Chen et al., 2023; Ochoa et al., 2021). Early immune modulation through interventions like oropharyngeal colostrum (EOC) may mitigate this risk by strengthening mucosal defenses early in the NICU course. Gender and mode of delivery did not show any significant relationship with sepsis prediction scores in either group, which is consistent with prior evidence that these variables exert limited influence on neonatal sepsis risk when compared to biological maturity and immune development (Zhang et al., 2021).

Importantly, the requirement for oxygen support was significantly associated with higher sepsis prediction scores in both groups (study: $F = 5.1$, $p = .00$; control: $F = 5.3$, $p = .00$). This association may reflect respiratory compromise as a clinical manifestation or consequence of underlying systemic infection, and it underscores the value of monitoring respiratory parameters as part of comprehensive sepsis prediction models (Shoji et al., 2023; Kusumaningrum et al., 2022).

Another key finding was the significant relationship between the method of feeding at discharge and sepsis risk, with exclusively breastfed or colostrum-fed infants showing lower sepsis prediction scores in both the study ($F = 5.5$, $p = .005$) and control groups ($F = 11.7$, $p < .001$). This outcome aligns with research indicating that breast milk and early colostrum contain immunoprotective components, such as lactoferrin, secretory IgA, and oligosaccharides, which help reduce infection risk by promoting gut barrier integrity and modulating inflammatory responses (Patel et al., 2023; Pérez et al., 2020). The protective effect of colostrum observed here supports the growing advocacy for its routine use in NICU protocols, especially for very low birth weight infants. Collectively, these correlations reinforce the immunological benefits of early oropharyngeal colostrum therapy, not only in reducing infection markers but also in influencing key clinical predictors of late-onset sepsis. These results support the integration of EOC as a targeted neonatal care intervention.

Conclusion:

The current study findings concluded that early oral administration of maternal colostrum is a feasible, safe, and potentially effective intervention associated with a significant reduction in the incidence of late-onset sepsis, suggesting that early immunomodulatory interventions may play a role in enhancing the preterm infants neonatal immune defines in this high-risk population. This study adds to the growing body of evidence supporting the use of early oral colostrum administration in preterm infants as a potentially beneficial intervention for infection prevention. Furthermore, the clinical outcomes observed such as improved physiological stability and reduced the length of preterm infants' hospital stay underscore the immunological and developmental relevance of colostrum exposure in the early neonatal period.

Recommendations:

Based on the findings of this study, the following recommendations are proposed:

1. Development of standardized early oropharyngeal colostrum administration protocols and integration of early oropharyngeal colostrum administration into standard NICU protocols particularly for preterm.

2. Further research with larger sample sizes and longer follow-up periods to strengthen the evidence base, larger randomized controlled trials across diverse healthcare settings are needed to assess the efficacy of EOC in reducing late-onset sepsis and other clinical outcomes. These studies should also explore optimal administration schedules and long-term neurodevelopmental impacts.

3. Promotion of early maternal milk expression: Maternal education and support to initiate breast milk expression within the first hour of birth should be prioritized to ensure timely availability of colostrum. Lactation support services should be made accessible and actively involved in NICU care.

4. Educating pregnant women and mothers about the importance and benefits of early colostrum feeding is crucial for newborn health.

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الملخص العربى

تأثير الإعطاء الفموى المبكر للبن السرسوب على الوقاية من تسمم الدم المتأخر لدى الخُدّج.

مقدمه: لا يزال **تسمم الدم** المتأخر سببًا رئيسيًا للوفاة بين الخُدّج. وقد برز الإعطاء المبكر للبن السرسوب عن طريق الفم كتدخل واعد لتعديل المناعة وتقليل خطر الإصابة بتسمم الدم لدى الخُدّج.

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الهدف: هدفت الدراسة إلى تقييم تأثير الإعطاء الفموى المبكر للبن السرسوب على الوقاية من تسمم الدم المتأخر لدى الخُدّج.

تصميم البحث: استُخدم تصميم بحث شبه تجريبي لتحقيق هدف الدراسة.

مكان الدراسة: أُجريت الدراسة في وحدة العناية المركزة لحديثي الولادة بمستشفى المنيل الجامعي.

العينة: قُسِّمت عينة غرضية من ثمانين رضيعًا خديجًا إلى مجموعتين: تلقت مجموعة الدراسة 2 مل من لبن سرسوب الأم،وأعطى داخل الفم كل ثلاث ساعات خلال أول 72 ساعة من الحياة، بينما تلقت مجموعة الضبط الرعاية الروتينية. أُجريت مراقبة سريرية لعلامات عدوى الدم حتى خروج الطفل من وحدة العناية المركزة لحديثي الولادة. جُمعت معلومات عن خصائص حديثي الولادة باستخدام استبيان مُنظَّم، واستُخدمت درجة التنبؤ بتسمم الدم لكلتا المجموعتين أربع مرات. حُلِّلت البيانات باستخدام برنامج (*SPSS*) الإصدار 29.

النتائج: كان معدل الإصابة بتسمم الدم المتأخر أقل بشكل ملحوظ في مجموعة الدراسة مقارنةً بالمجموعة الضابطة. بالإضافة إلى ذلك، أظهر الرضع في مجموعة الدراسة تحسنًا في الرضاعة الطبيعية، ومدة إقامة أقصر في وحدة العناية المركزة لحديثي الولادة، وانخفاضًا في علامات الالتهاب.

الخلاصه والتوصيات: يُعد الإعطاء الفموى المبكر للبن السرسوب تدخلاً آمنًا ومنخفض التكلفة وفعالًا للحد من خطر الإصابة بتسمم الدم المتأخر لدى الخدج. و يُوصى بتطبيق بروتوكولات الإعطاء الفموى المبكر للبن السرسوب في وحدات العناية المركزة لحديثي الولادة لتحسين نتائج هؤلاء الأطفال. ايضا يوصى باعطاء النساء الحوامل والأمهات توعية صحية حول أهمية وفوائد الرضاعة الطبيعية المبكرة واهمية اعطاء لبن السرسوب أمر بالغ الأهمية لصحة الأطفال حديثي الولادة.