

# **Serum Transforming Growth Factor beta 2 in Breast-fed versus Hydrolyzed formula-fed preterm Neonates**

*Thesis*

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*Presented by*

**Abdel-Rahem Ahmed Abdel-Rahem Hamed**

(M.B.B.Ch, 2008)

Faculty of Medicine, Ain Shams University

*Under the supervision of*

**Prof. Ibrahim Saad Abou Saif**

Professor of Pediatrics

Faculty of Medicine - Ain Shams University

**Ass.Prof.Rania Ibrahim Hossni Ismail**

Assistant Professor of Pediatrics

Faculty of Medicine- Ain Shams  
University

**Ass. Prof. Wafaa Khalil Zaky**

Assistant Professor of Microbiology

Faculty of Medicine – Ain Shams  
University

*Faculty of Medicine  
Ain Shams University  
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## *List of Abbreviations*

Abb.	Full term
AAP .....	American academy of pediatrics
BF .....	Breast-Fed
CBC.....	Complete blood count
CPAP .....	Continuous positive airway pressure
CRP.....	C-Reactive protein
CS.....	Cesarean section
CSF .....	Cerebro spinal fluid
DHM .....	Donor human milk
DM .....	Diabetes Mellitus
ELBW .....	Extremely low birth weight
FI.....	Feeding intolerance
GA.....	Gestational age
GIT.....	Gastrointestinal tract
HGS .....	Hepatocyte growth factor substrate
HPF.....	Hydrolyzed protein formula
Ig .....	Immunogloblin
IUGR.....	Intrauterine growth retardation
LBW .....	Low birth weight
MV .....	Mechanical ventilation
NEC .....	Necrotizing enterococitis
NICU .....	Neonatal intensive care unit
NS .....	Neonatal sepsis
NVD .....	Norma vaginal deliver
PDA.....	Patent ductus arteriosus

## *List of Abbreviations (cont...)*

Abb.	Full term
RDS.....	Respiratory distress syndrome
SIP .....	Spontaneous intestinal perforation
TGF- $\beta$ .....	Transforming growth factor- $\beta$
TPN.....	Total parental nutrition
VLBW .....	Very low birth weight

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## **Abstract**

TGF- $\beta$ 2 was not significantly related to gender, maternal illness or mode of delivery between the 2 groups. There was a highly significant correlation between the TGF- $\beta$ 2 serum level and birth weight, gestational age and HB% level. On the other hand, there was a highly significant negative correlation between TGF- $\beta$ 2 serum level and N.sepsis, mortality.

Finally, the study support our hypothesis that BF preterm neonates exhibit higher level of serum TGF- $\beta$ 2 and lower incidence of FI compared to HPF preterm neonates.

**Key words:** Necrotizing enterocolitis - Very-low-birth-weight- Intra-Uterine growth retardation- Low birth weight infants

## INTRODUCTION

It is well established that breast-feeding confers protection against infectious diseases, particularly those of the gastrointestinal tract, via antimicrobial molecules such as immunoglobulins, lysozyme, lactoferrin, defensins, and oligosaccharides (*Newberg and Walker, 2007*).

Accumulating evidence suggests that in addition to this passive immunoprotection, bioactive molecules in breast milk modulate the infant's mucosal and systemic immune responses and may thereby promote adequate and appropriate immune responsiveness against both potentially pathogenic and indigenous microbes and harmless environmental and dietary antigens (*Rautava and Walker, 2009*).

One of the most striking differences between breast-fed and formula-fed infants was evident in the serum concentrations of the Transforming Growth Factor beta 2 (TGF- $\beta$ 2) isoform, TGF- $\beta$ 2, with breast-fed infants exhibiting significantly higher levels of this anti inflammatory cytokine. Breast milk provides infants with direct anti-pathogenic effects via maternal microbe-specific Ig and various other antimicrobial substances (*Newberg and walker, 2007*).

TGF- $\beta$ 2 is an important growth factor present in human and bovine milk (*Gauthier et al., 2006; Chatterton et al., 2013*). TGF- $\beta$  is an immunomodulatory cytokine that is

secreted in breast milk in significant quantities. Of the 3 human TGF- $\beta$  isoforms (TGF- $\beta$ 1, 2, and 3), TGF- $\beta$ 2 is most abundant in breast milk. Breast milk TGF- $\beta$ 2 may be an important source of TGF- $\beta$  during the neonatal period when endogenous production of TGF- $\beta$  in the gut is still inadequate (*Maheshwari et al., 2011; Zhang et al., 1999*).

In the intestine, TGF- $\beta$ 2 is decreased in premature infants and especially in those experiencing necrotizing enterocolitis (NEC) as compared with term infants (*Maheshwari et al., 2011*). TGF- $\beta$ 2 may promote intestinal immune responses and gut functions, such as the intestinal adaptation to bacterial colonization and establishing oral tolerance by regulatory T cells, inducing IgA production and enhancing the intestinal epithelial barrier function, in newborn infants (*Gauthier et al., 2006; Chatterton et al., 2013*).

The deficiency of TGF- $\beta$ 2 may partly account for intestinal disorders, for instance the high incidence of NEC in formula-fed preterm infants (*Boyd et al., 2007*).

In neonates, extensively hydrolyzed protein formula has been shown to reduce gastro- esophageal reflux (*Corvaglia et al., 2013*), to treat allergy and food intolerance (*Osborn and Sinn, 2006*) and to accelerate gastrointestinal transit of milk and stools (*Mihatsch et al., 2001*).

In NICU, hydrolyzed protein formula has been used to feed the preterm infants when breast milk is not available (*Obsorn and sinn, 2006*). Whether it enables a more rapid establishment of full enteral feeding in preterm infants needs to be investigated (*Mihatsch et al., 2001*).

We hypothesis that breast fed preterm neonates exhibit higher level of serum TGF- $\beta$ 2 and lower incidence of feeding intolerance compared to hydrolyzed formula fed preterm neonates.

## **AIM OF THE WORK**

To study the feeding tolerance and its relation to serum TGF- $\beta$ 2 in breast fed versus hydrolyzed formula fed in preterm neonates.

## Chapter 1

# PREMATURITY

### Definition

Premature infants are live born infants delivered before completed 37 weeks from the first day of the last menstrual period (*Stoll and Kliegman, 2004*). Low birth weight infants (LBW) are infants weighing 2500 gm or less at birth, may be caused by a short gestation (prematurity), intra-uterine growth retardation (IUGR) or both (*Beherman et al., 2000*). Very-low-birth-weight (VLBW) infants are those who weigh less than 1500 gm at birth, while extremely low birth weight (ELBW) are infants who weigh less than 1000gm at birth (*Cockburn, 2000*).

### Incidence

In developing countries, approximately 70% of LBW infants have IUGR, while in developed countries 30 % of LBW infants have IUGR. Infants with IUGR have greater morbidity and mortality than appropriate for gestational age (*Beherman et al., 2000*).

In Egypt, only 42% of mothers were able to provide birth weight information about their babies. Amongst those births, 11% were classified as LBW, the percentage of children with LBW was higher in urban areas than in rural ones (12%in urban