# Study of Necrotizing Enterocolitis in Neonatal Intensive Care Unit of Cairo University Pediatric Hospital

## Thesis

**Submitted for Fulfillment of Master. Degree(M.Sc.) in Pediatrics**


**By**

**Tarek Rashad Abdalla Masoud**

**(M.B.B.Ch.)**

**Cairo University**

**Supervisors**

**Prof. Dr. Laila Hussein Mohamed Hussein**

**Professor of Pediatrics**

**Faculty of Medicine**

**Cairo University**

**Dr. Mai Ahmed Khairy**

**Assistant Professor of Pediatrics**

**Faculty of Medicine**

**Cairo University**

**Dr. Nermen Ramy Mohamed**

**Lecturer of Pediatrics**

**Faculty of Medicine**

**Cairo University**



**Faculty of Medicine - Cairo University**

**2010**

**بسم الله الرحمن الرحيم**

**(قالوا سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم)**

**صدق الله العظيم**

(سورة البقرة، آية ٣٢)

# Abstract

Necrtizing Enterocolitis(NEC) is a common gastrointestinal emergency.Prematurity is major risk factor . Pathogenesis is poorly understood but appears to be multi factorial . NEC is suspected clinically and confirmed by laboratory and radiological studies. Management of NEC is medical and surgical. Prevention and treatment have priority of reseach due to increased number of preterm survival at risk and high mortality and morbidity .



## Key words :

Necrotizing Enterocolitis – Prematurity .

# ACKNOWLEDGEMENT

First and foremost thanks and praise Allah, most gracious, most merciful by whose abundant grace, this work has come to life.

I would like to express my deep everlasting gratitude, thanks and respect to our eminent **Prof. Dr. Laila Hussein Mohamed Hussein,** professor of pediatrics, Faculty of Medicine, Cairo University for granting me the privilege of work under her supervision, kind help, indispensable advice and encouragement from the start of this work.

I would like to express my deep appreciation to **Dr. Mai Ahmed Khairy**, assistant professor of pediatrics, Faculty of Medicine, Cairo University for her great help, careful supervision and her continuous guidance to perform this work.

I would like to express my deep appreciation to **Dr. Nermin Rami Mohamed**, lecture of pediatrics, Faculty of Medicine, Cairo University for her great support and valuable advice to perform this work.

Special thanks is given to **Dr. Nagy El Hussiny**, fellow of pediatrics, Ahmed Maher Teaching Hospital, for his valuable cooperation to fulfill this work.

I am very grateful to all staff members of NICU in, Cairo University – Pediatrics Hospital. Faculty of Medicine

I would like to express my warm gratitude to my parents and members of my family for their kindness and unfailing support and much needed encouragement.

# CONTENTS

## List of Tables

## List of Figures

# LIST OF FIGURES

## List of Abbreviations

| | | |
|---|---|---|
| AP | : | Anteroposterior |
| aPTT | : | Activated Partial Thromboplastin Time |
| CS | : | Cesarean section |
| CD14 | : | Cluster Of Differentiation 14 |
| CPAP | : | Continuous positive airway pressure |
| CPS | : | Carbamoyl Phosphate Synthetase |
| CONS | : | Coagulase-negative Staphylococcus |
| CRP | : | C-Reactive Protein |
| CSF | : | Cerebrospinal fluid |
| DIC | : | Disseminated Intravascular Coagulation |
| EGF | : | Epidermal Growth Factor |
| IκB | : | Inhibitor Of Kappa-Light-Chain-Enhancer Of Activated B Cells |
| GI | : | Gastro-Intestinal |
| IFABP | : | Intestinal Fatty Acid Binding Protein |
| IVIG | : | Intravenous Immunoglobulin |
| IL | : | Interleukins |
| LBW | : | Low Birth Weight |
| L-FABP | : | Liver Fatty Acid Binding Protein |
| LPS | : | Lipopolysaccharide |
| MAMPs | : | Microbial- Associated Molecular Patterns |
| NEC | : | Necrotizing Enterocolitis |
| NO | : | Nitric Oxide |

| | | |
|---|---|---|
| NOD2 | : | Nucleotide-Binding Oligomerization Domain Containing 2 |
| NF-κB | : | Nuclear Factor Kappa-Light-Chain-Enhancer Of Activated B Cell |
| NG | : | Naso Gastric |
| NICU | : | Neonatal Intensive Care Unite |
| NOS | : | Nitric Oxide Synthetase |
| NPO | : | Nothing By Mouth |
| NSAID | : | Non Steroidal Anti Inflammatory Drugs |
| PAF | : | Platelet activating factor |
| PDA | : | Patent Ductus Areteriosus |
| PRR | : | Pattern Recognition Receptor |
| PT | : | Prothrombin Time |
| PAF-AH | : | Platelet Activating Factor Acetyl Hydrolase |
| RDS | : | Respiratory Distress Syndrome |
| RLQ | : | Right Lower Quadrant |
| SIMV | : | Synchronized Intermittent Mechanical Ventilation |
| SGA | : | Small For Gestational Age |
| SNPs | : | Single Nucleotide Polymorphisms |
| TJs | : | Tight Junctions |
| TLR | : | Toll-Like Receptor |
| TNF | : | Tumor Necrosis Factor |
| Tpo | : | Thrombopoietin |
| TPN | : | Total Parental Nutrition |
| UAC | : | Umbilical Artery Catheters |

| | | |
|---|---|---|
| UVC | : | Umbilical Venous Catheter |
| VLBW | : | Very low birth weight |
| VEGF | : | Vascular Endothelial Growth Factor |

# Introduction

## Introduction

Necrotizing enterocolitis (NEC) is the most common gastrointestinal emergency in the preterm infant. Necrotizing enterocolitis initially was described in case reports of Gastro-Intestinal (GI) perforations as early as 1825 ***(Hughes et al., 2009).***

NEC affects 5–15% of all infants born at less than 30 weeks gestational age or <1500 g birth weight. However, up to 10% of all neonates who develop NEC are born at term **(Giannone *et al.,2008).***

Premature infants are at high risk for NEC because of developmental immaturity of key functions in particular gastrointestinal motility, digestive ability, circulatory regulation intestinal barrier function. Preterm infants also have immature mucin expression by goblet cells and decreased paneth cell number (***Lin and Stoll, 2006).***

The risk of NEC in neonates with congenital heart disease is substantial. Factors associated with an elevated risk of NEC in infants with heart disease include premature birth, hypo plastic left heart syndrome, truncus arteriosus, and episodes of poor systemic perfusion or shock**. *(McElhinney et al., 2000)*.**

Newborn infants of mothers with pregnancy-induced hypertension present with intrauterine growth retardation, prematurity, dysmaturity and necrotizing enterocolitis ***(Grujić and Milasinović , 2006)****.*

Impairment of mesenteric blood flow due to the use of umbilical artery catheters (UAC) may increase the risk of necrotizing enterocolitis (NEC) in newborn infants. ***(Rand et al.; 1996).***

H2-blocker therapy was associated with higher rates of NEC due to decrease the already low acid output of stomach ***(Guillet et al.; 2006).***

The pathogenesis of necrotizing enterocolitis (NEC) is poorly understood, but appears to be multi-factorial and highly associated with immaturity of the gastrointestinal tract, colonization of the intestinal microbiota, and immature innate immune system ***(Neu, 2005).***

An episode of ischemia can be an initiating event followed by a complex cascade of inflammatory mediators active in NEC: epidermal growth factor, platelet-activating factor, and nitric oxide ***(Henry and Moss, 2004).***

More recently, the pattern of bacterial colonization has been given emphasis rather than the particular species or strain of bacteria or their virulence. Gram-negative bacteria that form part of the normal flora are now speculated as important factors in triggering the injury process in a setting where there is a severe paucity of bacterial species and possible lack of protective Gram-positive organisms ***(Panigrahi, 2006).***

Studies have shown genetic polymorphisms associated with predisposition to the development and severity of NEC ***(Harding, 2007).***

Neonates commonly present with feeding intolerance, delayed gastric emptying, abdominal distension or tenderness (or both). Occult or gross blood

in the stool, lethargy, apnea, respiratory distress, or poor perfusion may also occur. Infants might either have a benign disease with mainly gastrointestinal symptoms or a catastrophic illness characterized by sudden fulminate onset with circulatory compromise, respiratory and metabolic acidosis, DIC, grossly bloody stool and multiorgan system failure and in severe cases of diseases, there is intestinal perforation, peritonitis, and profound shock ***(Lin and Stoll, 2006).***

The diagnosis is suspected from clinical presentation but must be confirmed by diagnostic radiograph surgery or autopsy. No laboratory tests are specific for NEC. Thrombocytopenia, persistence metabolic acidosis and severe refractory hyponatremia are the most common triad of signs that help to confirm diagnosis ***(Eichenwald, 2008).***

Treatment options are limited to gut rest, parenteral nutrition, broad-spectrum antibiotics, and surgical interventions for enteral perforation. Two commonly used methods for NEC with intestinal perforation are laparotomy or primary peritoneal drainage ***(Yurdakok, 2008).***

Probiotic supplementation appears to be a promising option for primary prevention of NEC but further large trials are necessary for documenting their safety in terms of sepsis as well as long-term neurodevelopment outcomes and immune function. The impact of well-established simple strategies like antenatal glucocorticoid therapy, and early use of breast milk must not be forgotten ***(Patole, 2007).***