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Faculty of Graduate Studies

**Risk Factors for Necrotizing Enterocolitis among
Palestinian Premature and Neonates: A Retrospective
study.**

By

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**This thesis was submitted in partial fulfillment of the
requirements for the Master`s degree in Neonatal
Nursing
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Thesis Approval

Risk Factors for Necrotizing Enterocolitis among Palestinian Premature and Neonates: A Retrospective Study

By

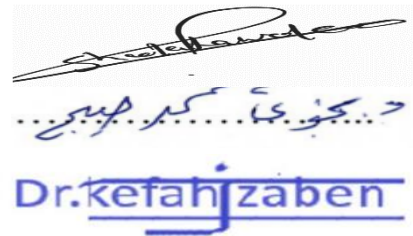
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Declaration

I declare that the work in this study titled “Risk Factors for Necrotizing Enterocolitis among Palestinian Premature and Neonates: A Retrospective Study” was carried out by me under the supervision of Dr. Waleed Shalata in the Department of Nursing .

In addition, I understand the nature of plagiarism and am aware of the University's policy on this .

The work provided in this thesis, unless otherwise referenced, is the researcher's work and has not been submitted by others elsewhere for any other degree or qualification.

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Abstract

Background: Necrotizing Enterocolitis is the most common gastrointestinal emergency in premature and neonates admitted to the neonatal intensive care unit. The most prevalent potentially fatal illness affecting the gastric tract among premature and neonates is Necrotizing Enterocolitis. There have been reports of mortality rates between 15% and 30%. Survivors are more likely to experience poor long-term growth and neurological damage, and surgical therapy is frequently required. Despite preventive measures like the use of donor milk, breastfeeding, prenatal glucocorticoid medication, and probiotic supplementation, Necrotizing Enterocolitis is still somewhat frequent in most neonatal intensive care units.

Aim: To study the Risk Factors for Necrotizing Enterocolitis among Palestinian Premature and Neonates.

Methodology: A qualitative, descriptive, retrospective study design was conducted at tertiary care hospitals (Governmental & Non-governmental) on the West Bank which contain neonatal intensive care units and treat necrotizing enterocolitis. The study population was all premature and neonates diagnosed with necrotizing enterocolitis who met the inclusion criteria. A convincing sample was composed of (191) premature neonates who participated in the study.

Result: The classification of births regarding gestational age, according to WHO standards, shows that in our study: 28.3% were extreme preterm births (24 to 27 weeks and 6 days), 48.7% were very preterm (28 to 31 weeks and 6 days), 15.7% were moderate to late preterm (32 to 36 weeks and 6 days), and 7.3% were term births (37 weeks or more). The average

birth weight was 1471 grams (with a standard deviation of 711 grams), and the average maternal age was 27 years (with a standard deviation of 5 years). Regarding the severity of necrotizing enterocolitis based on the modified Bell's Classification: 5.3% were stage IA (suspected), 13.7% were stage IB (suspected), 21.1% were stage IIA (definite, mildly ill), 17.4% were stage IIB (definite, moderately ill), 20.5% were stage IIIA (advanced, severely ill with bowel intact), and 22.1% were stage IIIB (advanced, severely ill with bowel perforation). Additionally, the maternal and sociodemographic data revealed varied rates of conditions such as hypertension, smoking, infections, and socio-economic status, offering a thorough overview of the health and socio-demographic characteristics of the sample.

Conclusion: While the average birth weight and maternal age were typical, the frequent occurrence of severe necrotizing enterocolitis highlights the serious health challenges these premature neonates face. Additionally, the varied maternal and sociodemographic factors, such as hypertension, smoking, infections, and socio-economic status, reveal the complex influences on both maternal and infant health.

Key Word: Necrotizing Enterocolitis, gastrointestinal emergency in infants, Premature and Neonates, Risk Factors

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List of Abbreviations

CRP: C-reactive protein

EPT: extremely preterm neonates

GA: gestational age

GIT: gastrointestinal tract

ICP: intrahepatic cholestasis of- pregnancy

IRB: Institutional Review Board

MAS: meconium aspiration syndrome

MPT: Moderately preterm newborns

NEC non-T: necrotizing enterocolitis non-total

NEC: Necrotizing Enterocolitis

NEC-T: necrotizing enterocolitis totalis

NICU: neonatal intensive care unit

OR: odds ratio

PDA: patent ductus arteriosus

PRBC: packed red blood cells

PTB: Pre-Term Birth

QUIPS: Quality in Prognosis Studies tool

SGA: small for gestational age

SPSS: Statistical Package for the Social Sciences

TLR4: Toll-like receptor 4

TPN: Total parenteral nutrition

VLBW: very low birth weight

WBC: white blood count

Chapter One

Introduction

1.1 Introduction

The inflammatory intestinal condition known as necrotizing enterocolitis (NEC), which is mainly observed in premature and neonates, is characterized by varying degrees of intestinal tract destruction, from mucosal injury to full-thickness necrosis and perforation (Temere et al., 2022).

According to a national prospective surveillance study, the incidence of necrotizing enterocolitis (NEC) varies from 2% to 7.5% in preterm infants and from 5% to 22% in kids with exceptionally low birth weights. For babies to have a good prognosis, problems related to low birth weight must be prevented and treated (Tan et al., 2022).

The incidence of NEC worldwide was 7.0%. In India, the prevalence of NEC was 1.26%. The incidence of NEC in low birth weight and premature neonates was 22% and 7%, respectively, in high-income nations. According to one study, 25.4% of enteral-fed preterm and low birth weight neonates had NEC. In 820 US centers, the NEC burden was 7.6%. Prematurity and NEC were highly correlated with early infant death in a variety of contexts, including Ethiopia. For neonates with confirmed NEC, the overall death rate was almost 25% (Temere et al., 2022).

The specific etiology of NEC has not been determined yet. Hemorrhagic and necrotizing inflammation inside the intestinal wall's layers is the hallmark of NEC. The Bell

staging criteria for NEC are used to classify the inflammation based on its severity. A major factor in the pathophysiology of the illness is the passage of gas-producing bacteria into the intestinal wall from the GIT lumen (Battersby and Modi, 2019).

While very preterm and low birth weight infants are the main patient of NEC, late preterm and term infants make up between 5% and 25% of all cases (Alsaied et al., 2020).

Very low birth weight (VLBW) infants that were admitted to the NICU had a prevalence of 7–13% of developing NEC, and a death rate of 10–44% (Alsaied et al., 2020).

There have been reports of mortality rates between 15% and 30%. Survivors are more likely to experience poor long-term growth and neurological damage, and surgical therapy is frequently required. Despite preventive measures like the use of donor milk, breastfeeding, prenatal glucocorticoid medication, and probiotic supplementation, NEC is still somewhat frequent in the majority of NICU (Berkhout et al., 2018).

The most risk factors for the development of NEC that were most frequently found were prematurity and low birth weight. There have been other reports of low Apgar scores, tiny for gestational age (GA), erythrocyte transfusions, treatment for patent ductus arteriosus (PDA), and nosocomial infections (Berkhout et al., 2018).

Necrotizing enterocolitis's complex pathogenesis is what makes it so unique. Prenatal risk factors like chorioamnionitis or genetic imprinting, perinatal risk factors like low birth weight, low gestational age at birth, or abnormal gut microbiota, and risk factors derived from neonatal care and stages like mechanical ventilation, feeding technique, or medication interventions are some of the most prevalent risk factors. Several factors, like as the kind of

delivery, the infant's feeding regimen, the baby's gestational age at birth, and the early use of antibiotics, might affect the premature and neonates colonization in the early stages of life. When a baby is delivered by cesarean, intestinal colonization may take longer to occur, as the premature and neonate's flora from the mother's skin colonizes them first. On the other hand, the flora from the birth canal colonizes more readily during vaginal deliveries (Martinez et al., 2022).

Necrotizing Enterocolitis is hard to forecast for a given situation. The cause is complicated and complex, involving a high level of immunoreactivity in the intestinal mucosa, aberrant microbial colonization, imbalance in microvascular tone, and hereditary susceptibility. Pneumatosis, necrosis, intestinal ischemia, and ultimately perforation are caused by a similar inflammatory mechanism (Samuels et al., 2017).

One of the prevalent illnesses that gravely endangers a newborn's life is NEC. Babies born prematurely with low birth weight (LBW) or under 36 weeks of gestation have greater rates of morbidity and mortality. Neonatal intensive care treatment technology and perinatal research have advanced rapidly in recent years, greatly increasing the survival rate of premature or low birth weight infants (Tan et al., 2022).

Once the illness has begun, it is challenging to terminate. The cornerstones of treatment are parenteral nutrition, broad-spectrum antibiotics, stomach decompression, and the suspension of enteral feedings. Choosing whether to do a laparotomy or implant a peritoneal drain for therapy or as a temporary solution is often challenging. A variety of tactics have been employed to stop NEC. The biggest advantage seems to be the supply of human milk. Regarding the prevention of non-essential cardiomyopathy, several widely held beliefs lack

supporting data. These beliefs include the very slow initiation of enteral feedings, the avoidance of feeding preterm infants during blood transfusions, and the refusal to feed infants with inserted umbilical venous or arterial lines (Neu, 2020).

1.2 Problem Statement

In recent years, there has been an increase in premature birth rates (less than 36 weeks), which has led to an increase in the entry of newborns to the NICU. One of the most common GI system problems in premature and neonates is NEC in the USA according to a systemic review study conducted by Martinez et al., 2022.

Necrotizing Enterocolitis is a life-threatening condition in the NICU. The cause of the disease remains unknown. Prematurity is the only known perinatal factor linked to an elevated risk of NEC in preterm newborns, according to studies (Neu, 2020).

Abdominal distention, metabolic acidosis, postnatal age, elevated blood glucose, and elevated liver enzymes are associated with bowel perforation in NEC. The study found that thrombocytopenia, elevated C-reactive protein (CRP), and anemia were associated with intestinal perforation in newborns with exceptionally low birth weights. It is unclear what risk factors neonates with NEC have for intestinal perforation (Tan et al., 2022).

The absence of any early diagnosis of this disease and failure to give the appropriate treatment promptly, whether, with antibiotics or surgery, will lead to a high death rate in Palestinian hospitals. There are lack of studies conducted in Palestine related to this topic.

1.3 Significant of the Study

The importance of this study lies in the urgent need to develop and improve the means and methods of early detection and treatment of NEC, to reduce the mortality rate and work to generalize this study outcomes to Palestinian hospitals.

It seems unlikely that novel approaches to diagnosis and treatment will lead to breakthroughs in lowering the related mortality and morbidity. Finding potential risk factors increases the likelihood of getting better results.

Conducting a study, especially on Palestinian Premature and Neonates provides important insights into the unique characteristics that contribute to NEC in this community. The occurrence and severity of NEC can be influenced by socioeconomic factors, healthcare procedures, and cultural influences. By evaluating these elements in the context of Palestine, the study may make specific suggestions to regional healthcare practitioners and authorities.

The study's findings can serve as a platform for future research aiming at better understanding NEC risk factors in the Palestinian population and developing targeted treatments to reduce their prevalence. The study may also motivate collaboration among researchers, healthcare professionals, and policymakers to promote evidence-based NEC prevention and management initiatives.

There is a lack of studies in Palestine about this disorder. As NEC progresses, it can lead to intestinal perforation causing peritonitis, sepsis, and death. The signs and symptoms of NEC, poor feeding, vomiting, lethargy, and abdominal tenderness, are nonspecific, so clinicians must remain suspicious when presented with these signs and symptoms in the neonatal population

While there is research on NEC risk factors in diverse groups, there may be minimal evidence available for the Palestinian setting. This work fills a vacuum by giving region-specific information on NEC risk factors, which can supplement and improve our overall understanding of the disorder.

1.4 Study Objective

1.4.1 General Objective

- To study the Risk Factors for Necrotizing Enterocolitis among Palestinian Premature and Neonates

1.4.2 Specific Objective

1. To evaluate risk factors for NEC in Palestinian Premature and Neonates.-
2. To assess the relationship between intrahepatic cholestasis of- pregnancy (ICP) and NEC in Palestinian Premature and Neonates.
3. To assess the relationship between a family history of allergic - disease and NEC in Palestinian Premature and Neonates.
4. To assess the relationship between meconium aspiration syndrome (MAS) and NEC in Palestinian Premature and Neonates.
5. To assess NEC risk variables across various GA groups.
6. To assess the relationship between Transfusion of Pack Red Blood Cells (PRBC) and NEC in Palestinian Premature and Neonates.
7. To assess the relationship between Asphyxia after birth and NEC in Palestinian Premature and Neonates.

8. To assess the relationship between Demographic characteristics and NEC in Palestinian Premature and Neonates.
9. To assess the relationship between type of delivery and NEC in Palestinian Premature and Neonates.

1.5 Study Question

1.5.1 Main Question

1. What are the risk factors for NEC in Palestinian Premature and Neonates?

1.5.2 Specific Question

1. What is the relationship between ICP and NEC in Palestinian Premature and Neonates?
2. What is the relationship between a family history of allergic - disease and NEC in Palestinian Premature and Neonates?
3. What is the relationship between MAS and NEC in Palestinian Premature and Neonates?
4. What are the NEC risk variables across various GA groups?
5. What is the relationship between the Transfusion of PRBC and NEC in Palestinian Premature and Neonates?
6. What is the relationship between Asphyxia after birth and NEC in Palestinian Premature and Neonates?
7. What is the relationship between Demographic characteristics and NEC in Palestinian Premature and Neonates?

8. What is the relationship between Mode of delivery and NEC in Palestinian Premature and Neonates?

1.6 Study Variables

- Dependent Variables: Necrotizing Enterocolitis among Palestinian Premature and Neonates.
- Independent Variables: Gestational age (GA), Intrahepatic cholestasis of pregnancy (ICP), Family history of allergic disease, Meconium Aspiration Syndrome (MAS), Demographic characteristics, Birth-weight (g), Maternal age, Gender, Mode of delivery. Asphyxia after birth, Transfusion of PRBC.

1.7 Conceptual Definition

1. Necrotizing Enterocolitis (NEC): is a serious gastrointestinal illness mainly affecting premature and neonates with low birth weight. It is characterized by intestinal wall inflammation and bacterial invasion, which can result in intestinal perforation and necrosis.
2. Risk factors: are elements that raise the possibility of contracting an illness. These for NEC include low birth weight, low Apgar scores, small stature for gestational age, erythrocyte transfusions, nosocomial infections, patent ductus arteriosus, and various conditions related to prenatal, perinatal, and neonatal care.
3. Premature infants: are those who are born before 37 weeks of pregnancy. These newborns' immature organs put them at risk for several problems, including NEC.

4. Very low birth weights (VLBW): Babies weighing fewer than 1500 grams at birth. These babies are especially susceptible to NEC.
5. Intrahepatic cholestasis of pregnancy (ICP): The liver condition might raise the risk of fetal problems, such as preterm birth and perhaps NEC.
6. Meconium Aspiration Syndrome (MAS): A respiratory distressing syndrome caused by a neonate inhaling a mixture of amniotic fluid and meconium. The possible connection between this disease and NEC is being looked at.

1.8 Operational Definition

1. NEC diagnosis: Using the Bell staging criteria, NEC will be diagnosed based on clinical symptoms such as abdominal distension, metabolic acidosis, and radiographic evidence of intestinal perforation or pneumatosis intestinalis.
2. Prematurity: According to early ultrasound readings or the mother's most recent menstrual cycle, a baby born before 37 weeks of gestation is considered premature.
3. Very low birth weights (VLBW): A birth weight of less than 1500 grams, as documented in the neonatal medical records, is considered a very low birth weight.
4. Gestational Age (GA): The number of completed weeks from the start day of the previous menstrual cycle to the day of birth.
5. Birth Weight: The newborn's weight, expressed in grams.
6. Maternal Age: The mother's age, expressed in years, at the time of delivery.
7. Type of Delivery: Based on what is documented in the medical records, the delivery was either vaginal or by cesarean section.
8. Asphyxia after Birth: Based on the requirement for resuscitation and the Apgar scores at 1 and 5 minutes after birth, the diagnosis was made.

9. PRBC transfusion: Documented if the baby had transfusions of packed red blood cells while in the intensive care unit.
10. Intrahepatic Cholestasis of Pregnancy (ICP): a diagnosis made in the medical records of the mother based on clinical symptoms such as pruritus and high serum bile acids during pregnancy.
11. Meconium Aspiration Syndrome (MAS): This condition is identified in medical records when meconium-stained amniotic fluid is found and the infant exhibits respiratory difficulty.

Chapter Two

Literature Review

2.1 Introduction

This chapter provides a synthesis of recent research found concerning Necrotizing Enterocolitis. Concepts that are critical to the study of this phenomenon include demographic data, clinical presentation, risk factors, and Necrotizing Enterocolitis among Premature and Neonates. Each concept is individually discussed.

The collection of literature was conducted utilizing a computerized search of databases. Databases were used for relevant articles and journals. The studies reviewed were published from 2014 to 2023.

2.2 Review of the studies

2.2.1 Risk Factors and Preventive Measures

Su et al. (2023) meta-analysis study in China sought to determine the risk variables for neonatal necrotizing enterocolitis (NEC) and offer suggestions for preventing it. The Chinese Biomedical Literature Database, China National Knowledge Infrastructure, Wanfang Database, Weipu Periodical Database, PubMed, Web of Science, Embase, and Cochrane Library were among the databases the writers examined for literature. They examined data from 52 studies, 48 case-control and 4 cohort studies, totaling 166,580 neonates, 33,522 in the case group and 133,058 in the control group, using Stata software. Premature membrane rupture (OR = 3.81, 95% CI:1.16-12.52), low birth weight (OR = 3.00,

95% CI:2.26-3.97), being small for gestational age (OR = 1.85, 95% CI:1.15-2.97), septicemia (OR = 4.34, 95% CI:3.16-4.15), blood transfusion (OR = 3.08, 95% CI:2.16-4.38), and congenital heart disease (OR = 2.73, 95% CI:1.55-4.81) were found to be significantly higher risk factors for NEC. This analysis was conducted. On the other hand, it was discovered that probiotic use (OR = 0.30, 95% CI: 0.22-0.40) and nursing (OR = 0.37, 95% CI: 0.23-0.59) decreased the risk. The study concluded that while breastfeeding, probiotics, prenatal glucocorticoids, and hyperbilirubinemia may lower the risk of NEC, factors like gestational diabetes, preterm membrane rupture, low birth weight, being small for gestational age, septicemia, blood transfusion, congenital heart disease, respiratory distress syndrome, early birth, and pneumonia may increase the risk.

A study by Zozaya et al (2020), aims to describe the changes in NEC mortality, therapy, and incidence in Spain throughout the previous ten years. Data from the Spanish Neonatal Network–SEN1500 database, which covered January 2005 to December 2017, were used in this multicenter cohort study. Preterm infants born at fewer than 32 weeks gestational age were included in the research; however, significant congenital deformities were excluded. The incidence of NEC, associated comorbidities (such as acute kidney injury, retinopathy of prematurity, cystic periventricular leukomalacia, late-onset sepsis, and bronchopulmonary dysplasia), mortality rates, and the proportion of surgical versus non-surgical treatments were the main outcomes that were investigated. Across four-year subperiods, the total incidence of NEC was 8.8% among 25,821 babies. On the other hand, the percentage of cases that required surgery rose dramatically from 48.8% in 2005–2008 to 70.2% in 2015–2017 ($p < 0.001$). From 36.7% in 2005–2008 to 26.6% in 2015–2017

($p < 0.001$), mortality rates decreased. The average gestational age of newborns was constant at 28.5 weeks ($p = 0.20$), while breastfeeding rates increased dramatically from 24.3% to 40.5% ($p < 0.001$). In certain units, probiotics have been used as a preventative measure; by 2015–2017, 18.6% of babies were getting them. Although the prevalence of NEC remained steady, there was a discernible rise in the number of surgical procedures performed, a decline in the death rate, and advancements in protective factors including

Campos-Martinez et al. (2022) conducted a comprehensive review that examined necrotizing enterocolitis (NEC), a devastating condition associated with preterm and the start of enteral feeding. The review looked at the most recent research on intestinal dysbiosis, low-weight formula, preterm, and human or donor milk, as well as probiotic administration, oligosaccharide supplementation, probiotic administration, and disease prediction biomarkers, as protective factors against NEC. The purpose of the study was to determine risk, predicting, and preventative variables for neonatal enterocolitis (NEC) in infants born before 37 weeks of gestation. Clinical trials, meta-analyses, randomized controlled trials, and systematic reviews that were published between January 2018 and October 2021 were included in the review. The studies were retrieved from the Cochrane Library, MEDLINE, and PubMed databases. 19 publications (out of 113) satisfied the inclusion and exclusion requirements for additional examination. The results showed that the incidence of NEC in premature newborns can be decreased by altering risk variables as gut microbiota, oxidative stress, metabolic dysfunction at birth, and immunological modulation. Gut health can be enhanced by adding human milk oligosaccharides to enteral nutrition, mixing probiotics (especially *Lactobacillus* and *Bifidobacterium* species), and supplementing with bioactive

metabolites. Finding NEC predictors such as fecal calprotectin, increased Toll-like receptor 4 (TLR4) activity, and IL6 receptor can help with early diagnosis. Although further investigation is required to establish the best probiotic doses and lactoferrin and oligosaccharide strains, encouraging results have been found recently.

During a seven-year case-control study directed by Beeby & Jeffery (2015), necrotizing enterocolitis (NEC) was identified in 82 neonates. Analysis of 74 preterm babies was done as part of the study to determine the factors influencing the development of NEC. A comparative analysis showed that the 35 children diagnosed with NEC had significantly lower birth weights, cord pH levels, and 1-minute Apgar scores when compared to control infants of the same gestational age. There were no significant differences found between the 39 infants with NEC and the controls in the 25–29-week gestational age group, except a lower percentage of the former receiving breast milk. Remarkably, every one of the eight full-term infants exhibited unique risk indicators. According to the study's conceptual framework, gestational age and vulnerability to NEC are closely related. More specifically, all newborns born between 25- and 29-weeks' gestation are at increased risk of extreme preterm. During the 30–36-week period, infants with hypoxia and developmental delays are more vulnerable; nonetheless, at term, a major predisposing event is considered necessary.

According to a study by Terrin et al (2014), necrotizing enterocolitis (NEC) is a common and fatal illness that affects infants. Although there have been great advancements in basic and clinical science research, the exact etiology of NEC is still unknown, there are few available treatments, and the rates of morbidity and death are still quite high. Understanding the history of NEC better may open up important therapy options. Innovative

methods offer promising approaches to treat and prevent NEC, such as dietary modifications, microbiome manipulation, and pharmaceutical suppression of toll-like receptor signaling. Starting with recent advances in our understanding of the pathogenic mechanisms underlying NEC, this review explores both existing and potential therapy options for this condition.

2.2.2 Long-term Outcomes and Gestational Age Impact

In a study conducted by Tan et al (2022), to improve clinical management, it is necessary to look into the factors that affect low birth weight (LBW) neonates' necrotizing enterocolitis (NEC). From January 1, 2019, to June 30, 2021, newborns admitted to our hospital were the subject of this retrospective cohort study. To determine risk factors for NEC in LBW newborns, logistic regression analyses were performed on the clinical features of both NEC and non-NEC infants. There were 192 LBW newborns in all, with a 35.42% NEC incidence. Regarding congenital heart disease, sepsis, nursing, blood transfusion, and probiotic feeding, there were notable distinctions between the NEC and non-NEC groups (all $P < .05$). Birth weight, gestational age, premature membrane rupture, maternal pregnancy-induced hypertension, amniotic fluid pollution, fetal hypoxia, neonatal respiratory distress syndrome, and mechanical ventilation did not differ significantly (all $P > .05$). Severe sepsis, blood transfusions, and congenital heart disease were independent risk factors for NEC in LBW newborns. Breastfeeding and probiotic feeding were protective factors. The prognoses of NEC infants who had surgery were better than those of infants who had conservative care ($P = .043$). Numerous factors contribute to the high incidence of NEC in infants born before full term. To improve the prognosis of infants born with low birth weight, comprehensive interventions focusing on these risk and protective variables are required.

A study conducted by Walsh & McGuire (2019), a very preterm newborn care and outcomes are improving, but prolonged hospitalization is still associated with major causes of mortality and both acute and long-term morbidity. The leading causes of mortality after the early newborn period are necrotizing enterocolitis (NEC) and late-onset infections, both of which increase the risk of neuro disability in these babies. While the precise etiology of these disorders is yet unknown, enteral feeding practices seem to play a role, particularly in the impact of immunonutrients from human breast milk on the microbial and metabolic balance of the developing gut. There is evidence to support the recommendation that mothers express breast milk as the primary food source for their extremely premature newborns. Pasteurized donor breast milk protects against NEC in situations where the mother's milk is not accessible. Randomized controlled trials have not shown that supplementing with certain immune nutrients, such as lactoferrin and immunoglobulins, is useful in avoiding infections or NEC. Although there is more proof supporting the use of probiotics and prebiotics, there are still questions about the selection, security, and accessibility of these formulations. Other tactics that are becoming increasingly important in lowering NEC, infections, and related growth and developmental problems in extremely preterm infants include staying away from medications like gastric acid suppressants that impair innate immunity and implementing evidence-based progressive feeding practices to reduce the need for invasive interventions.

Ohana et al (2020) cohort research sought to determine the crucial threshold for preterm about children's long-term digestive morbidity. This population-based study, which divided preterm newborns into four groups according to the degree of their prematurity, looked at the long-term occurrence of digestive illnesses in these infants. Hospitalizations

classified with particular ICD9 codes were used to identify digestive morbidity. A Kaplan-Meier survival curve was utilized to compare the cumulative incidence of digestive morbidity, and a Cox proportional hazards model was employed to account for confounding variables. 220,563 patients who satisfied the inclusion criteria were enrolled in the study. It was discovered that, in comparison to term newborns, preterm infants had a higher risk of digestive complications requiring hospitalization. The Kaplan-Meier survival curve showed that the risk of long-term digestive morbidity increased significantly with decreasing gestational age (Log-rank $p < 0.001$), peaking at 28 weeks of gestation. Being born severely or moderately preterm or late preterm was independently linked to long-term digestive illness, as confirmed by the Cox proportional hazards model. Preterm delivery is an independent risk factor for long-term digestive morbidity, with a critical cut-off point of 28 weeks gestation for substantial digestive difficulties.

According to a retrospective case-control study by Lu et al (2016), identifying the risk factors for neonatal necrotizing enterocolitis (NEC) is crucial to preventing its debilitating effects. The purpose of the study was to assess NEC risk variables for various gestational age (GA) groups. Bell's stage NEC II patients were divided into three groups according to GA: Group I (less than 34 weeks), Group II (more than 34 weeks but less than 37 weeks), and Group III (more than 37 weeks). Every instance had two controls that were comparable in terms of weight and GA. Medical record data were taken out and put through conditional and univariate logistic regression analysis. The study comprised 476 controls and 238 cases in total. The risk of NEC was markedly increased in preterm infants with intrahepatic cholestasis of pregnancy (ICP) and in those undergoing packed red blood cell

infusions. Furthermore, among full-term newborns, meconium aspiration syndrome (MAS) has been identified as a separate risk factor for the development of NEC. Probiotic use was linked to a lower incidence of NEC, whereas postnatal hypoxia and sepsis were linked to an elevated risk across all GA groups. Furthermore, compared to controls, babies older than 34 weeks who had congenital heart defects had a greater likelihood of developing NEC. ICP and MAS are highlighted in the paper as possible new risk factors for NEC.

Necrotizing enterocolitis (NEC) is a serious illness that mostly affects preterm babies, with the highest risk being extremely preterm infants (EPT ≤ 28 weeks), according to a study by Nair et al (2018). Additionally, a sizable fraction of NICU admissions are moderately preterm babies (MPT 28–34 weeks). NEC was discovered in 10% of EPT and 7% of MPT admissions, according to the study, which examined data from a single regional perinatal facility. In contrast, NEC was found in only 0.7% of late-preterm and term patients. The postnatal age at NEC onset and the gestational age at birth had an inverse association. Maternal hypertension problems (29%), as well as small for gestational age (SGA) (15%), were more common in MPT infants with NEC than in EPT infants (11.6% and 4.6%, respectively). Congenital gastrointestinal anomalies were present in a large number of late preterm and term infants with NEC. Mothers who have hypertensive disorders put their babies at risk for NEC and need to be closely watched. Clinical professionals can more effectively adapt interventions to prevent NEC by identifying risk factors unique to gestational age.

In a study conducted by Yu et al (2016) focused on determining the clinical outcomes and risk variables linked to intestinal perforation in preterm infants with necrotizing

enterocolitis (NEC). The study looked at clinical data from 57 premature babies who were admitted to our Neonatal Intensive Care Unit (NICU) between January 2010 and December 2012 who were diagnosed with NEC. Based on whether they had an intestinal perforation, these infants were split into two groups: those with a perforated NEC (n = 10) and those without (n = 47). A comparative examination was conducted between the two groups on several criteria, including general characteristics, clinical manifestations, and laboratory results. Significantly lower gestational age, birth weight, apnea incidence, need for mechanical ventilation, sepsis and shock incidence, lower blood pH, higher blood glucose levels, aberrant white blood cell (WBC) count, thrombocytopenia, and elevated C-reactive protein (CRP) levels were all seen in the group with perforated NEC (all with $p < 0.05$). In addition, compared to the nonperforated NEC group, the perforated NEC group had longer durations of fasting and total parenteral nutrition (TPN) usage, higher rates of cholestasis and extrauterine growth restriction (EUGR), longer durations of antibiotic treatment, higher rates of advanced antibiotic use, and a worse prognosis (all with $p < 0.05$). The study emphasizes that among premature infants diagnosed with NEC, there are several risk factors linked to intestinal perforation. By reducing the likelihood of intestinal perforation, early identification of these risk factors in premature infants with NEC may improve prognosis outcomes.

2.2.3 Clinical Characteristics and Epidemiology

According to a study by Wertheimer et al (2018), necrotizing enterocolitis (NEC) is still the most prevalent surgical emergency that poses a serious risk to a newborn's life, even after being diagnosed for almost 50 years. Although NEC is now far less common in preterm and very low birth weight infants than it was a few decades ago, it is still uncommon in term

babies and infants weighing more than 2,500 grams. According to recent research, NEC should be taken into consideration for term children with chromosomal and congenital abnormalities, especially if they have heart or gastrointestinal disorders or exhibit symptoms like feeding aversion, abdominal pain, or infection. NEC has serious short- and long-term effects on infants, making early diagnosis and treatment crucial, as well as encouraging breastfeeding as a vital preventive approach. This study addresses several NEC-related topics, including its etiology, clinical manifestations, and risk factors for term and preterm newborns, current therapies, and preventive measures. It also explores the long-term effects of NEC and emphasizes the critical role primary care physicians have in continuing to treat newborns after hospitalization.

According to a prospective multicenter case-control study by Berkhout et al (2018), identifying neonates at risk and developing focused preventative interventions can be greatly aided by identifying unique clinical risk factors for necrotizing enterocolitis (NEC). Using a sizable multicenter cohort, the study sought to identify independent risk variables linked to the development of NEC. This prospective cohort study, which involved nine newborn critical care units, enrolled children born at or below thirty weeks gestation. Up until 28 days after delivery, demographic and clinical data were continuously collected every day. In a 1:1 matched case-control cohort, univariate and multivariable analyses were used to find predictive factors for the development of NEC. Of the 843 babies in the research, 56 had been found to have NEC. Sepsis and formula feeding were associated with a higher risk of NEC incidence in the case-control study. On the other hand, giving antibiotics soon after delivery was linked to a lower incidence of NEC. The duration of parenteral feeding and the

kind of enteral feeding were found to be strongly correlated with non-essential carbohydrate consumption (NEC) in a multivariate logistic regression model. Notably, the risk of NEC was negatively linked with the early postpartum use of antibiotics. Long-term parenteral feeding and formula feeding are risk factors for NEC. Contrary to predictions, the start of antibiotic therapy within 24 hours of delivery was surprisingly inversely related to the occurrence of NEC.

2.2.4 Pathogenesis and Early Indicators

A study conducted by Temere et al (2022), premature infants are the main target of necrotizing enterocolitis (NEC), a common and serious gastrointestinal problem. In this study, the prevalence of NEC and risk factors for it in preterm newborns in Gurage Zone hospitals' Neonatal Intensive Care Units (NICUs) were to be ascertained. A straightforward random sample strategy was employed to collect data from a structured questionnaire as part of an institution-based cross-sectional study design. Following data cleaning, consistency checks, coding, and entry into EPI Data 3.1, the data were exported to Stata version 14 for additional analysis aimed at estimating the prevalence of NEC. The newborns, 28 (9.7%) had NEC, with a 95% confidence interval ranging from 6.8 to 13.7%. Birth weight, maternal illness, duration of hospital stay, and trophic feeding were factors linked to non-essential cardiomyopathy (NEC). In conclusion, there was a notable prevalence of NEC in preterm newborns. Premature newborns with low birth weights and those whose moms contracted infections during pregnancy require special care. Cutting down on hospital stays could be a big help in avoiding NEC.

Necrotizing enterocolitis (NEC) is the most frequent significant gastrointestinal problem affecting premature neonates, according to a study by Rose & Patel (2017). Although several risk factors for non-essential cardiomyopathy (NEC) have been identified in the literature, there is still some debate as to the causal importance of these factors, which go beyond gestational age, birth weight, and formula feeding. It is possible to identify risk factors for NEC before it manifests, possibly even before birth. This review's goal is to define these risk variables using the body of information that is currently available. By doing this, the review hopes to better understand the epidemiology of NEC and make it easier to identify risk factors for the next studies and attempts to improve the condition.

According to a comprehensive study by Samuels et al (2017), necrotizing enterocolitis (NEC) is a serious and complex illness that causes significant morbidity and mortality in premature newborns. A thorough understanding of the prognostic factors linked to NEC is essential for the successful identification of neonates at risk for the disorder. Through a thorough analysis of the body of available research, the study aimed to identify independent risk factors for NEC. Using multivariable analysis approaches, the author painstakingly searched databases such as Medline, Cochrane, Embase, PubMed, and Google Scholar to find cohort studies that focused on predicting factors for neonatal NEC. The chosen studies' quality was evaluated using the Quality in Prognosis Studies tool (QUIPS). After a thorough search yielding 5,154 results, 14 prognostic studies with a variety of designs were selected. Eleven research were classified as moderate or low quality, while three studies were evaluated as high quality. Significant prognostic factors for NEC were identified in some studies, along with cesarean section (associated with lower risk) and low birth weight,

small for gestational age, low gestational age, assisted ventilation, premature membrane rupture, black ethnicity, sepsis, being born outside of a hospital, hypotension, and surfactant therapy (with conflicting results). Still, it was decided that performing a meta-analysis was not viable. The review emphasized how little high-caliber research has been done on prognostic factors for NEC. It also emphasized the correlation—though not always the direct relationship—between the occurrence of NEC and several prognostic variables. To determine the predictive value of these factors, the study stressed the necessity of doing high-quality prognostic research.

2.2.5 Interventions and Treatment

The aim of a study conducted by Zhang et al (2017) was to identify perinatal risk factors for necrotizing enterocolitis (NEC) in very preterm infants. A retrospective analysis was carried out on all preterm neonates admitted to our institution between 2013 and 2016, having a gestational age of less than 32 weeks. The NEC group in this cohort consisted of patients who fulfilled inclusion requirements. The controls were chosen from the database and matched according to birth weight, gestational age, and gender. The chi-square test (χ^2) was used to compare the data, which were given as percentages (%). Using Student's t-test, quantitative data, represented as mean (standard deviation), were compared. To identify traits that were strongly correlated with NEC, conditional logistic regression was used. 46 (4.87%) of the 945 extremely preterm babies admitted to the neonatal critical care unit during the study were later diagnosed with NEC. 33 cases from the NEC group and 33 matched controls from the database were included in the study. Significant differences were found between the groups based on univariate analysis about intravenous aminophylline administration, signs

of neonatal infection, septicemia, and the prevalence of maternal placenta previa ($p < .05$). Neonatal septicemia (odds ratio [OR] = 4.000, $p = .043$) and intravenous aminophylline usage (OR = 4.922, $p = .035$) were found to be substantially linked with the development of NECs by conditional logistic regression analysis. The study thus highlights the correlation between the start of NEC in extremely preterm neonates and the administration of intravenous aminophylline and neonatal septicemia.

In a study conducted by Muller, Paula, and Seeliger (2016) in Germany, Necrotizing enterocolitis (NEC) is the most prevalent disease of the gastrointestinal tract (GIT) in premature babies and neonates. It is characterized as an ulcerative inflammation of the intestinal wall. Incipient NEC symptoms, ranging from localized digestive symptoms to sepsis-like indications, might be subtle. NEC is divided by severity into illness states using the modified Bell's Classification. Depending on severity, NEC can be treated conservatively or surgically with excision of the damaged intestine. Approximately 42% of tiny preterm newborns die. Early prevention of NEC can include breastfeeding or using pasteurized donor milk from a milk bank, administering probiotics, avoiding histamine type II receptor antagonists, and restricting antibiotic use.

2.3 Gap in the Studies

Important gaps in our understanding of necrotizing enterocolitis (NEC) persist despite a wealth of research. There are no standardized guidelines for prevention and management, and the quality of studies varies, thus large-scale, high-quality randomized controlled trials are required to corroborate findings. Further research on the long-term prognosis for NEC survivors is necessary, as the predictive usefulness of some prognostic markers is uncertain.

Furthermore, more research is needed to understand the fundamental principles of NEC etiology and innovative treatment strategies. To enhance outcomes for preterm newborns, tailored therapies based on gestational age and other risk factors must be developed.

Chapter Three

Research Methodology

3.1 Introduction

To answer our research questions, we need to choose an appropriate research design that will contribute to the following process of data collection and analysis, to check if what we claimed is right or wrong, the following parts will clarify the design that will be used and all other methodology-related questions. It covers the following sections: study design, study setting, study duration, study population, sampling, and sample size, inclusion and exclusion criteria, study instruments, validity of questionnaire, reliability of questionnaire, pilot study, data collection, ethical considerations, and data analysis.

3.2 Study design

A quantitative, descriptive, retrospective, study design was conducted to describe the risk factors for necrotizing enterocolitis among Palestinian premature and neonates.

The researcher chose governmental and non-governmental hospitals in the West Bank as research setting that contains a NICU. Hospitals have a fully computerized database for all procedures containing all data about premature and neonates.

3.3 Study Setting

The study was conducted at 10 tertiary care hospitals (Governmental & Non-governmental) on the West Bank which contain neonatal intensive care units (NICU) and treat necrotizing enterocolitis (Rafidia Hospital, Specialized Arab Hospital, Specialized

Nablus Hospital, Women's Union Hospital, Ibn Sena Hospital, Khalil Suliman Hospital, Thabit Thabit Hospital, Palestine Medical Complex, Alia Hospital), had a fully computerized health information system containing all the information related to their cases and the treatment or any procedure that was made in full details with the name and note of each health care provider contacted with neonate.

3.4 Study Duration

The study sample of data was selected from the beginning of January 2023 until the end of December 2023.

3.5 Study population

The study population was Palestinian preterm and neonates diagnosed with necrotizing enterocolitis in governmental and non-governmental hospitals in the West Bank of Palestine, who met the inclusion criteria. The accessible records of neonates in targeted hospitals were those neonates whose records were available at targeted hospitals. It was estimated to be about (378).

3.6 Sample and Sampling

A sample was taken from tertiary care hospitals in the West Bank, which included data from last year's database. Convenience sample methods were used to select data.

Convenience sampling was used, which a type of non-probability is sampling method that is also used in quantitative approaches. This form of sampling was used for the study because it was convenient for respondents. The researcher uses this strategy to choose the

appropriate sample while keeping in mind the need to include certain criteria and elements inside the study.

The total number of premature and neonates was (378). A convincing sample was composed of (191) premature and neonates who participated in the study during the data collection period. Data were collected by the researcher himself, from computerized health information system files containing all the information related to their cases and the treatment plans. The data collection procedure started by having IRB and ethical approval from universities and hospitals to collect the data from neonates' files, attaching forms of approval in Appendix II. The data collection procedure was taking all ethical considerations in order not to be annoying.

3.7 Inclusion Criteria

Full-term neonates and premature newborns who have entered the NICU with a diagnosis of necrotizing enterocolitis and the availability of a complete medical file.

3.8 Exclusion Criteria

- 1- Immunodeficiency disease,
- 2- Inherited metabolic disorder,
- 3- Major gastrointestinal malformations,
- 4- Those who had undergone abdominal surgery before enrollment.

3.9 Sample Size

The total population of premature and neonates was (378). Based on alpha 0.05, and power of 0.80, and a medium effect size, the sample included premature and neonate

necrotizing enterocolitis cases and met the pre-determined inclusion criteria. The estimated sample size is 191.

3.10 Study Instrument

The data collection tool was self-developed. The questionnaire contained three parts. Where part I was the demographic data including birth weight, maternal age, and NEC stage.

Part II Maternal characteristics of the study population according to gestational age at birth, which include maternal age, place of residence, and education level.

Part III Pregnancy characteristics and perinatal outcomes of the study population according to gestational age at birth which include gender, Apgar score, and other medical characteristics.

Necrotizing enterocolitis (NEC) can be staged into three groups, to guide appropriate treatment based on the work of Bell et al. In general, stage I and II are managed medically whereas stage III is managed surgically.

Stage I:

Clinical signs: lethargy, temperature instability, apnea, bradycardia, emesis, abdominal distension, hematochezia. Radiographic findings: intestinal dilatation. Treatment: oral feeding cessation, parenteral nutrition, nasogastric tube suction, antibiotics

Stage II

IIa: mildly ill & IIb: moderately ill

Clinical signs: as in stage I metabolic acidosis, thrombocytopenia, abdominal tenderness, absent bowel signs. Radiographic findings: intestinal dilatation, portal venous gas, pneumatosis intestinalis. Treatment: as in stage I, correction of metabolic acidosis

Stage IIIa: shock

Clinical signs: as in stage II, respiratory or circulatory arrest. Radiographic findings: as in stage II, ascites. Treatment: inotropes, etc. as in stage II

Stage IIIb: perforation

Clinical signs: any. Radiographic findings: pneumoperitoneum. Treatment: surgery

3.11 Study Validity and Reliability

The study tools evaluated by pediatric specialists and a jury group (5) of faculty staff with Ph.D. degrees in nursing specialties including the supervisor of this thesis. All their comments were taken into consideration and adjusted accordingly.

The questionnaire was evaluated by a statistician to measure reliability (calculating Cronbach's Alpha coefficient). It was validated for included intensivists, pediatricians who worked in hospitals, and nursing faculty staff members and experts.

The researcher had feedback on the questionnaire and verified the validity and reliability of the questionnaire; identified areas of vagueness; determined the real time needed to fill the questionnaire; pointed out weaknesses in wording; and got a clear opinion about the questionnaire. The researcher considered that it was a clear questionnaire, without comments regarding information from files and from a Jury group of different specialties

who evaluated the questionnaire content, therefore, the neonates were included in the actual study.

Reliability and internal consistency of the used tool showed very good reliability with a Cronbach alpha of (.762) in all variables of the used tool.

3.12 Pilot Study

The researcher conducted a pilot study with a total number of 15 premature and neonates who achieved the inclusion criteria, after they were included in the total study samples, none of the data collection tool domains had any modification, the internal consistency of the questionnaire was very good, and no further adjustment on the data collection tool was made.

3.13 Ethical Considerations

Ethical approval was obtained from Arab American University (AAUP), Institutional Review Board (IRB), and registered under the number (R-2024/A/62/N) as indicated in the Appendix 2, and permission for conducting the study in hospitals was taken from their administrative department. All data was kept confidential and only for the use of research purposes, no names of any neonates will be mentioned or used, no other information will be used in any context other than this research.

3.14 Analysis Plan

A software program was used in analyzing the data, SPSS v27, and different tests were run to test the significance changes in each independent variable on the dependent variable, including measures of central tendency and inferential statistics, testing questions via T-test,

ANOVA was used in the analysis of the gathered data. The correlation test was used to test the significance between categorical variables, and the ANOVA test was employed in testing the significance between the groups of different level measurements and other variables.

Chapter Four

Results

4.1 introduction

Data were tested for normality and results showed that the data were normally distributed, parametric analysis was used in analysis to test the research hypothesis and answer our research questions ($\alpha = 0.05$):

1. What are the risk factors for NEC in Palestinian Premature and Neonates?
2. What is the relationship between intrahepatic cholestasis of- pregnancy (ICP) and NEC in Palestinian Premature and Neonates?
3. What is the relationship between a family history of allergic - disease and NEC in Palestinian Premature and Neonates?
4. What is the relationship between meconium aspiration syndrome (MAS) and NEC in Palestinian Premature and Neonates?
5. What are the NEC risk variables across various gestational age (GA) groups?
6. What is the relationship between the Transfusion of PRBC and NEC in Palestinian Premature and Neonates?
7. What is the relationship between Asphyxia after birth and NEC in Palestinian Premature and Neonates?
8. What is the relationship between Demographic characteristics and NEC in Palestinian Premature and Neonates?

9. What is the relationship between Mode of delivery and NEC in Palestinian Premature and Neonates?

4.2 Demographics

The following table presents the distribution of births by gestational age according to the WHO classification. Among the cases, 28.3% were classified as extreme preterm births (24 to 27 weeks and 6 days), 48.7% as very preterm births (28 to 31 weeks and 6 days), 15.7% as moderate to late preterm births (32 to 36 weeks and 6 days), and 7.3% as term births (37 weeks or more)

Table 1, Gestational age

		N	N %
Q1) Gestational age by the WHO:	extreme PTB: 24 + 0–27 + 6,	54	28.3%
	very PTB: 28 + 0–31 + 6,	93	48.7%
	moderate to late PTB: 32 + 0–36 + 6 weeks)	30	15.7%
	Term Births (> 37 + 0 weeks)	14	7.3%

Table 2 provides data on birth weight and maternal age. The mean birth weight is 1471 grams, with a standard deviation of 711 grams, indicating considerable variability in birth weights among the sample. The mean maternal age is 27 years, with a standard deviation of 5 years, suggesting that most mothers are in their late twenties, with moderate age variation.

Table 2, Birth weight and maternal age.

Variable	M	SD
Q2) Birth weight (g)	1471	711
Q3) Maternal age (y)	27	5

Table 3 details the staging of necrotizing enterocolitis (NEC) according to the modified Bell's Classification, which includes radiologic and intestinal signs. The distribution is as follows: 5.3% of cases are classified as stage IA (suspected NEC), 13.7% as stage IB (suspected NEC), 21.1% as stage IIA (definite NEC, mildly ill), 17.4% as stage IIB (definite NEC, moderately ill), 20.5% as stage IIIA (advanced NEC, severely ill with bowel intact), and 22.1% as stage IIIB (advanced NEC, severely ill with bowel perforation). This indicates that most cases fall into the more severe categories of NEC.

Table 3, sample NEC staging

Q4) NEC staging according to modified Bell's Classification		
Variable	Frequency	%
IA- Suspected NEC	10	5.3
IB- Suspected NEC	26	13.7
IIA Definite NEC: mildly ill	40	21.1
IIB Definite NEC: moderately ill	33	17.4
IIIA Advanced NEC: severely ill, bowel intact	39	20.5
IIIB Advanced NEC severely ill, bowel perforated	42	22.1

Table 4 summarizes maternal and sociodemographic characteristics. For maternal chronic hypertension, 65.4% of mothers did not have it, while 34.6% did. Regarding smoking, 70.7% of mothers were non-smokers, and 29.3% were smokers. For maternal urinary tract infections, 62.3% had an infection, and 37.7% did not. In terms of maternal Group B Streptococcus (GBS) status, 66.0% were negative, and 34.0% were positive. Concerning the place of residence, 64.9% of mothers lived in a city, while 35.1% resided in a village. Educational levels varied, with 14.1% having less than a high school education, 15.2% having a high school education, 20.4% holding a diploma, 38.2% possessing a bachelor's degree, 12.0% earning a master's degree, and none having a Ph.D.

Table 4, sample response q6-11

Variable	Category	N	N %
Q6) Maternal chronic hypertension	No	125	65.4%
	Yes	66	34.6%
Q7) Smoking	No	135	70.7%
	Yes	56	29.3%
Q8) Maternal urinary tract infection	No	72	37.7%
	Yes	119	62.3%
Q9) Maternal GBS	No	126	66.0%
	Yes	65	34.0%
Q10) Place of residence	Village	67	35.1%
	City	124	64.9%
Q11) educational level	Less than high school	27	14.1%

	high school	29	15.2%
	diploma	39	20.4%
	BA	73	38.2%
	MASTER	23	12.0%
	PHD	0	0.0%

Table 5 provides a detailed breakdown of various medical conditions and complications observed in the sample population. Mild preeclampsia affected 53.4% of cases, while severe preeclampsia affected 42.4%, and eclampsia affected 47.1%. Intrauterine growth restriction was observed in 45.5% of cases, while maternal diabetes affected 38.7%. Placental abruption occurred in 29.8% of cases, and Caesarean delivery was performed in 86.4% of cases. Other conditions such as oligohydramnios affected 31.9% of cases, while polyhydramnios affected 29.3%. Notably, a significant proportion experienced a low Apgar score (< 7) in the 5th minute (74.3%), and 63.9% were small for gestational age, Gender distribution reveals that 54.5% of newborns were male, while 45.5% were female.

The immaturity of the gastrointestinal tract was prevalent, with 86.4% of cases affected. Congenital heart defects were observed in 58.1% of cases, while respiratory insufficiency affected 85.3% and sepsis affected 84.3%. Neonatal seizures were present in 48.2% of cases, and hypoglycemia affected 80.1%. Additionally, severe intrauterine growth retardation was noted in 60.7% of cases, Polycythemia affected 36.1% of cases, while gastroschisis was present in 9.4% of cases. Congenital herpes infection affected 31.4% of cases, while hemodynamic instability was observed in 80.1%. Erythrocyte transfusions were

required in 78.0% of cases, and phases of hypoxia and ischemia were noted in 29.8%. Additionally, hypothermia affected 29.3% of cases, while hyperthermia was observed in 27.7%. Abnormal bacterial accumulation in the gastrointestinal tract affected 56.5% of cases, while excessive and prolonged use of antibiotics was noted in 82.2%. Formula feeding was common, affecting 64.4% of cases. Asphyxia after birth was observed in 38.7% of cases, and meconium aspiration syndrome affected 36.6%.

Table 5, sample response q12-43

Variables	Category	N	N %
Q12) Mild preeclampsia	No	89	46.6%
	Yes	102	53.4%
Q13) Severe preeclampsia	No	110	57.6%
	Yes	81	42.4%
Q14) Eclampsia	No	101	52.9%
	Yes	90	47.1%
Q15) Intra uterine growth restriction*	No	104	54.5%
	Yes	87	45.5%
Q16) Maternal diabetes	No	117	61.3%
	Yes	74	38.7%
Q17) Placental abruption	No	134	70.2%
	Yes	57	29.8%
Q18) Caesarean delivery	No	26	13.6%
	Yes	165	86.4%

Q19) Oligohydramnios	No	130	68.1%
	Yes	61	31.9%
Q20) Polyhydramnios	No	135	70.7%
	Yes	56	29.3%
Q21) Low Apgar score (< 7) in 5th minute	No	49	25.7%
	Yes	142	74.3%
Q22) Small for gestational age	No	69	36.1%
	Yes	122	63.9%
Q23) Gender	Male	104	54.5%
	Female	87	45.5%
Q24) immaturity of the GIT	No	26	13.6%
	Yes	165	86.4%
Q25) congenital heart defects	No	80	41.9%
	Yes	111	58.1%
Q26) respiratory insufficiency	No	28	14.7%
	Yes	163	85.3%
Q27) sepsis	No	30	15.7%
	Yes	161	84.3%
Q28) neonatal seizures	No	99	51.8%
	Yes	92	48.2%
Q29) hypoglycemia	No	38	19.9%
	Yes	153	80.1%

Q30) severe intrauterine growth retardation	No	75	39.3%
	Yes	116	60.7%
Q31) Polycythemia	No	122	63.9%
	Yes	69	36.1%
Q32) gastroschisis	No	173	90.6%
	Yes	18	9.4%
Q33) congenital herpes infection	No	131	68.6%
	Yes	60	31.4%
Q34) Hemodynamic instability	No	38	19.9%
	Yes	153	80.1%
Q35) erythrocyte transfusions	No	42	22.0%
	Yes	149	78.0%
Q36) phases of hypoxia and ischemia	No	134	70.2%
	Yes	57	29.8%
Q37) hypothermia	No	135	70.7%
	Yes	56	29.3%
Q38) hyperthermia	No	138	72.3%
	Yes	53	27.7%
Q39) abnormal bacteria to accumulate in the GIT	No	83	43.5%
	Yes	108	56.5%
Q40) excessive and prolonged use of antibiotics	No	34	17.8%
	Yes	157	82.2%

Q41) Formula feeding	No	68	35.6%
	Yes	123	64.4%
Q42) Asphyxia after birth	No	117	61.3%
	Yes	74	38.7%
Q43) meconium aspiration syndrome	No	121	63.4%
	Yes	70	36.6%

Table 6 presents birth weight statistics categorized by stages of necrotizing enterocolitis (NEC). For infants suspected of NEC (stages IA and IB), the mean birth weight was 1406 grams with a standard deviation of 522 grams for stage IA, and 1998 grams with a standard deviation of 782 grams for stage IB. In cases of definite NEC, mildly ill infants (stage IIA) had a mean birth weight of 1419 grams with a standard deviation of 462 grams, while moderately ill infants (stage IIB) had a mean birth weight of 1725 grams with a standard deviation of 743 grams. For advanced NEC, severely ill infants with an intact bowel (stage IIIA) had a mean birth weight of 1212 grams with a standard deviation of 709 grams, and severely ill infants with a perforated bowel (stage IIIB) had a mean birth weight of 1259 grams with a standard deviation of 675 grams.

Table 6, NEC stages with birth weight.

Variables	Q2) Birth weight (g)	
	M	SD
IA- Suspected NEC	1406	522
IB- Suspected NEC	1998	782

IIA Definite NEC: mildly ill	1419	462
IIB Definite NEC: moderately ill	1725	743
IIIA Advanced NEC: severely ill, bowel intact	1212	709
IIIB Advanced NEC severely ill, bowel perforated	1259	675

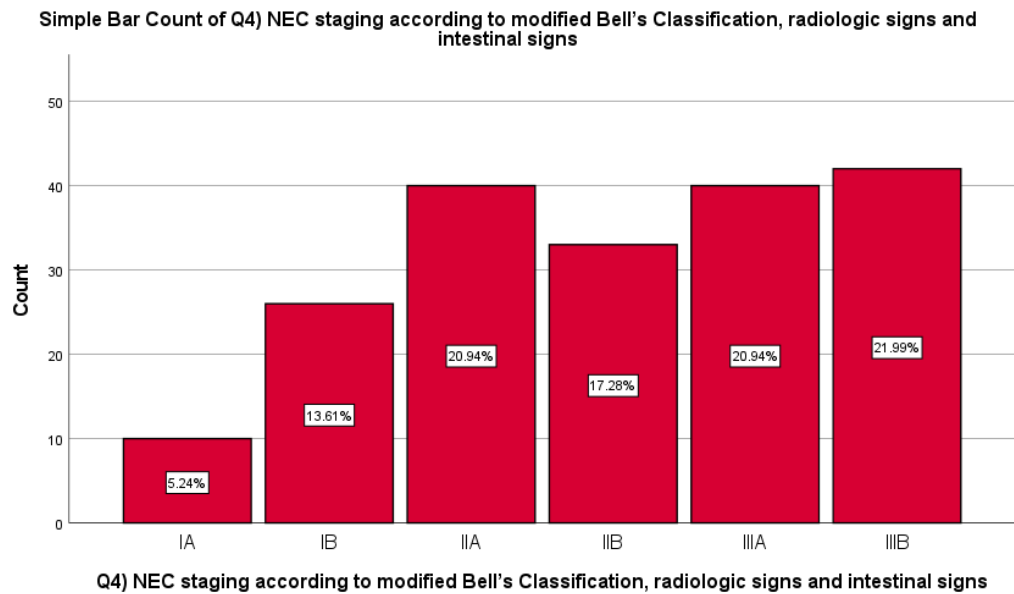


Figure 1, NEC staging distribution.

Table 7 details the distribution of NEC stages by gestational age according to WHO classifications. Among infants with suspected NEC (IA), 3.7% were born at 24–27 weeks (extreme preterm), 2.2% at 28–31 weeks (very preterm), and 20.0% at 32–36 weeks (moderate to late preterm), with no term births. For suspected NEC (IB), 7.4% were extremely preterm, 6.5% very preterm, 33.3% moderate to late preterm, and 42.9% term births. In the mildly ill definite NEC (IIA) group, 11.1% were extremely preterm, 30.1% very preterm, 13.3% moderate to late preterm, and 14.3% term births. The moderately ill definite

NEC (IIB) group had 0.0% extreme preterm, 29.0% very preterm, 20.0% moderate to late preterm, and no term births. For advanced NEC with bowel intact (IIIA), 31.5% were extremely preterm, 20.4% were very preterm, no moderate to late preterm, and 28.6% were term births. In the most severe stage, with bowel perforated (IIIB), 46.3% were extremely preterm, 11.8% very preterm, 13.3% moderate to late preterm, and 14.3% term births.

Table 7, NEC stages with Gestational age.

Variables	Q1) Gestational age by the WHO:							
	extreme PTB: 24 + 0–27 + 6,		very PTB: 28 + 0–31 + 6,		moderate to late PTB: 32 + 0–36 + 6 weeks)		Term Births (> 37 + 0 weeks)	
	N	N %	N	N %	N	N %	N	N %
IA- Suspected NEC	2	3.7%	2	2.2%	6	20.0%	0	0.0%
IB- Suspected NEC	4	7.4%	6	6.5%	10	33.3%	6	42.9%
IIA Definite NEC: mildly ill	6	11.1%	2	30.1	4	13.3%	2	14.3%
			8	%				
IIB Definite NEC: moderately ill	0	0.0%	2	29.0	6	20.0%	0	0.0%
			7	%				
IIIA Advanced NEC: severely ill, bowel intact	1	31.5%	1	20.4	0	0.0%	4	28.6%
	7		9	%				
IIIB Advanced NEC severely ill, bowel perforated	2	46.3%	1	11.8	4	13.3%	2	14.3%
	5		1	%				

Table 8 provides the mean maternal age and its standard deviation for each NEC stage. For infants with suspected NEC (IA), the mean maternal age was 29 years with a standard deviation of 5 years. For those with suspected NEC (IB), the mean maternal age was also 29 years, but with a higher standard deviation of 7 years. In the mildly ill definite NEC (IIA) group, the mean maternal age was 26 years with a standard deviation of 5 years. For the moderately ill definite NEC (IIB) group, the mean maternal age was 26 years with a standard deviation of 3 years. In the advanced NEC groups, the severely ill with bowel intact (IIIA) group had a mean maternal age of 26 years with a standard deviation of 4 years, and the severely ill with bowel perforated (IIIB) group had a mean maternal age of 26 years with a standard deviation of 5 years. This table indicates that maternal age varies slightly across different stages of NEC, with the most severe cases having younger mothers on average compared to those in the suspected NEC stages.

Table 8, NEC stages with maternal age.

Variables	Q3) Maternal age (y)	
	M	SD
IA- Suspected NEC	29	5
IB- Suspected NEC	29	7
IIA Definite NEC: mildly ill	26	5
IIB Definite NEC: moderately ill	26	3
IIIA Advanced NEC: severely ill, bowel intact	26	4

IIIB Advanced NEC severely ill, bowel perforated	26	5
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In Table 9, the significant correlations with suspected NEC (IA) include the following variables: maternal chronic hypertension had a weak negative correlation of -0.171 ($p = 0.018$), smoking had a weak negative correlation of -0.151 ($p = 0.037$), place of residence had a weak positive correlation of 0.173 ($p = 0.017$), eclampsia had a moderate negative correlation of -0.222 ($p = 0.002$), placental abruption had a weak positive correlation of 0.155 ($p = 0.032$), polyhydramnios had a weak negative correlation of -0.151 ($p = 0.037$), low Apgar score (< 7) in the 5th minute had a moderate negative correlation of -0.292 ($p < 0.001$), gender had a weak positive correlation of 0.163 ($p = 0.025$), immaturity of the GIT had a weak negative correlation of -0.181 ($p = 0.012$), severe intrauterine growth retardation had a weak negative correlation of -0.196 ($p = 0.007$), and asphyxia after birth had a weak negative correlation of -0.187 ($p = 0.010$).

Table 9, IA- Suspected NEC correlation with other variables.

Correlations		
		IA-Suspected NEC
Q1) Gestational age by the WHO:	Pearson	.104
	Correlation	
	Sig. (2-tailed)	.152

Q2) Birth weight (g)	Pearson	-.022
	Correlation	
	Sig. (2-tailed)	.767
Q3) Maternal age (y)	Pearson	.091
	Correlation	
	Sig. (2-tailed)	.210
Q5) Maternal age, year	Pearson	.091
	Correlation	
	Sig. (2-tailed)	.210
Q6) Maternal chronic hypertension	Pearson	-.171
	Correlation	
	Sig. (2-tailed)	.018
Q7) Smoking	Pearson	-.151
	Correlation	
	Sig. (2-tailed)	.037
Q8) Maternal urinary tract infection	Pearson	.086
	Correlation	
	Sig. (2-tailed)	.238
Q9) Maternal GBS	Pearson	-.070
	Correlation	
	Sig. (2-tailed)	.339

Q10) Place of residence	Pearson	.173
	Correlation	
	Sig. (2-tailed)	.017
Q11) educational level	Pearson	.002
	Correlation	
	Sig. (2-tailed)	.976
Q12) Mild preeclampsia	Pearson	.031
	Correlation	
	Sig. (2-tailed)	.669
Q13) Severe preeclampsia	Pearson	-.107
	Correlation	
	Sig. (2-tailed)	.142
Q14) Eclampsia	Pearson	-.222
	Correlation	
	Sig. (2-tailed)	.002
Q15) Intra uterine growth restriction*	Pearson	-.121
	Correlation	
	Sig. (2-tailed)	.097
Q16) Maternal diabetes	Pearson	.103
	Correlation	
	Sig. (2-tailed)	.158

Q17) Placental abruption	Pearson	.155
	Correlation	
	Sig. (2-tailed)	.032
Q18) Caesarean delivery	Pearson	.093
	Correlation	
	Sig. (2-tailed)	.199
Q19) Oligohydramnios	Pearson	.041
	Correlation	
	Sig. (2-tailed)	.577
Q20) Polyhydramnios	Pearson	-.151
	Correlation	
	Sig. (2-tailed)	.037
Q21) Low Apgar score (< 7) in 5th minute	Pearson	-.292
	Correlation	
	Sig. (2-tailed)	.000
Q22) Small for gestational age	Pearson	-.019
	Correlation	
	Sig. (2-tailed)	.795
Q23) Gender	Pearson	.163
	Correlation	
	Sig. (2-tailed)	.025

Q24) immaturity of the GIT	Pearson	-.181
	Correlation	
	Sig. (2-tailed)	.012
Q25) congenital heart defects	Pearson	.009
	Correlation	
	Sig. (2-tailed)	.902
Q26) respiratory insufficiency	Pearson	-.035
	Correlation	
	Sig. (2-tailed)	.626
Q27) sepsis	Pearson	-.028
	Correlation	
	Sig. (2-tailed)	.703
Q28) neonatal seizures	Pearson	-.038
	Correlation	
	Sig. (2-tailed)	.598
Q29) hypoglycaemia	Pearson	-.118
	Correlation	
	Sig. (2-tailed)	.103
Q30) severe intrauterine growth retardation	Pearson	-.196
	Correlation	
	Sig. (2-tailed)	.007

Q31) Polycythaemia	Pearson	.019
	Correlation	
	Sig. (2-tailed)	.795
Q32) gastroschisis	Pearson	-.076
	Correlation	
	Sig. (2-tailed)	.297
Q33) congenital herpes infection	Pearson	.043
	Correlation	
	Sig. (2-tailed)	.550
Q34) Hemodynamic instability	Pearson	-.118
	Correlation	
	Sig. (2-tailed)	.103
Q35) erythrocyte transfusions	Pearson	.125
	Correlation	
	Sig. (2-tailed)	.085
Q36) phases of hypoxia and ischemia	Pearson	.052
	Correlation	
	Sig. (2-tailed)	.473
Q37) hypothermia	Pearson	.055
	Correlation	
	Sig. (2-tailed)	.449

Q38) hyperthermia	Pearson	-.146
	Correlation	
	Sig. (2-tailed)	.044
Q39) abnormal bacteria to accumulate in the GIT	Pearson	-.078
	Correlation	
	Sig. (2-tailed)	.281
Q40) excessive and prolonged use of antibiotics	Pearson	-.014
	Correlation	
	Sig. (2-tailed)	.853
Q41) Formula feeding	Pearson	.077
	Correlation	
	Sig. (2-tailed)	.292
Q42) Asphyxia after birth	Pearson	-.187
	Correlation	
	Sig. (2-tailed)	.010
Q43) meconium aspiration syndrome	Pearson	.016
	Correlation	
	Sig. (2-tailed)	.822

In Table 10, for suspected NEC (IB), significant correlations include gestational age by the WHO with a strong positive correlation of 0.311 ($p = 0.000$) and birth weight with a strong positive correlation of 0.295 ($p = 0.000$). Maternal age also displayed a significant

positive correlation of 0.200 ($p = 0.006$), as did maternal urinary tract infection with a notable negative correlation of -0.258 ($p = 0.000$). Educational level showed a significant negative correlation of -0.208 ($p = 0.004$), while mild preeclampsia had a significant positive correlation of 0.187 ($p = 0.010$). Severe preeclampsia demonstrated a significant negative correlation of -0.217 ($p = 0.003$), and Caesarean delivery showed a strong negative correlation of -0.377 ($p = 0.000$).

Table 10, IB- Suspected NEC correlation with other variables.

Correlations		
		IB- Suspected NEC
Q1) Gestational age by the WHO:	Pearson	.311
	Correlation	
	Sig. (2-tailed)	.000
Q2) Birth weight (g)	Pearson	.295
	Correlation	
	Sig. (2-tailed)	.000
Q3) Maternal age (y)	Pearson	.200
	Correlation	
	Sig. (2-tailed)	.006
Q5) Maternal age, year	Pearson	.200
	Correlation	
	Sig. (2-tailed)	.006

Q6) Maternal chronic hypertension	Pearson	.097
	Correlation	
	Sig. (2-tailed)	.183
Q7) Smoking	Pearson	-.054
	Correlation	
	Sig. (2-tailed)	.455
Q8) Maternal urinary tract infection	Pearson	-.258
	Correlation	
	Sig. (2-tailed)	.000
Q9) Maternal GBS	Pearson	.037
	Correlation	
	Sig. (2-tailed)	.610
Q10) Place of residence	Pearson	.004
	Correlation	
	Sig. (2-tailed)	.958
Q11) educational level	Pearson	-.208
	Correlation	
	Sig. (2-tailed)	.004
Q12) Mild preeclampsia	Pearson	.187
	Correlation	
	Sig. (2-tailed)	.010

Q13) Severe preeclampsia	Pearson	-.217
	Correlation	
	Sig. (2-tailed)	.003
Q14) Eclampsia	Pearson	-.130
	Correlation	
	Sig. (2-tailed)	.073
Q15) Intra uterine growth restriction*	Pearson	-.056
	Correlation	
	Sig. (2-tailed)	.438
Q16) Maternal diabetes	Pearson	-.065
	Correlation	
	Sig. (2-tailed)	.372
Q17) Placental abruption	Pearson	-.059
	Correlation	
	Sig. (2-tailed)	.420
Q18) Caesarean delivery	Pearson	-.377
	Correlation	
	Sig. (2-tailed)	.000
Q19) Oligohydramnios	Pearson	-.010
	Correlation	
	Sig. (2-tailed)	.891

Q20) Polyhydramnios	Pearson	.013
	Correlation	
	Sig. (2-tailed)	.862
Q21) Low Apgar score (< 7) in 5th minute	Pearson	-.046
	Correlation	
	Sig. (2-tailed)	.523
Q22) Small for gestational age	Pearson	-.019
	Correlation	
	Sig. (2-tailed)	.791
Q23) Gender	Pearson	-.118
	Correlation	
	Sig. (2-tailed)	.105
Q24) immaturity of the GIT	Pearson	-.199
	Correlation	
	Sig. (2-tailed)	.006
Q25) congenital heart defects	Pearson	-.282
	Correlation	
	Sig. (2-tailed)	.000
Q26) respiratory insufficiency	Pearson	-.267
	Correlation	
	Sig. (2-tailed)	.000

Q27) sepsis	Pearson	-.164
	Correlation	
	Sig. (2-tailed)	.023
Q28) neonatal seizures	Pearson	.106
	Correlation	
	Sig. (2-tailed)	.144
Q29) hypoglycaemia	Pearson	-.185
	Correlation	
	Sig. (2-tailed)	.011
Q30) severe intrauterine growth retardation	Pearson	-.306
	Correlation	
	Sig. (2-tailed)	.000
Q31) Polycythaemia	Pearson	.083
	Correlation	
	Sig. (2-tailed)	.254
Q32) gastroschisis	Pearson	.290
	Correlation	
	Sig. (2-tailed)	.000
Q33) congenital herpes infection	Pearson	-.006
	Correlation	
	Sig. (2-tailed)	.940

Q34) Hemodynamic instability	Pearson	-.185
	Correlation	
	Sig. (2-tailed)	.011
Q35) erythrocyte transfusions	Pearson	-.305
	Correlation	
	Sig. (2-tailed)	.000
Q36) phases of hypoxia and ischemia	Pearson	.008
	Correlation	
	Sig. (2-tailed)	.912
Q37) hypothermia	Pearson	.080
	Correlation	
	Sig. (2-tailed)	.273
Q38) hyperthermia	Pearson	.095
	Correlation	
	Sig. (2-tailed)	.191
Q39) abnormal bacteria to accumulate in the GIT	Pearson	-.083
	Correlation	
	Sig. (2-tailed)	.252
Q40) excessive and prolonged use of antibiotics	Pearson	-.214
	Correlation	
	Sig. (2-tailed)	.003

Q41) Formula feeding	Pearson	.104
	Correlation	
	Sig. (2-tailed)	.153
Q42) Asphyxia after birth	Pearson	-.128
	Correlation	
	Sig. (2-tailed)	.078
Q43) meconium aspiration syndrome	Pearson	-.175
	Correlation	
	Sig. (2-tailed)	.015
IB- Suspected NEC	Pearson	1
	Correlation	

In Table 11, significant variables correlated with IIA Definite NEC (mildly ill) include smoking, which shows a negative correlation of -0.162 ($p = 0.025$), indicating that smoking is associated with a lower incidence of this NEC stage. Maternal urinary tract infection has a negative correlation of -0.210 ($p = 0.003$), suggesting that UTIs are associated with lower incidences of mild NEC. Place of residence shows a strong negative correlation of -0.350 ($p = 0.000$), indicating a significant link between residence and NEC incidence. Immaturity of the gastrointestinal tract has a positive correlation of 0.204 ($p = 0.005$), suggesting that immaturity of the GIT increases the likelihood of developing mild NEC. Hyperthermia is significantly positively correlated at 0.342 ($p = 0.000$), showing that higher temperatures are linked to an increased risk of mild NEC. Finally, meconium aspiration

syndrome has a positive correlation of 0.169 ($p = 0.019$), indicating an association with higher rates of mild NEC.

Table 11, IIA Definite NEC: mildly ill correlation with other variables.

Correlations		
		IIA Definite NEC: mildly ill
Q1) Gestational age by the WHO:	Pearson Correlation	.017
	Sig. (2-tailed)	.810
Q2) Birth weight (g)	Pearson Correlation	-.038
	Sig. (2-tailed)	.600
Q3) Maternal age (y)	Pearson Correlation	-.031
	Sig. (2-tailed)	.671
Q5) Maternal age, year	Pearson Correlation	-.031
	Sig. (2-tailed)	.671
Q6) Maternal chronic hypertension	Pearson Correlation	.005
	Sig. (2-tailed)	.947
Q7) Smoking	Pearson Correlation	-.162

	Sig. (2-tailed)	.025
Q8) Maternal urinary tract infection	Pearson Correlation	-.210
	Sig. (2-tailed)	.003
Q9) Maternal GBS	Pearson Correlation	.092
	Sig. (2-tailed)	.206
Q10) Place of residence	Pearson Correlation	-.350
	Sig. (2-tailed)	.000
Q11) educational level	Pearson Correlation	-.119
	Sig. (2-tailed)	.100
Q12) Mild preeclampsia	Pearson Correlation	.042
	Sig. (2-tailed)	.562
Q13) Severe preeclampsia	Pearson Correlation	.027
	Sig. (2-tailed)	.711
Q14) Eclampsia	Pearson Correlation	.055
	Sig. (2-tailed)	.446

Q15) Intra uterine growth restriction*	Pearson	.124
	Correlation	
	Sig. (2-tailed)	.089
Q16) Maternal diabetes	Pearson	.013
	Correlation	
	Sig. (2-tailed)	.855
Q17) Placental abruption	Pearson	.002
	Correlation	
	Sig. (2-tailed)	.981
Q18) Caesarean delivery	Pearson	-.021
	Correlation	
	Sig. (2-tailed)	.775
Q19) Oligohydramnios	Pearson	-.077
	Correlation	
	Sig. (2-tailed)	.292
Q20) Polyhydramnios	Pearson	.036
	Correlation	
	Sig. (2-tailed)	.621
Q21) Low Apgar score (<7) in 5th minute	Pearson	.008
	Correlation	
	Sig. (2-tailed)	.916

Q22) Small for gestational age	Pearson	.092
	Correlation	
	Sig. (2-tailed)	.204
Q23) Gender	Pearson	-.032
	Correlation	
	Sig. (2-tailed)	.665
Q24) immaturity of the GIT	Pearson	.204
	Correlation	
	Sig. (2-tailed)	.005
Q25) congenital heart defects	Pearson	-.085
	Correlation	
	Sig. (2-tailed)	.244
Q26) respiratory insufficiency	Pearson	.068
	Correlation	
	Sig. (2-tailed)	.351
Q27) sepsis	Pearson	-.061
	Correlation	
	Sig. (2-tailed)	.404
Q28) neonatal seizures	Pearson	-.058
	Correlation	
	Sig. (2-tailed)	.422

Q29) hypoglycaemia	Pearson	.128
	Correlation	
	Sig. (2-tailed)	.079
Q30) severe intrauterine growth retardation	Pearson	-.113
	Correlation	
	Sig. (2-tailed)	.119
Q31) Polycythaemia	Pearson	.068
	Correlation	
	Sig. (2-tailed)	.348
Q32) gastroschisis	Pearson	.010
	Correlation	
	Sig. (2-tailed)	.889
Q33) congenital herpes infection	Pearson	.095
	Correlation	
	Sig. (2-tailed)	.190
Q34) Hemodynamic instability	Pearson	-.130
	Correlation	
	Sig. (2-tailed)	.072
Q35) erythrocyte transfusions	Pearson	-.100
	Correlation	
	Sig. (2-tailed)	.171

Q36) phases of hypoxia and ischemia	Pearson	.086
	Correlation	
	Sig. (2-tailed)	.236
Q37) hypothermia	Pearson	-.105
	Correlation	
	Sig. (2-tailed)	.147
Q38) hyperthermia	Pearson	.342
	Correlation	
	Sig. (2-tailed)	.000
Q39) abnormal bacteria to accumulate in the GIT	Pearson	.062
	Correlation	
	Sig. (2-tailed)	.395
Q40) excessive and prolonged use of antibiotics	Pearson	.105
	Correlation	
	Sig. (2-tailed)	.148
Q41) Formula feeding	Pearson	.033
	Correlation	
	Sig. (2-tailed)	.647
Q42) Asphyxia after birth	Pearson	-.040
	Correlation	
	Sig. (2-tailed)	.587

Q43) meconium aspiration syndrome	Pearson	.169
	Correlation	
	Sig. (2-tailed)	.019

In Table 12, significant variables correlated with IA-Suspected NEC using ANOVA analysis include place of residence and gender. Place of residence has a significant F-value of 5.816 ($p = 0.017$), indicating that mother living in the cities were significantly at higher risk of IA suspected NEC. Gender also shows a significant F-value of 5.132 ($p = 0.025$), suggesting that females were at a significantly higher risk than males in the likelihood of developing IA suspected NEC. Other variables such as birth weight, maternal age, meconium aspiration syndrome, gestational age by WHO, phases of hypoxia and ischemia, and caesarean delivery did not show significant associations with IA-Suspected NEC.

Table 12, IA- Suspected NEC ANOVA with other variables.

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
Q2) Birth weight (g)	Between Groups	44720.823	1	44720.823	.088	.767
	Within Groups	96046898.287	189	508184.647		
	Total	96091619.110	190			

Q3) Maternal age (y)	Between Groups	36.577	1	36.577	1.58 4	.210
	Within Groups	4364.334	189	23.092		
	Total	4400.911	190			
Q43) meconium aspiration syndrome	Between Groups	.012	1	.012	.051	.822
	Within Groups	44.334	189	.235		
	Total	44.346	190			
Q1) Gestational age by the WHO:	Between Groups	1.516	1	1.516	2.07 1	.152
	Within Groups	138.400	189	.732		
	Total	139.916	190			
Q36) phases of hypoxia and ischemia	Between Groups	.109	1	.109	.516	.473
	Within Groups	39.881	189	.211		
	Total	39.990	190			
Q10) Place of residence	Between Groups	1.298	1	1.298	5.81 6	.017
	Within Groups	42.199	189	.223		
	Total	43.497	190			
	Between Groups	.196	1	.196	1.66 0	.199

Q18)	Within Groups	22.265	189	.118		
Caesarean delivery	Total	22.461	190			
Q23) Gender	Between Groups	1.252	1	1.252	5.13 2	.025
	Within Groups	46.119	189	.244		
	Total	47.372	190			

In Table 13, the significant variables correlated with IB-Suspected NEC using ANOVA analysis include birth weight, maternal age, meconium aspiration syndrome, gestational age by the WHO, and caesarean delivery. Birth weight has a significant F-value of 17.977 ($p = 0.000$), indicating a strong association with suspected NEC. Maternal age shows a significant F-value of 7.856 ($p = 0.006$), suggesting that the age of the mother is significantly related to the incidence of suspected NEC. Meconium aspiration syndrome also presents a significant F-value of 5.984 ($p = 0.015$). Gestational age by WHO has a significant F-value of 20.292 ($p = 0.000$), highlighting its strong correlation with suspected NEC. Additionally, cesarean delivery shows a significant F-value of 31.253 ($p = 0.000$), indicating a significant relationship with suspected NEC. Other variables such as phases of hypoxia and ischemia, place of residence, and gender did not show significant associations with IB-Suspected NEC.

Table 13, IB- Suspected NEC ANOVA with other variables.

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Q2) Birth weight (g)	Between Groups	8345889.996	1	8345889.996	17.977	.000
	Within Groups	87745729.114	189	464263.117		
	Total	96091619.110	190			
Q3) Maternal age (y)	Between Groups	175.623	1	175.623	7.856	.006
	Within Groups	4225.288	189	22.356		
	Total	4400.911	190			
Q43) meconium aspiration syndrome	Between Groups	1.361	1	1.361	5.984	.015
	Within Groups	42.985	189	.227		
	Total	44.346	190			
Q1) Gestational age by the WHO:	Between Groups	13.566	1	13.566	20.292	.000
	Within Groups	126.351	189	.669		
	Total	139.916	190			
	Between Groups	.003	1	.003	.012	.912

Q36) phases of hypoxia and ischemia	Within Groups	39.987	189	.212		
	Total	39.990	190			
Q10) Place of residence	Between Groups	.001	1	.001	.003	.958
	Within Groups	43.497	189	.230		
	Total	43.497	190			
Q18) Caesarean delivery	Between Groups	3.187	1	3.187	31.25	.000
	Within Groups	19.274	189	.102	3	
	Total	22.461	190			
Q23) Gender	Between Groups	.658	1	.658	2.660	.105
	Within Groups	46.714	189	.247		
	Total	47.372	190			

In Table 14, the significant variables correlated with IIA Definite NEC (mildly ill) using ANOVA analysis include meconium aspiration syndrome and place of residence. Meconium aspiration syndrome shows a significant F-value of 5.578 ($p = 0.019$), indicating a significant relationship with the incidence of IIA Definite NEC. Place of residence has a highly significant F-value of 26.328 ($p = 0.000$), suggesting a strong correlation with the occurrence of IIA Definite NEC. Other variables such as birth weight, maternal age,

gestational age by the WHO, phases of hypoxia and ischemia, cesarean delivery, and gender did not show significant associations with IIA Definite NEC.

Table 14, IIA Definite NEC: mildly ill ANOVA with other variables.

ANOVA							
			Sum of Squares	df	Mean Square	F	Sig.
Q2) Birth weight (g)	Between Groups		139984.276	1	139984.276	.276	.600
	Within Groups		95951634.834	189	507680.608		
	Total		96091619.110	190			
Q3) Maternal age (y)	Between Groups		4.203	1	4.203	.181	.671
	Within Groups		4396.708	189	23.263		
	Total		4400.911	190			
Q43) Meconium aspiration syndrome	Between Groups		1.271	1	1.271	5.578	.019
	Within Groups		43.074	189	.228		
	Total		44.346	190			

Q1) Gestational age by the WHO:	Between Groups	.043	1	.043	.058	.810
	Within Groups	139.874	189	.740		
	Total	139.916	190			
Q36) Phases of hypoxia and ischemia	Between Groups	.297	1	.297	1.413	.236
	Within Groups	39.693	189	.210		
	Total	39.990	190			
Q10) Place of residence	Between Groups	5.318	1	5.318	26.32 8	.000
	Within Groups	38.179	189	.202		
	Total	43.497	190			
Q18) Caesarean delivery	Between Groups	.010	1	.010	.082	.775
	Within Groups	22.451	189	.119		
	Total	22.461	190			
Q23) Gender	Between Groups	.047	1	.047	.188	.665

	Within Groups	47.325	189	.250		
	Total	47.372	190			

Chapter Five

Discussion

5.1 Introduction

The study involving 191 participants provides a detailed look at factors associated with necrotizing enterocolitis (NEC) in Palestinian premature and neonates. The data collection tool was reliable, with a Cronbach's alpha of 0.762, indicating good consistency across the 48 variables measured.

5.2 Demographic and gestational age

GA categorized the participants as extreme PTB with a prevalence (28.3%), this result is similar to Lu et al., 2016 (30.7%) and Zozaya et al., 2020 (28.5%) but was not similar to Ohana et al., 2021 (0.4%). On the other hand, very PTB (48.7%) is not similar to Ohana et al., 2021 (0.1%) and Lu et al., 2016 (34.8%).

Related to moderate to late PTB (15.7%) is similar to Ohana et al., 2021 (6.0%). The last category is term birth (7.3%) was not similar to Ohana et al., 2021 (93.5%) and Lu et al., 2016 (39.4%).

Gestational age influences how severe NEC stages are. Severe NEC stages IIIA and IIIB are associated with a higher incidence of extreme preterm deliveries (24–27 weeks), this result is consistent with Ohana et al., 2021 and Nair et al., 2018.

This high percentage of very preterm births (48.7%) suggests that a large portion of the population is at increased risk for NEC, as prematurity is a major risk factor.

5.3 Birth Weight and Maternal Age

As shown in the result, the mean birth weight is (1471 gm) which is consistent with Campos-Martinez et al., 2022 show (1760 gm) and Berkhout et al., 2018 show (1810 gm), and consistent with Tan et al., 2022 (1838 gm). The variation in birth weight indicates a wide range of neonatal sizes, from extremely low to higher birth weights, which can impact the severity and incidence of NEC.

The mean maternal age is (27 years) similar to Ohana et al., 2021 (28.47 years) and Berkhout et al., 2018 (25 years). Maternal age doesn't vary much across NEC stages, averaging between 26 and 29 years. However, there's a slight tendency to indicate younger mothers might have infants in more severe NEC stages.

5.4 NEC Staging (Modified Bell's Classification)

The distribution of NEC stages was as follows, stage IA (Suspected NEC) which shows in result (5.3%), this result is not similar to Berkhout et al., 2018 (85%) of term infants have Stage IA.

There are weak to moderate connections between suspected NEC (IA) and variables such as maternal chronic hypertension, smoking, and place of residence, eclampsia, placental abruption, low Apgar score, gender, GIT immaturity, severe intrauterine growth retardation, and post-birth hypoxia. There is a substantial correlation between suspected NEC (IA) and female gender and urban living, suggesting a higher risk factor connected with these characteristics.

Related to Stage IB (Suspected NEC) (13.7%) that's not similar to Wertheimer et al., 2019 which shows (77.3%). The prevalence of term births in suspected NEC stages (IA and IB) suggests a connection between the severity of NEC and gestational age, it consistent with Berkhout et al., 2018 and Nair et al., 2018.

Suspected NEC (IB) has a negative correlation with maternal urinary tract infection and educational attainment, and a strong positive correlation with gestational age, birth weight, and mother age. Strong correlations have been found between birth weight, mother age, meconium aspiration syndrome, cesarean delivery, and gestational age by the World Health Organization (IB) and probable NEC (IB).

While Stage IIA (Definite NEC, mildly ill) is (21.1%) that's similar to Berkhout et al., 2018 (33.9%) and Wertheimer et al., 2019 (25%); About Stage IIB (Definite NEC, moderately ill) (17.4%) which similar to Berkhout et al., 2018 (28.6%).

There is a substantial correlation between location of residency and meconium aspiration syndrome in IIA Definite NEC (Mildly Ill), suggesting potential roles as risk factors.

Several risk factors for mild NEC are highlighted by the substantial correlations observed between IIA Definite NEC and smoking, maternal urinary tract infection, place of residency, GIT immaturity, hyperthermia, and meconium aspiration syndrome.

On the other hand, Stage IIIA (Advanced NEC, severely ill with bowel intact) is (20.5%) similar to Berkhout et al., 2018 (14.3%); Stage IIIB (Advanced NEC, severely ill with bowel perforation) is (22.1%) which is similar to Berkhout et al., 2018 (23.2%).

Most cases were in the severe stages (IIIA and IIIB), highlighting the significant burden and severity of NEC in this group.

5.5 Maternal and Sociodemographic Characteristics

When we talk about Maternal and Sociodemographic Characteristics, the prevalence of chronic hypertension is (34.6%) which consistent with Nair et al., 2018 is (30.1%) and Ohana et al., 2021 (27.3%); Maternal smoking (29.3%) consistent with Campos-Martinez et al., 2022 (34.3%); Urinary tract infection (62.3%) that inconsistent with Zhang et al., 2017 (25.9%) and inconsistent with Beeby& Jeffery (2015) (37.2%).

City residents (64.9%) which is similar to Lu et al., 2016 (51.5%) and Berkhout et al., 2018 (61.1%); Education (bachelor's degree) (38.2%) not similar to Rose & Patel (2018) that show (74.2%).

These maternal factors, such as chronic hypertension and infections, can adversely affect fetal development and increase NEC risk. The high level of education among mothers might influence their healthcare practices and access.

5.6 Medical Conditions and Complications

The prevalence of various conditions included mild preeclampsia which shows in the result is (53.4%) this result is similar to Rose & Patel, 2018 mild preeclampsia (61.2%) and similar to Berkhouta et al., 2018 (59.3%); Severe preeclampsia (42.4%) which similar to Campos-Martinez et al., 2022 (51.6%); Eclampsia (47.1%) that not similar to Nair et al., 2018 (11.7%) but similar with Muller et al., 2016 (41.3%).

On the other hand, Maternal diabetes (38.7%) that not consistent with Su et al., 2023 (80.6%) and Rose & Patel 2018 (67.5%); Caesarean delivery (86.4%) which is consistent with Su et al., 2023 (80.7%) and Lu et al., 2016 (58.9%); Respiratory insufficiency (85.3%) that consistent with Su et al., 2023 (79.8%) and Ohana et al., 2021 (76.3%).

Sepsis (84.3%) similar to Su et al., 2023 (88.9%) and Luquan et al., 2020 (74.8%); Hypoglycemia (80.1%) similar to Zhang et al., 2017 (69.9%) and Berkhout et al., 2018 (76.6%). PRBC (78%) which is consistent with Janjindamai et al., 2019.

High rates of preeclampsia, and maternal diabetes are significant as they complicate pregnancies and impact neonatal outcomes, increasing the risk for NEC. The high percentage of Caesarean deliveries and respiratory issues highlight the medical complexity faced by these newborns.

Chapter Six

Conclusion and Recommendation

6.1 Conclusion

Necrotizing enterocolitis (NEC) in preterm and neonatal Palestinians offers important information about the severity and risk factors of the condition. It demonstrates that a significant percentage of cases of NEC are in very preterm (48.7%) and severe preterm (28.3%) newborns, underscoring the greater risk associated with lower gestational ages at birth. At 1471 grams, the average birth weight is low and highly variable, suggesting a substantial correlation between lower birth weights and more severe NEC stages. The majority of cases are in severe phases IIIA (20.5%) and IIIB (22.1%), which emphasizes the significance of low birth weight even more.

The prevalence of maternal health conditions such as smoking (29.3%), urinary tract infections (62.3%), and chronic hypertension (34.6%) suggests that these conditions raise the risk of NEC. The majority of women reside in cities (64.9%) and have a bachelor's degree (38.2%), suggesting that sociodemographic and educational characteristics affect the health of newborns. NEC development is further aided by the prevalence of medical disorders such as preeclampsia, intrauterine growth restriction, and maternal diabetes.

A strong correlation between the severity of NEC and gestational age, with extremely preterm and extreme newborns having a higher risk of developing severe NEC. These results highlight the necessity of addressing maternal and neonatal health variables to lower the

prevalence and severity of NEC. For high-risk populations, they stress the significance of focused interventions and specialized care.

6.2 Recommendation

1. Focus on improving prenatal care for mothers with chronic hypertension, urinary tract infections, and smoking habits. Regular monitoring and early interventions can help manage these risks.
2. Provide nutritional support for pregnant women to improve birth weights and overall neonatal health.
3. Implement regular screening for early signs of NEC in premature infants to ensure timely treatment.
4. Monitor High-Risk Groups, pay particular attention to Extreme Preterm Births (24–27 weeks) and Very Preterm Births (28–31 weeks), as these cases exhibited greater rates of severe NEC stages (IIIA and IIIB).
5. Increase the level of care and surveillance during and after cesarean sections, particularly as 86.4% of NEC cases involved cesarean sections.
6. Infants with low Apgar scores (< 7) at the fifth minute should receive extra attention because there is a strong correlation between them and a higher risk of NEC.
7. Educate expecting mothers on the importance of managing infections, particularly urinary tract infections, during pregnancy, and help pregnant women quit smoking reducing the risk of NEC and other complications.

8. Train healthcare providers in the latest NEC management and prevention strategies to ensure they can offer the best care. On the other hand, support research into the causes of NEC and the development of new treatments and prevention methods.

6.3 Study Limitation

1. The study is retrospective, it relies on existing records and data, which may not have been collected with the same rigor as prospective data. This can introduce recall bias and limit the ability to establish causality.
2. The study might lack long-term follow-up data to assess the outcomes of infants with NEC, limiting the understanding of the condition's impact over time.
3. Difficulty moving between cities due to the occupation situation during data collection.
4. Missing data could not be retrieved such as feeds could not be analyzed as data regarding the type of feeds was missing.
5. We can only describe the association between the risk factors and NEC; further studies would be needed to address effects.

References

Al Tawil, K., Sumaily, H., Ahmed, I. A., Sallam, A., Al Zaben, A., Al Namshan, M., & Crankson, S. (2013). Risk factors, characteristics and outcomes of necrotizing enterocolitis in late preterm and term infants. *Journal of neonatal-perinatal medicine*, 6(2), 125-130.

Alsaied A, Islam N, Thalib L. Global incidence of necrotizing enterocolitis: a systematic review and meta-analysis. *BMC Pediatr.* 2020;20(1):1–15. doi:10.1186/s12887-020-02231-5

Battersby C, Modi N. Challenges in advancing necrotizing enterocolitis research. *Clin Perinatol.* 2019;46(1): 19–27

Beeby, P. J., & Jeffery, H. (1992). Risk factors for necrotising enterocolitis: the influence of gestational age. *Archives of disease in childhood*, 67(4 Spec No), 432-435.

Berkhout, D. J., Klaassen, P., Niemarkt, H. J., de Boode, W. P., Cossey, V., van Goudoever, J. B., ... & de Meij, T. G. (2018). Risk factors for necrotizing enterocolitis: a prospective multicenter case-control study. *Neonatology*, *114*(3), 277-284.

Campos-Martinez, A. M., Expósito-Herrera, J., Gonzalez-Bolívar, M., Fernández-Marin, E., & Uberos, J. (2022). Evaluation of risk and preventive factors for necrotizing enterocolitis in premature newborns. A systematic review of the literature. *Frontiers in Pediatrics*, *10*, 874976.

Chekole Temere, B., Aynalem Mewahegn, A., Tefera Zewudie, B., Alebel GebreEyesus, F., Kassaw, A., Gelaw Walle, B., ... & Seid, W. (2022). Necrotizing enterocolitis and its predictors among preterm neonates admitted in neonatal intensive care units of Gurage zone public hospitals, Southwest Ethiopia, 2021. *Pediatric health, medicine and therapeutics*, 95-102.

Drenckpohl, D., Knaub, L., Schneider, C., McConnell, C., Wang, H., & Macwan, K. (2010). Risk factors that may predispose premature infants to increased incidence of necrotizing enterocolitis. *ICAN: Infant, Child, & Adolescent Nutrition*, 2(1), 37-44.

Gregory, K. E., DeForge, C. E., Natale, K. M., Phillips, M., & Van Marter, L. J. (2011). Necrotizing enterocolitis in the premature infant: neonatal nursing assessment, disease pathogenesis, and clinical presentation. *Advances in Neonatal Care*, 11(3), 155-164.

Hall, N. J., Eaton, S., & Pierro, A. (2013). Necrotizing enterocolitis: Prevention, treatment, and outcome. *Journal of pediatric surgery*, 48(12), 2359-2367.

Janjindamai, W., Prapruettrong, A., Thatrimontrichai, A., Dissaneevate, S., Maneenil, G., & Geater, A. (2019). Risk of necrotizing enterocolitis following packed red blood cell transfusion in very low birth weight infants. *The Indian Journal of Pediatrics*, 86, 347-353.

Lu, Q., Cheng, S., Zhou, M., & Yu, J. (2017). Risk factors for necrotizing enterocolitis in neonates: a retrospective case-control study. *Pediatrics & Neonatology*, 58(2), 165-170.

Luquan, L., Lu, G., & Zhongyao, Z. (2020). Advances in the diagnosis and medical treatment of neonatal necrotizing enterocolitis. *Chinese Journal of Practical Pediatrics*, 35(5), 5–9.

Müller, M. J., Paul, T., & Seeliger, S. (2016). Necrotizing enterocolitis in premature infants and newborns. *Journal of neonatal-perinatal medicine*, 9(3), 233-242.

Nair, J., Longendyke, R., & Lakshminrusimha, S. (2018). Necrotizing enterocolitis in moderate preterm infants. *BioMed research international*, 2018.

Neu, J. (2020). Necrotizing Enterocolitis: The Future. *Neonatology*, 117:240-4.

Ohana, O., Wainstock, T., Sheiner, E., Leibson, T., & Pariente, G. (2021). Long-term digestive hospitalizations of premature infants (besides necrotizing enterocolitis): is there a critical threshold?. *Archives of gynecology and obstetrics*, 304(2), 455-463.

Rose, A. T., & Patel, R. M. (2018, December). A critical analysis of risk factors for necrotizing enterocolitis. In *Seminars in Fetal and Neonatal Medicine* (Vol. 23, No. 6, pp. 374-379). WB Saunders.

Samuels, N., van de Graaf, R. A., de Jonge, R. C., Reiss, I. K., & Vermeulen, M. J. (2017). Risk factors for necrotizing enterocolitis in neonates: a systematic review of prognostic studies. *BMC pediatrics*, 17, 1-9.

Singh, R., Visintainer, P. F., Frantz, I. D., Shah, B. L., Meyer, K. M., Favila, S. A., ... & Kent, D. M. (2011). Association of necrotizing enterocolitis with anemia and packed red blood cell transfusions in preterm infants. *Journal of Perinatology*, *31*(3), 176-182.

Su, Y., Xu, R. H., Guo, L. Y., Chen, X. Q., Han, W. X., Ma, J. J., ... & Ren, C. J. (2023). Risk factors for necrotizing enterocolitis in neonates: a meta-analysis. *Frontiers in pediatrics*, *10*, 1079894.

Tan, X., Zhou, Y., Xu, L., Zhang, L., Wang, J., & Yang, W. (2022). The predictors of necrotizing enterocolitis in newborns with low birth weight: A retrospective analysis. *Medicine*, *101*(7), e28789.

Terrin, G., Scipione, A., & De Curtis, M. (2014). Update in pathogenesis and prospective in treatment of necrotizing enterocolitis. *BioMed research international*, 2014.

Thompson, A., Bizzarro, Yu, M., Diefenbach, K., Simpson, B., & Moss, R. (2011). Risk factors for necrotizing enterocolitis totalis: A case-control study. *Journal of Perinatology*, 31(11): 730-738

Walsh, V., & McGuire, W. (2019). Immunonutrition for preterm infants. *Neonatology*, 115(4), 398-405.

Wertheimer, F., Arcinue, R., & Niklas, V. (2019). Necrotizing enterocolitis: enhancing awareness for the general practitioner. *Pediatrics in review*, 40(10), 517-527.

Yu, L., Tian, J., Zhao, X., Cheng, P., Chen, X., Yu, Y., ... & Xiao, Z. (2016). Bowel perforation in premature infants with necrotizing enterocolitis: risk factors and outcomes. *Gastroenterology research and practice*, 2016.

Zhang, L. P., Lei, X. P., Luo, L. J., & Dong, W. B. (2019). Risk factors for necrotizing enterocolitis in very preterm infants: a case–control study in southwest China. *The Journal of Maternal-Fetal & Neonatal Medicine*, 32(6), 896-901.

Zozaya C, García González I, Avila-Alvarez A, Oikonomopoulou N, Sánchez Tamayo T, Salguero E, Saenz de Pipaón M, García-Muñoz Rodrigo F, and Couce ML (2020). Incidence, treatment, and outcome trends of necrotizing enterocolitis in preterm infants: A multicenter cohort study. **Front. Pediatr.** 8:188. doi: 10.3389/fped.2020.00188.

Appendices

Appendix 1: Research Instrument

Risk Factors for Necrotizing Enterocolitis among Palestinian Premature and Neonates: A Retrospective Case-Control Study

Demographic characteristics and clinical variables

Q1) Gestational age by the WHO:

- A. extreme PTB: 24 + 0–27 + 6,
- B. very PTB: 28 + 0–31 + 6,
- A. moderate to late PTB: 32 + 0–36 + 6 weeks)

- B. Term Births (> 37 + 0 weeks)

Q2) Birth weight (g): _____

Q3) Maternal age: _____

Q4) NEC staging according to modified Bell's Classification, radiologic signs and intestinal signs

- A) IA- Suspected NEC
- B) IB- Suspected NEC
- C) IIA Definite NEC: mildly ill
- D) IIB Definite NEC: moderately ill
- E) IIIA Advanced NEC: severely ill, bowel intact
- F) IIIB Advanced NEC severely ill, bowel perforated

Table 1- Maternal characteristics of the study population according to gestational age at birth.

Maternal characteristics	extreme PTB: 24 + 0-27 + 6,	very PTB: 28 + 0-31 + 6,	moderate to late PTB: 32 + 0-36 + 6 weeks)	Term Births (> 37 + 0 weeks)
Q5) Maternal age, year				
Q6) Maternal chronic hypertension				
Q7) Smoking				
Q8) Maternal urinary tract infection				
Q9) Maternal GBS				
Q10) Place of residence	Village			
	City			
Q11) educational level	Less than high school			
	high school diploma			
	BA			
	MASTER			
	PHD			

Table 2 Pregnancy characteristics and perinatal outcomes of the study population according to gestational age at birth.

Pregnancy characteristics	extreme PTB: 24 + 0–27 + 6,	very PTB: 28 + 0–31 + 6,	moderate to late PTB: 32 + 0–36 + 6 weeks)	Term Births ($> 37 + 0$ weeks)
Q12) Mild preeclampsia				
Q13) Severe preeclampsia				
Q14) Eclampsia				
Q15) Intra uterine growth restriction*				
Q16) Maternal diabetes				
Q17) Placental abruption				
Q18) Cesarean delivery				
Q19) Oligohydramnios				
Q20) Polyhydramnios				
Q21) Low Apgar score (< 7) in 5th minute				
Q22) Small for gestational age				
Q23) Gender	Male			
	Female			
Q24) immaturity of the GIT				
Q25) congenital heart defects				
Q26) respiratory insufficiency				
Q27) sepsis				
Q28) neonatal seizures				
Q29) hypoglycemia				
Q30) severe intrauterine growth retardation				
Q31) Polycythemia				
Q32) gastroschisis				
Q33) congenital herpes infection				
Q34) Hemodynamic instability				
Q35) erythrocyte transfusions				
Q36) phases of hypoxia and ischemia				
Q37) hypothermia				
Q38) hyperthermia				
Q39) abnormal bacteria to accumulate in the GIT				
Q40) excessive and prolonged use of antibiotics				
Q41) Formula feeding				

Q42) Asphyxia after birth				
Q43) meconium aspiration syndrome				

Appendix 2: IRB Approval

Arab American University
Institutional Review Board - Ramallah



الجامعة العربية الأمريكية
مجلس أخلاقيات البحث العلمي - رام الله

IRB Approval Letter

Study Title: "Risk Factors for Necrotizing Enterocolitis among Palestinian Premature and Neonates: A Retrospective Study".

Submitted by: Ameer Omar Mohamad Shanableh

Date received: 6th April 2024

Date reviewed: 14th May 2024

Date approved: 14th May 2024

Your Study titled "Risk Factors for Necrotizing Enterocolitis among Palestinian Premature and Neonates: A Retrospective Study" with the code number "R-2024/A/62/N" was reviewed by the Arab American University Institutional Review Board - Ramallah and it was approved on the 14th of May 2024.

Sajed Ghawadra, PhD
IRB-R Chairman
Arab American University of Palestine





General Conditions:

1. Valid for 6 months from the date of approval.
2. It is important to inform the IRB-R with any modification of the approved study protocol.
3. The Bord appreciates a copy of the research when accomplished.

رام الله - فلسطين

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تسهيل المهمة: Appendix 3

Arab American University
Faculty of Graduate Studies



الجامعة العربية الأمريكية
كلية الدراسات العليا

2024/5/27

إلى من يهمة الأمر

تسهيل مهمة بحثية

تحية طيبة وبعد،

أهدىكم كلية الدراسات العليا في الجامعة العربية الأمريكية أطيب التحيات، وبالإشارة إلى الموضوع أعلاه، تشهد كلية الدراسات العليا في الجامعة أن الطالب عميد عمر محمد شقابلة والذي يصل الرقم الجامعي 202113175 هو طالب ماجستير في برنامج تريض حديثي الولادة ويعمل على رسالة الماجستير الخاصة به بعنوان:

" Risk Factors for Necrotizing Enterocolitis among Palestinian Premature and Neonates: A Retrospective study"

تحت إشراف الدكتور وليد شلاطة. نأمل من حضوركم الإيعاز لمن يلزم لمساعدته للحصول على المعلومات اللازمة للدراسة، علماً أن المعلومات مستخدم لغاية البحث فقط وسيتم التعامل معها بداية السرية، وقد أعطي هذه الرسالة بناءً على طلبه.

وتفضلوا بقبول فائق الاحترام

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الملخص

الخلفية: التهاب الأمعاء والقولون الناخر (NEC) هو حالة الطوارئ المعدية المعوية الأكثر شيوعًا عند الرضع المقبولين في وحدة العناية المركزة لحديثي الولادة (NICU). أكثر الأمراض القاتلة انتشارًا التي تؤثر على الجهاز الهضمي (GIT) بين الخدج وحديثي الولادة هو التهاب الأمعاء والقولون الناخر. وكانت هناك تقارير عن معدلات وفيات تتراوح بين 15% و 30%. من المرجح أن يعاني الناجون من ضعف النمو على المدى الطويل والأضرار العصبية، وكثيرًا ما يكون العلاج الجراحي مطلوبًا. على الرغم من التدابير الوقائية مثل استخدام الحليب المتبرع به، والرضاعة الطبيعية، والأدوية القشرية السكرية قبل الولادة، ومكملات البروبيوتيك، لا يزال NEC متكررًا إلى حد ما في غالبية وحدات العناية المركزة لحديثي الولادة (NICU).

الهدف: دراسة عوامل الخطر للإصابة بالتهاب الأمعاء والقولون الناخر لدى الأطفال الخدج والأطفال الفلسطينيين.

المنهجية: تم إجراء تصميم دراسة وصفية وكمية بأثر رجعي في مستشفيات الرعاية الثالثة (الحكومية والخاصة) في الضفة الغربية والتي تحتوي على وحدات العناية المركزة لحديثي الولادة (NICU) وعلاج التهاب الأمعاء والقولون الناخر. كان مجتمع الدراسة جميع الولدان الذين تم تشخيص إصابتهم بالتهاب الأمعاء والقولون الناخر والذين استوفوا معايير الاشتمال. وتكونت عينة مقنعة من (191) من حديثي الولادة الذين شاركوا في الدراسة خلال فترة جمع البيانات.

النتيجة: يُظهر توزيع الولادات حسب عمر الحمل، وفقًا لمعايير منظمة الصحة العالمية، أنه في دراستنا: 28.3% كانت ولادات مبكرة جدًا (24 إلى 27 أسبوعًا و 6 أيام)، و 48.7% كانت ولادات مبكرة جدًا (28 إلى 31 أسبوعًا و 6 أيام)، و 15.7% كانت ولادة مبكرة متوسطة إلى متأخرة (32 إلى 36 أسبوعًا و 6 أيام)، و 7.3% كانت ولادة مبكرة (37 أسبوعًا أو أكثر). وكان متوسط الوزن عند الولادة 1471 جرامًا (بانحراف معياري 711 جرامًا)، وكان متوسط عمر الأم 27 عامًا (بانحراف معياري 5 سنوات). فيما يتعلق بخطورة التهاب الأمعاء والقولون الناخر (NEC) بناءً على تصنيف بيل المعدل: 5.3% كانوا في المرحلة IA (مشتبه بهم)، و 13.7% كانوا في المرحلة IB (مشتبه بهم)، و 21.1%

كانوا في المرحلة) IIA مؤكد، مريض بشكل معتدل)، 17.4% كانوا في المرحلة) IIA IIB مؤكد، مريض بشكل معتدل)، 20.5% كانوا في المرحلة) IIIA متقدم، مريض بشدة مع سلامة الأمعاء)، و22.1% كانوا في المرحلة) IIIB متقدم، مريض بشدة مع ثقب الأمعاء). تسلط هذه الأرقام الضوء على ارتفاع معدل انتشار مراحل NEC الشديدة. بالإضافة إلى ذلك، كشفت البيانات الأمومية والاجتماعية والديموغرافية عن معدلات متنوعة من الحالات مثل ارتفاع ضغط الدم والتدخين والالتهابات والحالة الاجتماعية والاقتصادية، مما يوفر نظرة عامة شاملة على الخصائص الصحية والاجتماعية والديموغرافية للعينة.

الاستنتاج: في الختام، أظهرت دراستنا عددا كبيرا من الولادات المبكرة، وهي حالات مبكرة جدا. في حين أن متوسط الوزن عند الولادة وعمر الأم كانا نموذجيين، فإن تكرار حدوث التهاب الأمعاء والقولون الناخر الوخيم (NEC) يسلط الضوء على التحديات الصحية الخطيرة التي يواجهها هؤلاء الرضع. بالإضافة إلى ذلك، فإن العوامل الأمومية والاجتماعية والديموغرافية المتنوعة، مثل ارتفاع ضغط الدم والتدخين والالتهابات والحالة الاجتماعية والاقتصادية، تكشف عن التأثيرات المعقدة على صحة الأم والطفل. تؤكد هذه النتائج الحاجة الملحة إلى الرعاية المتخصصة والتدخلات لدعم الخدج وأمهاتهم.

الكلمات المفتاحية: التهاب الأمعاء والقولون الناخر (NEC) ، حالة الطوارئ الهضمية عند الرضع، الخدج وحديثي الولادة، عوامل الخطر