

Correlation between Mean Platelet Volume and different morbidities in preterm infants

*Thesis submitted for partial fulfillment of Master degree in
pediatrics*

By

Michael Nabil Halim
M.B, B.Ch

Under supervision of

Prof. Dr. Mohamed Sami El Shimi
Professor of Pediatrics
Faculty of Medicine – Ain Shams University

Dr. Hebat Allah Ali Shaaban
Lecturer of Pediatrics
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
2014

ACKNOWLEDGEMENT

First of all I thank **GOD** to whom I relate all my success in achieving any work in my life.

I find no words by which I can express my sincere thanks, supreme gratitude to ***PROF. DR. MOHAMED SAMI ELSHIMI***, Professor of Pediatrics, Faculty of Medicine, Ain Shams University, who kindly offer the generous encouragement, supervision, guidance and continuous support.

Also, I am deeply grateful to **DR. HEBAT ALLAH ALI SHAABAN**, Lecturer of Pediatrics, Faculty of Medicine, Ain Shams University, for her kind patience, sincere advice, cooperation and tremendous effort although this study, any attempt to express my independence to her will be far from being complete.

Also, I am greatly honored to express my deepest gratitude to my Father, Mother and Sister for their love, care and everlasting support to my whole carrier.

MICHAEL NABIL

2014

LIST OF CONTENTS

TITLE	PAGE NO.
INTRODUCTION.....	1
AIM OF THE WORK.....	5
REVIEW OF LITERATURE:	
❖ PRETERM INFANTS.....	6
❖ NEONATAL SEPSIS.....	31
❖ NECROTIZING ENTEROCOLITIS.....	51
❖ INTRAVENTRICULAR HEMORRHAGE....	74
❖ MEAN PLATELET VOLUME.....	95
PATIENTS AND METHOD.....	105
RESULTS.....	110
DISCUSSION.....	127
RECOMMENDATIONS.....	136
SUMMARY AND CONCLUSION.....	137
REFERENCES.....	140
ARABIC SUMMARY.....	

LIST OF TABLES

TABLE NO.	TITLE	PAGE NO.
TABLE (1)	Normative values for CSF profiles in neonates compared with those who have neonatal meningitis	42
TABLE (2)	Results of CRP and Prolactin in differentneonatal groups	44
TABLE (3)	Modified Bell's staging of NEC	67
TABLE (4)	Postnatal pharmacologic preventions strategies for IVH	93
TABLE (5)	Descriptive data of all neonates included in the study	111
TABLE (6)	Distribution of morbidity and mortality among the studied neonates	112
TABLE (7)	TheClinical characteristics of the three studied groups	114
TABLE (8)	Comparison between different perinatal data between the three clinical groups	115
TABLE (9)	Causes of prematurity in different studied groups	116
TABLE (10)	Description of different CBC parameters on day 1 and day 3 of life for the studied preterms	117
TABLE (11)	Comparison between different CBC parameters on day 1 between the clinical groups	119
TABLE (12)	Comparison between CBC parameters on day 3 of life between the different clinical groups	120

TABLE (13)	Comparison between CBC parameters on day one and day three among no morbidity group	121
TABLE (14)	Comparison between CBC parameter on day one and day three of life among sepsis group	122
TABLE (15)	Comparison between CBC parameters on day and day three among necrotizing enterocolitis group	123
TABLE (16)	Relation between mean platelet volume on day 1 of life and different variables	124

LIST OF FIGURES

FIGURE NO.	TITLE	PAGE NO.
FIG. (1)	Algorithm for management of healthy appearing and high-risk infants	50
FIG. (2)	Abdominal distention and abdominal wall erythema in an infant with NEC	61
FIG. (3)	Typical, albeit marked, changes of necrotizing enterocolitis with very extensive gas outlining most of the bowel	65
FIG. (4)	Morphology of germinal matrix	75
FIG. (5)	Showing grading of IVH using transcranial ultrasonography	83
FIG. (6)	Coronal and sagittal ultrasound scans demonstrating hyperechogenic intraventricular hemorrhage	85
FIG. (7)	CT scan showing spontaneous intracerebral hemorrhage with bleeding in the third and both lateral ventricles and hydrocephalus	86
FIG. (8)	Showing serial cranial ultrasounds and MRI studies from a preterm male infant born at 24 weeks of gestation	88

FIG. (9)	Serial cranial ultrasounds of a 30 week preterm male with Grade 3 IVH and hemorrhagic PVL at age 10 days	90
FIG. (10)	The megakaryocytopoietic developmental pathway	96
FIG. (11)	Morbidities of prematurity	113
FIG. (12)	Relation between mean platelet volume on day 1 of life and gestational age	125
FIG. (13)	ROC curve analysis of mean platelet volume on day one of life	126

LIST OF ABBREVIATIONS

ABBREVIATION	FULL TERM
BFU-MK	Megakaryocyte burst-forming unit
BG	Basal ganglia
BM	Bone marrow
BPD	Broncho pulmonary dysplasia
CBC	Complete blood picture
CBF	Cerebral blood flow
CFU	Colony-forming units
CFU	Colony-forming unit
CMP	Common myeloid progenitor
CPAP	Continuous positive airway pressure
CPP	Cerebral perfusion pressure
CRP	C-reactive protein
CSF	Cerebrospinal fluid
CT	Computed tomography
DIC	Disseminated intravascular coagulation
ELBW	Extremely low birth weight
FFP	Fresh frozen plasma
FMF	Familial Mediterranean fever
GBS	Group B streptococci
GERD	Gastro esophageal Reflux
GFAP	Glial fibrillary acidic protein
GIR	Glucose infusion rate
GMH	Germinal matrix hemorrhage

HIE	Hypoxic-ischemic encephalopathy
HSC	Hematopoietic stem cells
I/T RATIO	Immature to total neutrophil ratio
ICP	Intracranial pressure
ICSI	Intra-cytoplasmic sperm injection
IGA	Immunoglobulin A
IUGR	Intrauterine growth restriction
IV	Intravenous
IVF	In vitro fertilization
IVH	Intraventricular hemorrhage
IVIG	Intravenous immune globulin
LBW	Low birth weight
MAP	Mean arterial pressure
MEP	MK-erythroid progenitor
MKS	Megakaryocytes
MPV	Mean platelet volume
MRI	Magnetic resonant imaging
NEC	Necrotizing Enterocolitis
NICHD	National Institute of Child Health and Human Development
NICU	Neonatal intensive care unit
NO	Nitric Oxide
PAF	Platelet activating factor
PDA	Patent ductus arteriosus
PHH	Post hemorrhagic hydrocephalus
PPROM	Preterm Premature Rupture of Membranes

PRBCS	Packed red blood cells
PROM	Premature rupture o membrane
PVL	Periventricular leukomalacia
PVL	Periventricular leukomalacia
RDS	Respiratory distress syndrome
ROP	Retinopathy of prematurity
SGS	Subgaleal shunt placement
TF	Transcription factors
TPN	Total parenteral nutrition
TTTS	Twin to twin transfusion syndrome
WHO	World Health Organization

INTRODUCTION

Preterm birth, defined as childbirth occurring at less than 37 completed weeks or 259 days of gestation, is a major determinant of neonatal mortality and morbidity and has long-term adverse consequences for health (*Wang, 2004*). The morbidity associated with preterm birth often extends to later life, resulting in enormous physical, psychological and economic costs (*Petrou, 2005*). Of all early neonatal deaths (deaths within the first 7 days of life) that are not related to congenital malformations, 28% are due to preterm birth. Preterm birth rates have been reported to range from 5% to 7% of live births in some developed countries, but are estimated to be substantially higher in developing countries (*Lawn, 2006*).

Neonatal sepsis is a single most important cause of neonatal deaths in the community, accounting for over half of them. If diagnosed early and treated aggressively it is possible to save most cases of neonatal sepsis (*Balachandran et al, 2006*). Neonatal sepsis is defined as a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. Incidence of neonatal sepsis in developed countries is 2.2-8.6 per 1,000 live births (*Shankar, 2008*).

Neonatal sepsis can be classified into two sub-types depending upon whether the onset of symptoms is before 72 hours of life (early onset) or later (late onset). Early-onset infections are caused by organisms prevalent in the maternal genital tract or in the delivery area. Risk factors for early-onset sepsis include prematurity, low birth weight, premature and prolonged rupture of membranes, maternal fever, uroinfection and chorioamnionitis(*Chacko, 2005*)

Necrotizing enterocolitis is a medical condition primarily seen in premature infants, where portions of the bowel undergo necrosis. It is the second most common cause of morbidity in premature infants and requires intensive care over an extended period (*Panigrahi, 2006*). Its incidence varies between 0.3 and 2.4 infants/1000 births and between 7-11% (range 3-22% in individual nursery data) amongst infants of less than 1500 g. Male and female are equally affected. There is a sharp decrease in its incidence around 35-36 weeks of post-conceptual age. The age of onset is inversely related to birth weight and gestational age. NEC mortality varies between 9-28%. (*Caplan, 2004*). Initial symptoms include feeding intolerance, increased gastric residuals, abdominal distension and bloody stools. Symptoms may progress rapidly to abdominal discoloration with intestinal perforation and peritonitis and systemic hypotension requiring intensive medical support.

Intraventricular haemorrhage occurs frequently in premature neonates. Large haemorrhages cause post-haemorrhagic ventricular dilatation, often requiring permanent cerebrospinal fluid diversion. Elevated intracranial pressure, inflammatory cytokines and periventricular white matter distortion causes significant and permanent neurological disability. Intraventricular haemorrhage (IVH) remains an important problem in neonatal care. Improvements in neonatal care have led to a persistent decline in the mortality associated with prematurity. Although advances in neonatal care have reduced the incidence of IVH in premature neonates, overall rates of IVH have generally been in the 20 to 25% range over the last two decades (*Horbar, 2002*).

The role of laboratory results and their notification of critical values in diagnosis of different neonatal morbidities can sometimes be crucial in the management of the patient. (*Plebani, 2010*). There are a variety of tests which are helpful for screening of neonates with sepsis, necrotizing enterocolitis & intraventricular hemorrhage.

There is a growing body of clinical evidence suggesting that platelets play an important role in the inflammatory response. Multiple inflammatory factors such as chemokines, cytokines and coagulation factors are secreted by platelets, which increase in size when they are activated.

Circulating platelets may differ in size and hemostatic potential (*Van der Loo, 1997*). Larger platelets contain more granules and produce greater amounts of vasoactive and prothrombotic factors, such as thromboxane A₂, serotonin and ATP; they aggregate more rapidly under the stimulus of agonists, such as ADP, collagen and adrenaline; and finally; they express a greater number of adhesion molecules, such as P-selectin and GpIIb/IIIa (*Bath, 1996*). All this leads to greater hemostatic efficiency: in fact, increased mean platelet volume (MPV) values are associated with shortened bleeding times (*Martin, 1983*).

AIM OF THE WORK

The aim of this work is:

To assess the correlation between mean platelet volume and the occurrence of various morbidities of prematurity; neonatal sepsis, necrotizing enterocolitis and intraventricular hemorrhage.