EFFECT OF GESTATIONAL AGE ON VITAMIN–K DEPENDENT COAGULATION FACTORS IN HEALTHY PRETERM NEONATES

Thesis

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By

Shaymaa Ahmed Fouad Fakher El Dien
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Under Supervision of

Prof. Dr./ Hanaa Mohammad El sayed Afifi
Professor of Clinical and Chemical Pathology
Faculty of Medicine – Ain Shams University

Dr./ Abeer Attia Saad Eldin
Assistant Professor of Clinical and Chemical Pathology
Faculty of Medicine - Ain Shams University

Dr/ Rania Ali Hassan El-Farrash
Lecturer of Pediatrics
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
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بسم الله الرحمن الرحيم

سبحانك لا علم لنا
إلا ما علمتنا
إنك أنت العليم الحكيم

سورة البقرة آية (٣٢)

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LIST OF ABBREVIATIONS

Abbrev.	Full term
γ	Gamma
ADP	Adenosine diphosphate
AGA	Appropriate gestational age
APC	Activated protein C
APTT	Activated partial thromboplastin time.
AT-III	Antithrombin III TAFI: thrombin-activatable fibrinolysis inhibitor
BMI	Body math index
CS	Cesarean section
D-dimer	Fibrin degradation fragment
Dex	*Dexamethazone*
EPCR	Endothelial protein C receptor
F	One-way analysis of variance (ANOVA)
FPA	Fibrinopeptides A
FPB	Fibrinopeptides B
FT	Full term
FV	Factor V
FVII	Factor VII
FVIIIa	Activated factor VIII
GA	Gestational age
Gla	Gamma carboxy-glutamic acid
HMW	Kininogen: high molecular weight kininogen
LGA	Large for gestational age
min	Minute
n	Number
ND	Neonatal death

LIST OF ABBREVIATIONS (Cont...)

Abbrev.	Full term
NEC	Necrotizing interocolitis
NICU	Neonatal intensive care unite
NS	Non- significant
NVD	Normal vaginal delivery
P –value	Probability value
P-C/S	Protein C and protein S
PIVKA	Protein Induced by Vitamin K Absence
PL	Phospholipid
PROM	Premature rupture of membrane
PS	Protein S
PT	Prothrombin time
PT	Preterm
PT	Prothrombin time
PTT	Partial thromboplastin time
P-value	Probability-value
R	Spearman correlation rho
RDS	Respiratory distress syndrome
S	Significant
SD	Standard deviation
SGA	Small for gestational age
TAFI	Thrombin-activated fibrinolytic inhibitor
TF	Tissue factor
TFPI	Tissue factor pathway inhibitor
TG	Thrombin generation
T-M Complex	Thrombomodulin Complex
TM	Thrombomodulin
tPA	Tissue plasminogen activator

LIST OF ABBREVIATIONS *(Cont...)*

Abbrev.	Full term
TXA2	Thromboxane A2
ULVWF	Ultra-large von Willebrand factor
US	Ultrasound
Vit	Vitamin
VKCFD	Vitamin K-dependent coagulation factor deficiencies
VKD	Vit k dependent
VKDB	Vitamin K deficiency-related bleeding
VLBW	Very low birth weight
vWF	vonWillibrand factor.
wks	Weeks
ZPI	Protein Z-dependent protease inhibitor
ZPI	Protein Z-related protease inhibitor
χ^2	Chi-square test

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INTRODUCTION

Physiology of neonatal haemostasis is inadequately understood in comparison to the adult model. In healthy preterm neonates the coagulation system is more immature at birth compared to full-terms and gradually evolves toward the mature adult system ***(Manco et al., 2005).***

Moreover, laboratories that work out on large amounts of neonatal samples should establish their own reference values, since results are strongly related to the specific analyzer device and the reagents that are being utilized; it is well known that there are many pitfalls and dilemmas in the evaluation of neonatal haemostasis ***(Monagle et al., 2010).***

The study of coagulation status has particular importance for premature babies who are at risk of serious health problems. Haemorrhagic and/or thrombotic complication may increase morbidity and mortality in this age group ***(Andrew et al., 1988).***

Vitamin- K is required for the insertion of an additional carboxyl group to glutamic acid residues (gamma-carboxylation) on factor II, VII, IX, X, and protein C and S resulting in their activation ***(Uzuki et al., 2001).***

Prematurity is considered the most important risk factor for periventricular-intraventricular hemorrhage (PIVH). The earlier birth occurs, the higher the incidence will be, and

consequently the more severe PIVH is expected. In addition, early onset PIVH is also likely to progress into a higher grade ***(Gleissner et al., 2000).***

In preterm neonates, the hepatic microsomal enzymatic systems that are responsible for the activation and synthesis of vitamin K precursor proteins may have been immature and unable to respond adequately ***(Kazzi et al., 1989).***

PIVH occurring in premature infants less than 35 weeks' gestation age is an important cause of mortality and it is associated with long-term morbidity, including neurodevelop-mental problems such as hydrocephalus, cerebral palsy, learning disabilities, delayed mental development, severe behavioral problems, etc ***(Van and Ouden, 2004).***

AIM OF THE WORK

The aim of this work is to detect effect of gestational age on vitamin -K dependent coagulation factors (II, VII, IX, X) in healthy preterm neonates.

HAEMOSTASIS

Haemostasis is defined as the process that provides rapid activation to stop bleeding and exert appropriate inhibition to prevent unwanted clot extension ***(Segel and Francis, 2001)***.

The haemostatic system is a complex interaction between the vasculature, cellular components and plasma proteins that interact to maintain haemostasis in the healthy body ***(Monagle and Massicotte, 2011).***

The haemostatic system can be further defined as primary, secondary and tertiary haemostasis to better define the interdependent mechanisms that combine to maintain haemostasis **Primary haemostasis** describes the cellular interaction of platelets and the endothelium and the initiation of the platelet plug that is localized to the point of injury at the vessel wall.**Secondary haemostasis** describes the activation of the coagulation system that is initiated, amplified and prolonged in a sequence of activations of coagulation proteins and regulated by a series of positive and negative feedback mechanisms. **Tertiary haemostasis** a description of the fibrinolytic system which regulates the breakdown of blood clots as healing vessels regain vascular integrity ***(Monagle and Massicotte, 2011).***