Necrotizing Enterocolitis and Its Predictors Among Preterm Neonates Admitted in Neonatal Intensive Care Units of Gurage Zone Public Hospitals, Southwest Ethiopia, 2021

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Background: Necrotizing Enterocolitis (NEC) is the most common multifactorial and devastating gastrointestinal emergency which primarily affects premature infants. The purpose of this study was to identify the prevalence of Necrotizing Enterocolitis and its associated factors among preterm neonates admitted to Neonatal Intensive Care Units in Gurage Zone hospitals.

Methods: Institution-based cross-sectional study design was employed. The simple Random Sampling Technique was applied to collect the data using a structured questionnaire. Data were cleaned, checked for inconsistencies, coded and entered via EPI data 3.1, and exported to Stata version 14 for further analysis. The data were processed by Stata 14 to estimate the prevalence of necrotizing enterocolitis.

Results: The prevalence of Necrotizing Enterocolitis among neonates was 28 (9.7%) 95%CI of 6.8–13.7%. Birth weight (AOR: 7.33 95% CI (2.04: 26.38)), presence of maternal infection (AOR: 6.09, 95% CI (1.31:28.26)), length of hospital stay (AOR: 3.28, 95% CI (1.20, 8.96)), and initiating trophic feeding (AOR: 5.89, 95% CI (2.27:15.33)) were associated with neonatal necrotizing enterocolitis.

Conclusion: The prevalence of Necrotizing Enterocolitis among preterm neonates was significant and special attention is needed for premature neonates with low birth weight and born from mothers with infection during pregnancy. Minimizing the length of hospital stay will be very useful to prevent the occurrence of Necrotizing Enterocolitis.

Keywords: necrotizing enterocolitis, low birth weight, trophic feeding

Introduction
Necrotizing enterocolitis (NEC) is an inflammatory intestinal disorder primarily seen in premature infants, characterized by variable damage to the intestinal tract, ranging from mucosal injury to full-thickness necrosis and perforation.1 The global incidence of NEC was 7.0%.2 The incidence of NEC in India was 1.26%.3 In high-income countries, the incidence of NEC among preterm and low birth weight babies was 7% and 22% respectively.4 In one study, the prevalence of NEC among enteral Feed preterm and low birth weight neonates was 25.4%.5 The burden of NEC in 820 US centers was (7.6%).6 Early neonatal death was strongly associated with prematurity and NEC in different settings, including Ethiopia.7–14 The overall mortality in neonates with confirmed NEC was about 25%.15–17 Necrotizing enterocolitis in premature infants impacts morbidity, mortality, and septic complications in developing countries.18 Budgetary issues are
the main challenge encountered during and after the commencement of neonatal units in developing countries. In sub-Saharan countries, inadequate facilities and a lack of trained personnel are the main obstacles to neonatal care.

There are variations in the incidence of necrotizing enterocolitis between high and low-income countries. The rate of neonatal necrotizing enterocolitis in high-income countries was ranged from 2% to 7%. The Ethiopian government have been planning and prepared treatment guideline to strengthen the neonatal intensive care unit to give care for babies who are born early, and who have problems like NEC.

There is limited evidence regarding the prevalence of Necrotizing Enterocolitis & its associated factors among premature infants. Therefore, The purpose of this study was to assess the prevalence and associated factors of Necrotizing Enterocolitis among preterm neonates admitted to Neonatal Intensive Care Units of Gurage Zone public hospitals.

Methods and Materials

Study Design
A cross-sectional study was employed to assess the prevalence of Necrotizing Enterocolitis & its associated factors among neonates admitted to Neonatal Intensive Care Units of Gurage Zone public hospitals.

Study Setting and Period
The study sites were Gunchire primary hospital, Atat hospital, and Wolkite University specialized and teaching hospital from June 2019 to June 2021. The Wolkite University specialized and teaching hospital is located in Wolkite town, located 150 km away from Addis Ababa.

Study Participants and Eligibility
In this study, all preterm neonates admitted to NICU in the selected hospitals of the Gurage zone from June 2019 to June 2021 were included, and neonates with incomplete data were excluded.

Sample Size Determinations
The sample size was determined using a single population proportion using the proportion of NEC 25.4%. Assuming the $Z_{α/2}$ -critical value for normal distribution at 95% confidence level, 5% margin of error (W). After adding a 5% non-response rate, the final sample size was 288.

Sampling Technique and Procedure
Random sampling was applied to select the three hospitals from all the public hospitals in the Gurage zone. Participants that fulfilled the inclusion criteria were randomly selected using excel (computer-generated random sample). Allocation of the study subjects was applied based on the proportion of the number of medical records of the neonates.

Data Collection Tool
Data were collected by reviewing the patients’ cards using the pretested checklist. NEC was confirmed by referring to the neonates’ medical charts.

Data Quality Control
A proper data abstraction tool, which evaluated by experienced researchers, and it was pretested on 5% of the given sample size to identify problems with the checklist. Based on the pretest, variables which have had the potential of being incomplete were excluded from the tool. For the data collectors and supervisors’ training was given.

Data was cleaned, checked for inconsistencies, coded and entered via EPI data 3.1, and exported to Stata version 14 for further analysis. The data were processed by Stata 14 to estimate the prevalence of necrotizing enterocolitis. The data were processed by state 14 to estimate the prevalence of necrotizing enterocolitis. The results of this study are displayed using tables, figures, and charts.
Definition of Terms
Necrotizing enterocolitis: an acute disorder of the gastrointestinal system which could affect every part of the bowel with a partial or diffuse intestinal necrosis.

Trophic feeding: The first minimum enteral feeding to initiate the neonate gut regardless of method or volume. Early trophic feeding: indicates when the neonate starts trophic feeding within 24 hours of birth. Delayed trophic feeding: indicates when the neonates start trophic feeding after 24 hours of birth.

Result
Socio-Demographic Characteristics
Of 288 neonates admitted to NICU selected for this study, about half (51.7%) were males (see Table 1).

Maternal Intra and antepartum Characteristics
More than half (58.3%) of neonates were born from multiparous mothers. About 134 (46.5%) neonates had a birth-related complication. Regarding the mode of delivery, 52.4% of neonates were via spontaneous vaginal delivery. (See Table 2).

Clinical and Feeding Characteristics
Among the study participants, 10 (3.5%) babies had congenital anomalies, 181 (62.9%) of the babies had developed failure to breathe, 155 (53.8%) babies had respiratory distress, 237 (82.3%) babies had received antibiotics, and 90 (68.%) had received trophic feeding (see Table 3).

Prevalence of Necrotizing Enterocolitis
The prevalence of Necrotizing Enterocolitis among 288 study participants was 28 (9.7%) with a CI of 6.8–13.7% (Figure 1).

Factors Associated with Necrotizing Enterocolitis among those Neonates
Birth weight, maternal infection, length of hospital stay, and initiating trophic feeding were found to be significant factors for the development of Necrotizing enterocolitis among preterm neonates. The odds of neonates necrotizing enterocolitis among neonates who wait more than a week in NICU were 3.28 times higher than those who wait less than a week (AOR: 3.28, 95% CI (1.20, 8.96)). The odds of neonates with birth weight <1500 gm were 7.33 times more likely to develop NEC than those with a birth weight of 2500 gm–4000 gm (AOR: 7.33 95% CI (2.04: 26.38)). The odds of necrotizing enterocolitis among neonates from mothers with maternal infection were 6.09 times higher (AOR: 6.09, 95%

Table 1 Socio-Demographic Characteristics of Neonates Attending NICU of Gurage Zone Public Hospital, Southwest Ethiopia, August 2021 (n=288)

| Study Variable                | Category | Frequency | Percent % |
|------------------------------|----------|-----------|-----------|
| Sex                          | Male     | 149       | 51.7      |
|                              | Female   | 139       | 48.3      |
|                              | Total    | 288       | 100.0     |
| Birth weight classification  | <1500 gm | 94        | 32.6      |
|                              | 1500–2500 gm | 26    | 9         |
|                              | 2500–4000 gm | 166  | 58.4      |
|                              | Total    | 288       | 100.0     |
| APGAR score                  | 4–6      | 80        | 27.8      |
|                              | ≥7       | 208       | 72.2      |
|                              | Total    | 288       | 100.0     |
CI (1.31:28.26)). The odds of necrotizing enterocolitis among neonates who start trophic feeding were 5.89 times higher (AOR: 5.89, 95% CI (2.27: 15.33)) (Table 4).

Discussion

The prevalence of necrotizing enterocolitis was 9.7% (95% CI: 6.8%- 13.7). The figure was consistent with studies conducted in Seoul National University Bundang Hospital, Seongnam, Korea (7.3%),24 US centers, in which the prevalence of NEC (7.6%),6 in Duke intensive care nursery in which the incidence of NEC as 10.7%.25 The finding is higher than studies conducted in several setting,14 in which the prevalence was 3.2%, United Kingdom, reported the prevalence as 1.8% for the winter season and 2.1% for the summer season.26 This difference may be due to the disparities in healthcare. But, the finding

| Study Variable | Category | Frequency | Percent % |
|----------------|----------|-----------|-----------|
| CI (1.31:28.26)) | The odds of necrotizing enterocolitis among neonates who start trophic feeding were 5.89 times higher | AOR: 5.89, 95% CI (2.27: 15.33) |

Table 2 Maternal Intra and Antepartum Characteristics of Neonates Attending NICU of Gurage Zone Public Hospital, Southwest Ethiopia, August 2021 (n=288)

| Study Variable                                      | Category | Frequency | Percent % |
|-----------------------------------------------------|----------|-----------|-----------|
| Mode of delivery                                    | C/S      | 104       | 36.1      |
|                                                      | SVD      | 151       | 52.4      |
|                                                      | Instrumental | 33       | 11.5      |
| Parity                                              | Primipara | 120       | 41.7      |
|                                                      | Multipara | 168       | 58.3      |
| Prolonged labor                                     | Yes      | 168       | 58.3      |
|                                                      | No       | 120       | 41.7      |
| Maternal chronic disease during pregnancy           | Yes      | 84        | 29.2      |
|                                                      | No       | 204       | 70.8      |
| Maternal infection during pregnancy                 | Yes      | 211       | 73.3      |
|                                                      | No       | 77        | 26.7      |
| Mother took any drug during pregnancy               | Yes      | 54        | 18.7      |
|                                                      | No       | 234       | 81.3      |
| The baby has a birth-related complication           | Yes      | 134       | 46.5      |
|                                                      | No       | 154       | 53.5      |

Table 3 Clinical and Feeding Characteristics of Neonates Attending NICU of Gurage Zone Public Hospital, Southwest Ethiopia, August 2021 (n=288)

| Study Variable                                      | Category | Frequency | Percent % |
|-----------------------------------------------------|----------|-----------|-----------|
| The baby has congenital anomalies                   | Yes      | 10        | 3.5       |
|                                                      | No       | 278       | 96.5      |
| Need for Resuscitation after birth                  | Yes      | 181       | 62.9      |
|                                                      | No       | 107       | 37.1      |
| Respiratory distress                                | Yes      | 155       | 53.8      |
|                                                      | No       | 133       | 46.2      |
| CPAP Support                                        | Yes      | 117       | 40.6      |
|                                                      | No       | 171       | 59.4      |
| Baby receive antibiotics                            | Yes      | 237       | 82.3      |
|                                                      | No       | 51        | 17.7      |
| The baby has been diagnosed with NEC                | Yes      | 28        | 9.7       |
|                                                      | No       | 260       | 90.3      |
| Trophic feeding                                     | Yes      | 90        | 68.7      |
|                                                      | No       | 198       | 1.6       |
| Length of hospital stay                             | <7 days  | 206       | 71.5      |
|                                                      | ≥7 days  | 82        | 28.5      |
was lower than studies conducted in Addis Ababa, Ethiopia (25.4%). This difference might be due to the differences in population segment, as the study in Addis Ababa includes low birth weight infants as an inclusion criterion.

Birth weight was a significant factor for NEC. There is evidence that low birth weight increases the morbidity and mortality of neonates with NEC, Sweden, recent advance evidence, systemic review evidence, Seoul National University Bundang Hospital, Seongnam, Korea, Mexico. Figure 1 Prevalence of NEC among preterm neonates attending NICU of Gurage zone public hospital, South west Ethiopia, August 2021 (n=288).

Table 4 Bivariable and Multivariable Logistic Regression Among Neonates Attending NICU Gurage Zone Public Hospital, Southwest Ethiopia, August 2021 (n=288)

| Variables          | Category | NEC | COR      | AOR       | p-value |
|--------------------|----------|-----|----------|-----------|---------|
|                    |          | No N(%) | Yes N(%) |           |         |         |
| Birth weight       | <1500    | 18 (69.2) | 8 (30.8) | 7.85 (2.69–22.89) | 7.33 (2.04–26.38) | 0.002 |
|                    | 1500–2500 | 83 (88.3) | 11 (1.7) | 2.34 (0.93–5.87) | 1.46 (0.52–4.1) | 0.470 |
|                    | 2500–4000 | 159 (94.6) | 9(5.4) | 5.27 (1.22–22.76) | 1 | |
| Maternal infections| Yes      | 185 (87.7) | 26 (12.3) | 1.62 (0.78–3.63) | 1 | |
|                    | No       | 75 (97.4) | 10 (2.6) | 1 | 1 |
| RDS                | Yes      | 137 (88.4) | 18 (11.6) | 6.79 (2.86–16.11) | 5.89 (2.27 15.33) <0.0001 |
|                    | No       | 123 (92.5) | 10 (7.5) | 1 | 1 |
| Early Trophic feeding | Yes    | 70 (77.8) | 20 (22.2) | 1.32 (0.44–3.99) | 0.82 (0.23–2.93) | 0.762 |
|                    | No       | 190 (96) | 8(4) | 2.03 (0.92–4.52) | 3.28 (1.20, 8.96) | 0.02 |

Note: Bold text: significant association with the outcome of interest.
Maternal infection was found to be a significant factor in developing NEC. This finding was supported by studies done in Sweden, Seoul National University Bundang Hospital, Seongnam, Korea, and other countries in which chorioamnionitis was significantly associated with the development of NEC.

Initiation of trophic feeding was associated with an increase in the risk of developing NEC, and it was evidenced by findings from a referral and training center in East Azerbaijan Province of Islamic Republic of Iran, in which delaying initiation was associated with less NEC and NEC associated death.

Length of hospital stay was significantly associated with NEC. This finding was evidenced by other studies in Iran. This present study does have some limitations. Since, the data were from medical records, socioeconomic factors, and some basic information was not possible to access.

**Conclusion and Recommendation**

The prevalence of Necrotizing Enterocolitis among neonates was significant and special attention is needed for premature neonates with low birth weight and born from mothers with infection during pregnancy. Minimizing the length of hospital stay will be very useful to prevent the occurrence of Necrotizing Enterocolitis.

**Data Sharing Statement**

The datasets analyzed during the current study are available from the corresponding author on reasonable request and will be attached to the editorial office when requested at any time.

**Ethical Consideration**

This study was approved by the Wolikite University College of Health science ethical review committee. After having the clearance, a permission letter was obtained from the managers of selected hospitals in the Gurage zone. The responsible bodies of pediatric inpatient care were tolled about the purpose of this study. Written informed consent was not sought from the legally authorized representatives of the patients directly since we used a medical record. When the data was recorded from their medical chart’s identification numbers were used for each individual patient so as to make it easy to identify the individuals’ profile while keeping patient’s medical secret. This study was conducted in accordance with the declaration of Helsinki.

**Acknowledgments**

Our gratitude goes to supervisors, the data collectors, and the staff of the selected hospitals for their cordial collaboration.

**Disclosure**

The authors have declared that there is no conflicts of interest in this work.

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