

Factors Contributing to Necrotizing Enter Colitis among Neonates in the Neonatal Intensive Care Unit of Public Hospital in Central Ethiopia: An Unmatched Case-Control Study

Abstract

Background: Necrotizing Enterocolitis (NEC) is a severe condition in newborns that causes intestinal inflammation, infection, and necrosis, with lasting impacts on survivors' health and quality of life. It remains a leading cause of neonatal morbidity and mortality, especially in developing countries. In Ethiopia, limited research exists on the factors contributing to NEC. This study aimed to identify the factors associated with NEC among neonates admitted to the neonatal intensive care unit of a public hospital in Central Ethiopia.

Methods: A facility-based unmatched case-control study was conducted from August 1 to 30, 2024, among neonates admitted to the NICU of public hospitals in Central Ethiopia. Cases were neonates diagnosed with Necrotizing Enterocolitis (NEC), while controls were those admitted without NEC. Data were collected *via* interviews and record reviews. Binary and multivariable logistic regression analyses were performed, with Adjusted Odds Ratios (AOR) and 95% Confidence Intervals (CI) reported. Associations with a p -value < 0.05 were considered statistically significant.

Result: This study included 133 cases and 397 controls. Factors significantly associated with necrotizing enterocolitis in neonates were chorioamnionitis (AOR 4.04; 95% CI: 2.33, 6.97), formula milk use (AOR 2.47; 95% CI: 1.50, 4.06), prolonged hospital stay (AOR 2.06; 95% CI: 1.27, 3.33), continuous positive airway pressure support (AOR 2.29; 95% CI: 1.36, 3.87), and premature rupture of membranes (AOR 2.52; 95% CI: 1.55, 4.12).

Conclusion: Chorioamnionitis, extended hospital stay, the use of continuous positive airway pressure support, and premature rupture of membranes were positively significantly associated with the development of necrotizing enterocolitis in newborns. Special attention should be given to the prevention, early detection, and treatment of necrotizing enterocolitis.

Keywords: Necrotizing enterocolitis • Neonates • Neonatal intensive care unit • Ethiopia

Abbreviations: ANC: Antenatal Care; APGAR: Appearance, Pulse Rate, Grimace, Activity, Respiration Rate; APH: Ante Partum Hemorrhage; CPAP: Continuous Positive Air Way Pressure; CS: Caesarean Section; GHTN: Gestational Hypertension; NEC: Necrotizing Enterocolitis; NICU: Neonatal Intensive Care Units; PROM: Premature Rupture of Membrane; SVD: Spontaneous Vaginal Delivery.

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Introduction

Necrotizing Enterocolitis (NEC) is a serious condition in newborns that causes inflammation, infection, and necrosis to the intestines [1]. Despite progress in newborn care, NEC remains a major cause of morbidity and mortality in premature babies. Its causes are still not fully understood due to its complex nature and varied symptoms [2,3]. Factors like an underdeveloped immune system, imbalanced gut bacteria, and inflammation worsened by formula feeding and prolonged antibiotic use are linked to NEC, especially in premature infants [4].

Globally, the incidence of NEC varies widely depending on healthcare settings. A systematic review estimated a pooled incidence rate of 6.62%, with the condition affecting approximately 10% of infants weighing less than 1,500 grams [5]. Alarming, NEC has a high mortality rate, particularly in low-birth-weight infants and those requiring surgical intervention. For Very Low Birth Weight (VLBW, $\leq 1,500$ g) and Extremely Low Birth Weight (ELBW, $\leq 1,000$ g) infants, mortality rates can rise to 30.1% and exceed 50% for those with surgical NEC [6-8].

The consequences of NEC extend beyond immediate neonatal care, leaving survivors to face lifelong challenges. These include gastrointestinal complications like intestinal strictures and short bowel syndrome, as well as neurodevelopmental disabilities [9]. These outcomes significantly affect survivors' mental and physical health, social experiences, and quality of life, with impacts persisting into adolescence and adulthood.

Despite ongoing research, the multifactorial nature of NEC continues to challenge our understanding. Genetics, inflammation, and environmental factors play a central role in its pathogenesis, while breastfeeding has been identified as a key preventative measure as well monitoring for feeding intolerance, abdominal distension, and bloody stools, are critical to improving outcomes in infants at risk for NEC. Furthermore, studies have identified critical risk factors, such as prematurity, low birth weight, and formula feeding. Additional factors, including antenatal steroid use, prolonged mechanical ventilation, and umbilical vein catheterization, have also been linked to increased NEC risk.

In the African context, the burden of NEC is particularly concerning. In a study conducted in Addis Ababa, Ethiopia, the prevalence of

NEC was reported at 25.4%, with significant associations identified between NEC and factors such as gestational age, birth weight, APGAR score, prolonged labor, maternal chronic diseases, and ventilation. Another study in southern Ethiopia highlighted risk factors such as body mass index, khat chewing, gestational age, and premature rupture of membranes. These findings emphasize the urgent need for region-specific strategies to address NEC.

Despite progress in understanding Necrotizing Enterocolitis (NEC), significant gaps remain, particularly in low-resource settings. This study aims to explore the contributing factors of NEC to provide insights for prevention and treatment. In Ethiopia, limited research exists on these factors, and this study seeks to identify the key factors associated with NEC among neonates admitted to a public hospital's neonatal intensive care unit in Central Ethiopia.

Materials and Methods

Study area, period, and design

An unmatched case-control study was conducted from August 1 to 30, 2024, in selected hospitals in the Central Ethiopia region. This region, with Hosanna as its center located 230 kilometers southwest of Addis Ababa, has a population of 4.2 million, with women making up 50.86% of the population, according to the 2017 Central Statistical Agency report. Of the region's 20 public hospitals, 14 offer neonatal intensive care services. The study was conducted in five hospitals: Worabe Comprehensive Specialized Hospital, Wachamo University Nigist Eleni Mohammed Memorial Comprehensive Specialized Hospital, Durame General Hospital, Dr. Bogalech Gebre Memorial Hospital, and Alaba Kulito General Hospital, which together manage an average of 926 neonatal admissions every two months.

Eligibility criteria

Inclusion criteria for cases: All neonates admitted to the NICU at the selected public hospitals during the data collection period who were diagnosed with Necrotizing Enterocolitis (NEC) by a physician, based on a standardized set of clinical and/or radiological criteria, or those who met the defined criteria for NEC and were admitted to the NICU during the study period, were included as cases.

Inclusion criteria for controls: All neonates admitted to the NICU at the selected public

hospitals during the data collection period who did not develop NEC or did not meet the diagnostic criteria for NEC were included as controls.

Exclusion criteria for cases: Neonates initially diagnosed with Necrotizing Enterocolitis (NEC) who later recovered but experienced other health complications during the data collection period were excluded from the study.

Exclusion criteria for controls: Neonates diagnosed with NEC or other neonatal diseases during the data collection period were excluded. Additionally, neonates admitted to the NICU with major congenital anomalies, genetic disorders, or whose mothers were absent, deaf, or unable to communicate were excluded. Neonates with incomplete medical records were also excluded, regardless of their group (cases or controls).

Sample size determination

The sample size for this unmatched case-control study was calculated using OpenEPI Info version 7 software with the double population proportion method. The calculation was based on data from a previous study conducted in Southern Ethiopia, which reported a maternal smoking history as a key variable. In this study, 11.7% of mothers in the control group had a smoking history, with an odds ratio of 2.1. A precision of 5%, a power of 80%, and a case-to-control ratio of 1:3 were assumed. After adjusting for a 5% non-response rate, the final sample size was determined to be 530, consisting of 133 cases and 397 controls.

Study variables

The study variables included a dependent variable, Necrotizing Enterocolitis (NEC), and several independent variables. The socio-demographic characteristics of the mother included maternal age, marital status, residence, occupation, and educational status. Obstetric factors examined were parity, mode of delivery, antenatal care follow-up, maternal chronic diseases during pregnancy, prolonged labor, Antepartum Hemorrhage (APH), Premature Rupture of Membranes (PROM), and chorioamnionitis. Neonatal factors considered included gender, gestational age, birth weight, APGAR score, antibiotic use, use of Continuous Positive Airway Pressure (CPAP), diagnosis of NEC, type of milk, and length of hospital stay.

Operational definitions

Necrotizing Enterocolitis (NEC) is a serious

gastrointestinal condition in neonates, characterized by clinical signs such as abdominal distention, redness of the abdominal wall, feeding intolerance, vomiting, and the presence of blood in the stool. Radiologically, it is diagnosed through the observation of dilated bowel loops, bowel wall edema, pneumatosis intestinalis, portal venous gas, and pneumoperitoneum.

Case: Neonates admitted to the Neonatal Intensive Care Unit (NICU) of a public hospital in Central Ethiopia who were diagnosed with Necrotizing Enterocolitis (NEC) by a physician, based on clinical and/or radiological criteria, during the study period.

Control: Neonates admitted to the NICU of the selected public hospitals in Central Ethiopia who were not diagnosed with Necrotizing Enterocolitis (NEC) during their stay in the NICU and did not meet the diagnostic criteria for NEC.

Sampling technique and procedure

From the 14 hospitals providing Neonatal Intensive Care Unit (NICU) services, we randomly selected five hospitals: Worabe Comprehensive Specialized Hospital, Wachamo University Nigist Eleni Mohammed Memorial Comprehensive Specialized Hospital, Durame General Hospital, Dr. Bogalech Gebre Memorial Hospital, and Alaba Kulito General Hospital. The sample size was proportionally allocated across these hospitals based on their average monthly admissions from the previous year. For each case, three controls were selected, with controls chosen systematically at five intervals.

Data collection instruments and procedures

The data collection instruments were developed based on a review of relevant literature on umbilical catheterization and included variables related to maternal sociodemographic, pregnancy, perinatal, and neonatal factors. Data were collected using a structured questionnaire administered through face-to-face interviews, alongside a medical record checklist. The questionnaire was initially prepared in English, translated into local languages, and then back-translated into English by a language expert to ensure accuracy and consistency. A team of five midwives, supervised by an MSc-level professional, collected the data. Respondents were informed about the study's purpose, and data were gathered through interviews and medical record reviews. Supervisors ensured the proper execution of the data collection process

and maintained the integrity of the study.

Data quality control

To ensure data quality, a pretest was conducted on 5% of the total sample size at Wolaita Sodo University Comprehensive Hospital. Based on the pretest results, necessary adjustments were made to the instruments, and the revised tools were used for the actual data collection. Data collectors and supervisors received training on the study objectives, data collection procedures, and ethical considerations. Throughout the data collection process, data collectors were closely supervised and instructed to verify the completeness of the data before submission.

Data analysis and processing

The collected data were cleaned, coded, and entered into EpiData version. Then, the data were exported to Statistical Package for the Social Sciences (SPSS) version 26 for analysis. Descriptive analysis was performed to describe the characteristics of participants, and the result was described in the form of text, tables, and figures. By using a binary logistic regression model, bivariable analysis was done to identify the association between each independent variable and the outcome variable. Independent variables with $p<0.25$ were included in the multi-variable analysis to exclude potential confounders and identify actual associations. Multi-collinearity was checked to see the linear correlation among the independent variables by using the variance inflation factor. None of the variables yield

variance inflation factor >5 . The model fitness was checked by the Hosmer Lemeshow goodness of fit test, it was found to be insignificant ($p\text{-value}=0.531$), which indicates that the model was fitted. Then, in the multivariable logistic regression analysis, adjusted odds ratio with a 95% Confidence Interval (CI) was reported, and variables with $p<0.05$ were declared to be significantly associated with non-reassuring fetal heart rate pattern.

Results

Socio-demographic characteristics of the participants

The study analyzed 133 cases and 397 controls, achieving a 100% response rate. Maternal age distribution revealed that the majority of participants in both groups were between 25 and 29 years old, comprising 77 cases (57.9%) and 225 controls (56.6%). Urban residence was more prevalent among cases, with 238 (51.7%) residing in urban areas, compared to only 44 controls (11.1%). Marital status indicated that most participants in both groups were married, with 114 cases (85.7%) and 364 controls (91.7%) reporting this status. Educational attainment showed a marked disparity, as a larger proportion of mothers in the case group (68, 51.1%) lacked formal education compared to the control group. Regarding occupational status, housewives represented the majority in both groups 80 cases (60.2%) and 201 controls (50.6%) while fewer participants were government employees (Table 1).

Variables	Categories	Case (n=133)	Control (n=397)
Maternal age in years	≤ 19	3 (2.3%)	6 (1.5%)
	20 to 24	30 (22.6%)	89 (22.4%)
	25 to 29	77 (57.9%)	225 (56.7%)
	30 to 34	21 (15.8)	71 (17.9%)
	≥ 35	2 (1.5%)	6 (1.5%)
Residence	Urban	44 (33.1%)	238 (59.9%)
	Rural	89 (66.9%)	159 (40%)
Current marital status	Married	114 (85.7%)	364 (91.7%)
	Divorced	15 (11.3%)	19 (4.8%)
	Widowed	4 (3%)	14 (3.5%)
Educational status	No formal education	68 (51.1%)	62 (15.6%)
	Primary school	30 (22.5%)	233 (58.7%)
	Secondary school	25 (18.8%)	58 (14.6%)
	College and above	10 (7.5%)	44 (11%)

Occupational status	Government employee	10 (7.5%)	44 (11%)
	Merchant	33 (24.8%)	130 (32.7%)
	Student	10 (7.5%)	22 (5.5%)
	Housewife	80 (60.2%)	201 (50.6%)

Table 1. Socio-demographic characteristics of participants in public hospitals of Central Ethiopia, (n=530).

Obstetric history related characteristics

The research findings reveal distinct differences in maternal and delivery-related variables between the case and control groups. Antenatal Care (ANC) follow-up was more frequent in the control group, with 335 participants (93.1%) attending ANC compared to 109 cases (81.9%), highlighting a higher level of maternal healthcare engagement among controls. Regarding the mode of delivery, Spontaneous Vaginal Delivery (SVD) was the most common in both groups,

with 89 cases (66.9%) and 268 controls (74.5%). Parity analysis indicated that multiparous women constituted the majority in the case group (320, 91.7%), whereas primiparous women were more prevalent among controls (77, 42.5%). Prolonged labor was reported in a higher proportion of controls (192, 48.4%) compared to cases (68, 51.1%), as was Premature Rupture of Membranes (PROM), occurring in 171 controls (43.1%) and 85 cases (64.0%). Antepartum Hemorrhage (APH) was rare in both groups, with only 3 cases (2.3%) and 6 controls (1.7%) (Table 2).

Variables	Categories	Case (133)	Control (397)
ANC follow up	Yes	109 (82%)	335 (84.3%)
	No	24 (18%)	62 (15.6%)
Mode of delivery	SVD	89 (66.9%)	268 (67.5%)
	C/S	37 (27.8%)	100 (25.2%)
	Instrumental assisted	7 (5.3%)	29 (7.3%)
Parity	Multiparous	104 (78.2%)	320 (80.6%)
	Primiparous	29 (21.8%)	77 (19.4%)
Prolonged labor	Yes	68 (51.1%)	192 (48.4%)
	No	65 (48.9%)	205 (51.6%)
PROM	Yes	85 (63.9%)	171 (43%)
	No	48 (36.1%)	226 (57%)
APH	Yes	3 (2.3%)	6 (1.5%)
	No	130 (97.7%)	391 (98.5%)
Chorioamnionitis	Yes	89 (66.9%)	184 (46.3%)
	No	44 (33.1%)	213 (53.7%)
Diabetes mellitus	Yes	13 (9.8%)	19 (4.8%)
	No	120 (90.2%)	368 (92.7%)
GHTN	Yes	36 (27.1%)	65 (16.4%)
	No	97 (72.9%)	332 (83.6%)
Anemia during pregnancy	Yes	46 (34.6%)	84 (21.2%)
	No	87 (65.4%)	313 (78.8%)

Table 2. Obstetric history related characteristics of the participants in public hospitals of Central Ethiopia, (n=530).

Newborn related characteristics

Among the participants, males accounted for a slightly higher proportion in both groups, with 75 cases (56.4%) and 209 controls (52.6%). Regarding gestational age, a similar distribution was observed across categories; however, cases showed a higher prevalence of births at the extremes of gestational age, with 43 cases (32.3%) born preterm (<37 weeks) and 45 cases (33.8%) born post-term (≥ 42 weeks), compared to 112 controls (28.2%) and 76 controls (19.1%), respectively. Birth weight varied significantly, as a larger proportion of cases (55, 41.4%) had low birth weight (<2.5 kg) compared to controls (164, 41.3%), while high birth weight (>4 kg) was slightly more common among cases (16, 12%) than controls (14, 3.5%).

APGAR scores at the 5th minute demonstrated

a striking disparity, with a greater percentage of cases (33, 24.8%) scoring ≤ 3 compared to controls (14, 3.5%), indicating higher severity of neonatal distress. The type of milk initiated showed that breast milk was less common among cases (79, 59.4%) compared to controls (305, 76.4%), while formula feeding was notably higher in cases (54, 40.6%). Birth asphyxia was more prevalent among cases (68, 51.1%) than controls (148, 37.3%), as was the need for CPAP support (63 cases, 47.4%, *vs.* 145 controls, 36.6%). Antibiotics were administered more frequently in the case group (67, 50.4%) than in the control group (168, 42.2%). Finally, a greater proportion of cases (87, 65.4%) stayed in the hospital for more than seven days compared to controls (198, 50.0%), underscoring the severity of complications among cases (Table 3).

Study variables	Categories	Case (133)	Control (397)
Sex	Male	75 (56.4%)	209 (52.6%)
	Female	58 (43.6%)	188 (47.4%)
Gestational age	<37 week	43 (32.3%)	112 (28.2%)
	37-42 week	45 (33.8%)	209 (52.6%)
	≥ 42 week	45 (33.8%)	76 (19%)
Birth weight	<2.5 kg	55 (41.4%)	164 (41.3%)
	2.5-4 kg	62 (46.6%)	219 (55.2%)
	>4 kg	16 (12%)	14 (3.5%)
APGAR score in 5 th minute	≤ 3	33 (24.8%)	14 (3.5%)
	04-Jul	81 (60.9%)	315 (79.3%)
	≥ 7	19 (14.3%)	68 (17.1%)
Type of milk started	Formula milk	54 (40.6%)	92 (23.2%)
	Breast milk	79 (59.4%)	305 (76.8%)
Birth asphyxia	Yes	68 (51.1%)	148 (37.3%)
	No	65 (48.9%)	249 (62.7%)
CPAP support	Yes	63 (47.4%)	145 (36.5%)
	No	70 (52.6%)	252 (63.5%)
Antibiotics used	Yes	67 (50.4%)	168 (42.3%)
	No	66 (49.6%)	229 (57.7%)
Length of stay in hospital	$\leq$ Seven days	46 (34.6%)	199 (50.1%)
	>Seven days	87 (65.4%)	198 (49.9%)

Table 3. Newborn related characteristics of the participants in public hospitals of Central Ethiopia, (n=530).

Determinants of necrotizing enterocolitis

To identify the determinants of necrotizing enterocolitis, variables with a p-value less than 0.25 in the bivariate analysis, along with those that had significant associations in previous studies, were included in the multivariable model for this study. In the binary logistic regression analysis, the following factors were identified as candidate variables for the final multivariable logistic regression analysis: Hypertensive disorders during pregnancy, chorioamnionitis, birth asphyxia, the type of food given to the newborn, the sex of the newborn, the length of hospital stay, the use of continuous positive airway pressure support, the use of antibiotics, and premature rupture of membranes.

However, in the final multivariable logistic regression analysis, chorioamnionitis, the length of hospital stay, the use of continuous positive airway pressure support, and premature rupture of membranes were found to be significantly associated with necrotizing enterocolitis at a 95% confidence level, with p-values less than 0.05.

The odds of developing necrotizing enterocolitis were four times higher among newborns whose mothers had chorioamnionitis compared to those whose mothers did not (AOR 4.04, 95% CI: 2.33, 6.97). Additionally, newborns who were started on formula milk were two times more likely to develop necrotizing enterocolitis compared to those who were started on breast milk (AOR 2.47, 95% CI: 1.50, 4.06).

Neonates who stayed in the hospital for seven days or more had two times higher odds of developing necrotizing enterocolitis compared to those who stayed less than seven days (AOR 2.06, 95% CI: 1.27, 3.33). Additionally, neonates who received continuous positive airway pressure support had 2.29 times higher odds of developing necrotizing enterocolitis compared to those who did not receive such support (AOR 2.29, 95% CI: 1.36, 3.87). Furthermore, newborns whose mothers experienced premature rupture of membranes had 2.5 times higher odds of developing necrotizing enterocolitis compared to those whose mothers did not (AOR 2.52, 95% CI: 1.55, 4.12) (Table 4).

Variables	Necrotizing enterocolitis		COR (95% CI)	AOR (95% CI)	p-value
	Case (133)	Control (397)			
Hypertensive disorders during pregnancy					
Yes	36 (27.1%)	65 (16.4%)	1.89 (1.19, 3.02)	1.20 (0.68, 2.11)	0.528
No	97 (72.9%)	332 (83.6%)	1	1	
Chorioamnionitis					
Yes	89 (66.9%)	184 (46.3%)	2.34 (1.55, 3.53)	4.04 (2.33, 6.97)*	0.001
No	44 (33.1%)	213 (53.7%)	1	1	
Birth asphyxia					
Yes	68 (51.1%)	148 (37.3%)	1.76 (1.18, 2.61)	1.25 (0.75, 2.07)	0.378
No	65 (48.9%)	249 (62.7%)	1	1	
Type of food given for the newborn					
Formula milk	54 (40.6%)	92 (23.2%)	2.26 (1.49, 3.44)	2.47 (1.50, 4.06)*	0.001
Breast milk	79 (59.4%)	305 (76.8%)	1	1	
Sex of the newborn					
Male	75 (56.4%)	209 (52.6%)	1.16 (0.78, 1.72)	1.02 (0.65, 1.59)	0.615
Female	58 (43.6%)	188 (47.4%)	1	1	
Length of stay in hospital					

Less than 7 days	46 (34.5%)	199 (50.1%)	1	1	0.003
7 and more days	87 (65.4%)	198 (49.9%)	1.90 (1.26, 2.85)	2.06 (1.27, 3.33)*	
Continuous positive airway pressure support					
Yes	63 (47.4%)	145 (36.5%)	1.56 (1.05, 2.32)	2.29 (1.36, 3.87)*	0.002
No	70 (52.6%)	252 (63.5%)	1	1	
Used antibiotics					
Yes	67 (50.4%)	168 (42.3%)	1.38 (0.93, 2.05)	1.39 (0.85, 2.28)	0.184
No	66 (49.6%)	229 (57.7%)	1	1	
Premature rupture of membranes					
Yes	85 (63.9%)	171 (43.1%)	2.34 (1.56, 3.51)	2.52 (1.55, 4.12)*	0.001
No	48 (36.1%)	226 (56.9%)	1	1	
Note: COR: Crude Odd Ratio; AOR: Adjusted Odd Ratio; CI: Confidence Interval, 1: Reference group, *Shows significance.					

Table 3. Newborn related characteristics of the participants in public hospitals of Central Ethiopia, (n=530).

Discussion

Necrotizing enterocolitis is one of the most prevalent gastrointestinal emergencies in newborns, representing a potentially life-threatening condition commonly encountered in neonatal intensive care units globally. This condition leads to ischemia and necrosis in certain areas of the infant's gastrointestinal system. This study aimed to identify the factors associated with necrotizing enterocolitis among newborns admitted to neonatal intensive care units in public hospitals in Central Ethiopia. The findings from a multivariable logistic regression analysis indicated that chorioamnionitis, extended hospital stay, the use of continuous positive airway pressure support, and premature rupture of membranes were significantly linked to the development of necrotizing enterocolitis in these newborns.

The odds of developing necrotizing enterocolitis were four times higher among newborns whose mothers had chorioamnionitis compared to those whose mothers did not. The finding of this study was supported by the studies conducted in Southwest Ethiopia, Sweden, and United States. The possible reason might be chorioamnionitis can initiate an inflammatory response in the newborn. Infants exposed to chorioamnionitis may also experience changes

in their gut microbiota due to the inflammatory environment and potential exposure to various pathogens. Furthermore, chorioamnionitis may impact the development of the newborn's immune system, increasing their susceptibility to infections.

Additionally, newborns who were started on formula milk were two times more likely to develop necrotizing enterocolitis compared to those who were started on breast milk. The finding of this study was supported by the study done in Southwest Ethiopia. The possible justification might be formula milk may lack some protective components that can increase susceptibility to NEC. Breast milk fosters a healthy gut microbiota, essential for digestion and immune defense, while formula feeding can disrupt the composition of gut bacteria. Additionally, breast milk offers passive immunity through immunoglobulins, helping to protect infants from infections. In contrast, formula-fed infants may not receive the same level of immune protection, making them more vulnerable to NEC.

Neonates who stayed in the hospital for seven days or more had two times higher odds of developing necrotizing enterocolitis compared to those who stayed less than seven days. The finding of this study was supported by the

studies conducted in southern Ethiopia, and Iran. The possible justification might be that prolonged hospital stays increase exposure to factors such as intravenous nutrition, antibiotic treatments, and medical devices, which can disrupt the balance of gut microorganisms, impair intestinal function, and raise the risk of infections. Delayed progression to feeding through the digestive tract further weakens the intestinal barrier, making it more susceptible to harmful bacteria. Additionally, the risk of hospital-acquired infections and the immature state of the neonatal immune system amplify this vulnerability. Together, these factors disrupt the delicate balance of the gut and immune system, significantly increasing the risk of developing necrotizing enterocolitis.

Additionally, neonates who received continuous positive airway pressure support had 2.29 times higher odds of developing necrotizing enterocolitis compared to those who did not receive such support. This finding was consistent with the result of studies done in Addis Ababa, Ethiopia. The possible justification might be neonates requiring continuous positive airway pressure often experience respiratory distress or other complications that may predispose them to NEC. Additionally, continuous positive airway pressure may trigger an inflammatory response that can impact the gastrointestinal tract. Furthermore, many infants with continuous positive airway pressure are preterm or have comorbidities that already increase their susceptibility to NEC.

Furthermore, newborns whose mothers experienced premature rupture of membranes had 2.5 times higher odds of developing necrotizing enterocolitis compared to those whose mothers did not. The finding of this study was supported by the studies conducted in Hawassa and Dilla town, Bahir Dar, Ethiopia, Netherlands, and Atlanta. The possible reason might be the increased likelihood of intra-amniotic infection and inflammation due to Premature Rupture of Membranes (PROM), which triggers a fetal inflammatory response. This inflammation can compromise the structural and functional development of the neonatal gut, weakening its barrier integrity. Additionally, PROM is associated with preterm birth, and preterm infants are inherently at higher risk of NEC due to immature intestinal and immune systems, poor gut perfusion, and a predisposition to abnormal microbiome colonization. These factors collectively create a

high-risk environment for the development of NEC in neonates exposed to PROM.

Conclusion

Chorioamnionitis, extended hospital stay, the use of continuous positive airway pressure support, and premature rupture of membranes were significantly associated with the development of Necrotizing Enterocolitis (NEC) in newborns. Special attention should be given to the prevention, early detection, and treatment of NEC, minimizing hospital stays of newborns, and timely and routine training of healthcare professionals. Additionally, strategies to promote breastfeeding and reduce the use of formula milk in at-risk neonates should be prioritized to mitigate NEC risk.

Limitations of the Study

The study design was facility-based and relied on medical records and interviews, which could have introduced information bias or inaccuracies stemming from incomplete documentation or recall errors by respondents.

Ethics Approval and Consent to Participate

This study adhered to the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Health Research Review Board of Arba Minch University, College of Medicine and Health Sciences (Reference number IRB/23189/2024), following a thorough review to ensure the protection and well-being of all participants. A formal letter of cooperation was provided by the School of Nursing to the public hospitals involved in the study. Before data collection, written permission was secured from the Medical Directors of each public hospital. In addition, all participants were fully informed about the nature and purpose of the study, and written voluntary consent was obtained from each participant prior to their involvement in the research.

Consent for Publication

Not applicable.

Availability of Data and Materials

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no conflicts

of interest.

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Author Contributions

AAL, AB, KK and TK contributed in the conception of the research problem, initiated the research, wrote the research proposal, and conducted the research. AH, AD and AA made data entry, data analysis, wrote interpretation and reviewed the final manuscript. Finally, all authors reviewed the manuscript.

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