INTERLEUKIN 1β in HUMAN COLOSTRUM in RELATION to NEONATAL JAUNDICE

Protocol 0of Thesis

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بسم الله الرخمن الرحيم
قَالُوا سُبْحَانَكَ لا عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْحَكِيمُ
صدق الله العظيم
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Dedication

To

My Mother

My Father

My Husband

My Sisters & Brothers

My Lovely Daughter & Son

And my all friends whose favors are beyond description, asking them to forgive me

Acknowledgement

First of all, thanks to Allah, the Most Gracious, Most Merciful, for any success in achieving any work in my life, and for guiding me through and giving me the strength to complete this work the way it is.

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List of Abbreviations

AA	arachidonic acid
ASBT	apical sodium- dependent bile acid transporters
APR	acute phase reactant
BMJ	breast milk jaundice
COPD	chronic obstructive pulmonary disease
CRP	c-reactive protein
CTL	cytotoxic T lymphocyte
COX2	cyclo-oxygenase 2
CNS	central nervous system
CS	cesarean section
DHA	docosahexaenoic acid
DC	denteritic cell
DPD	2,5 dichloro phenyl diazonium
EPA	eicosa-pentaenic acid
EP	epinephrine
EGF	epidermal growth factor
FA	fatty acid
FHF	fulminant hepatic failure
G6PD	glucose-6-phosphate dehydrogenase enzyme
GA	gestational age
IDDM	insulin dependent diabetes mellitus

IL-1β	interleukin beta
IL1RA	interleukin-1 receptor antagonist
ICE	interleukin -1 converting enzyme
Ig	immunoglobulin
LCH	langerhans cell histiocytosis
LPUFAs	long chain poly-unsaturated fatty acids
MS	multiple sclerosis
MHC	major histocompatibility complex
NFKB	nuclear factor kappa B
NPY	neuropeptide y
NJ	neonatal jaundice
NE	norepinephrine
PGE2	prostaglandine E2
RBCs	red blood cells
TGF β	transforming growth factor β
TcB	trans-cutaneous bilirubinometer
TSB	total serum bilirubin
TNF	tumour necrotic factor
Th2	T helper 2 lymphocyte
UDPGT	uridine diphosphate – glucuronyl transferase
Ws	weeks
Wt	weight

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Introduction

Breast—fed infants have higher bilirubin levels than formula-fed infants. The jaundice of breast—fed infants is commonly of undetermined etiology. Suggested mechanisms for these findings include insufficient milk transfer to the neonate inhibition of hepatic excretion of biIirubin, and increased intestinal absorption of bilirubin (**Bertini et al., 2001**).

Inhibition of hepatic excretion of bilirubin could explain the jaundice associated with human milk consumption, and early studies suggested that exposure to acquired cholestatic injury such as drugs, hormones, proinflamatory cytokines, or biliary obstruction or destruction results in an altered expression and function of hepatic uptake and excretory systems, changes that may maintain and contribute to cholestasis and jaundice. In particular, increased production of IL8 and IL10 has been reported in patients with biliary obstruction and jaundice (**Trauner et al.,2005**).

Moreover the cholestatic effect of cytokines (IL1 **β** ,IL6) is believed to result from the repression of genes that normally mediated the hepatic uptake, metabolism, and biliary excretion of bile salts and various nonbile salt organic anions such as bilirubin. In addition lL1α,IL6, and tumor necrosis factor were found to decrease the glucuronidation activities dose dependently (**Bolder et al.,1997**).

Intestinal absorption is a key step in the enterohepatic circulation of bilirubin because bilirubin is more easily absorbed from intestine than are bilirubin glucuronides. Increased intestinal absorption of bilirubin, facilitated by breast milk rich in **β** -glucuronidase or via some other mechanisms such as delayed passage of meconiurn, the establishment of a population of intestinal bacteria that converts bilirubin glucuronides to various urobilinoids and therefore reduces the availability of bilirubin for intestinal absorption, and casin hydrolysates that inhibit **β** -glucuronidase in the intestine currently appear to be another likely mechanism that explain neonatal jaundice associated with breast-feeding (**Gourley,1998**).

Several studies have shown that enterocytes can constitutively express pro-inflamatory cytokines, and this response is up-regulated by inflammatory stimuli such as endotoxin and IL1 **β**. Although cytokines are known to play a critical role both in the function of hepatie uptake and excretory systems and in the enterohepatic circulation, little is known concerning their concentrations and associations within breast milk of mothers feeding, neonates with neonatal jaundice (**Gourley,2002**).