Assessment of Correlation between Change in Level of Maternal serum Alfa Fetoprotein and Fetomaternal Hemorrhage after Elective Cesarean Section

Thesis

Submitted for partial fulfillment of master degree
in Obstetrics & Gynecology

Presented by

Osama Salah El-Dine Badwai
M.B.B.Ch. 2010
Resident of Obstetrics & Gynecology
Ain Shams University Hospital

Under Supervision of

Prof. Dr./ Magdy Mohamed Kamal
Professor of Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University

Assistant Prof./ Tamer Ahmed El refaey
Assistant Professor of Obstetrics & Gynecology
Faculty of Medicine – Ain Shams University

Dr./ Ayman Abd-Elkader Mohamed
Lecturer of Obstetrics & Gynecology
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University

2015

سورة البقرة الآية: ٣٢

Acknowledgments

First and foremost, I feel always indebted to ***Allah*** *the Most Beneficent and Merciful.*

I wish to express my deepest gratitude and thanks to **Prof. Dr./ Magdy Mohamed Kamal,** *Professor of Obstetrics and Gynecology, Faculty of Medicine – Ain Shams University, for his constructive criticism, unlimited help and giving me the privilege to work under his supervision.*

My most sincere gratitude is also extended to Assistant **Prof./ Tamer Ahmed El refaey,** *Assistant Professor of Obstetrics & Gynecology, Faculty of Medicine – Ain Shams University, for his enthusiastic help, continuous supervision, guidance and support throughout this work.*

Words fail to express my appreciation to **Dr./ Ayman Abd-Elkader Mohamed,** *Lecturer of Obstetrics & Gynecology, Faculty of Medicine – Ain Shams University, for his enthusiastic help, continuous supervision, guidance and support throughout this work.*

I can't forget to thank **Dr. Rasha Mohammed,** *Lecturer of Clinical Pathology, for her great efforts and help during the practical part in this thesis.*

Last but not least, I can't forget to thank all members of my Family, especially my ***Parents****, for pushing me forward in every step in the journey of my life.*

Candidate

Osama Salah

List of Contents

List of Abbreviations

Abbr.	Full-term
AUROC	: Area under Receiver-operating characteristic curve
CSF	: Cerebrospinal fluid
CTG	: Cardiotocography
CVS	: Chorionic villious sampling
DAT	: Direct antiglobin test
EDTA	: Ethylenediaminetetraacetic acid
ELISA	: Enzyme-linked imunnosorbent assay
EST	: Endodermal sinus tumour
FHR	: Fetal heart rate
FMH	: Fetomaternal haemorrhage
HCC	: Hepatocellular carcinoma
IUD	: intrauterine death
IVT	: Intravascular intrauterine transfusion
KBT	: Kleiheauer-Betke test
MCA	: Middle cerebral artery
MoM	: Multiples of median
MSAFP	: Maternal serum alfa-feto protein
NICE	: National institute for clinical experience
NPV	: Negative predictive value
PBS	: Phosphate buffered saline
PPS	: Phosphate buffered saline
PPV	: Positive predictive value
PSV	: Peak systolic velocity
PV	: Per-vaginal
RAAP	: Routine antenatal anti-D prophylaxis

List of Abbreviations *(Cont.)*

Abbr.	Full-term

RBCs : Red blood cells
Rh D : Rhesus D
ROC curve : Receiver-operating characteristic curve
VFEM : Volume of fetal erythrocytes in maternal circulation

List of Tables

List of Tables *(Cont.)*

List of Figures

List of Figures *(Cont.)*

List of Figures *(Cont.)*

Introduction

Fetal and maternal circulations normally are supposed not to be in direct contact. The placental barrier is found there to play the role of separation between them in a way that receiving nutrients by the fetus and gas exchange between mother and fetus, are not compromised whatsoever. That is why the placental abnormalities are the most encountered risk factor in cases that are confirmed to be suffering from fetomaternal hemorrhage ***(Bernstein et al., 1992).***

In normal pregnancy this abnormal contact between the fetal and maternal circulations may occur so late during delivery. Up to 1 ml of blood may pass. But in an abnormal pregnancy, fetomaternal hemorrhage is defined as the hemorrhage of 30 ml or more, of whole blood from a fetus into the maternal circulation. As less than 30 ml is considered benign and passes without any remarkable side effects ***(Sebring et al., 1990).***

The problem in fetomaternal hemorrhage appears when fetal blood escapes into the maternal circulation in a considerable amount 30 ml or more. That shall compromise the fetal condition leading to many morbidities and mortalities. The result varies from minimal degree of fetal anemia up to severe degree of fetal anemia. And lethal

hydrops fetalis may follow that, leading to fetal cerebral edema, kernicterus, fluid collection in all body spaces, severe pallor and failed circulation (due to the escaping red cells) and eventually ending in death of the fetus ***(Zizka et al., 2001).***

Occurrence of fetomaternal hemorrhage is not a predictable event. Even some actual cases are listed to be of unknown cause ***(Bird et al., 1999).***

Also as a clinical wise, most of the fetomaternal hemorrhage cases never produce these evident signs or symptoms by which a confirmed diagnosis can be made upon, until it is very late ***(Kecskes et al., 2003).***

But somehow it might be linked to certain risk factors which if happened to the pregnant lady before in her obstetrical medical history, it gives a clue that this lady in particular is more susceptible for having fetomaternal hemorrhage in her next pregnancies. So more antenatal care and cautious follow up must be given to such lady in order to avoid any complications as possible and also to detect occurrence of the fetomaternal hemorrhage as earliest so that the management she will be having, could give more optimum outcome ***(Sebring et al., 1990).***

These risk factors include a previous history of spontaneous stillbirth, placental disruption and abnormalities, anterior position of the placenta, surgical and manual removal of the placenta, twin (monochorionic, monozygotic) pregnancy, premature rupture of membranes, invasive diagnostic procedures as cordocentesis, preterm labor, postmaturity, maternal trauma, external version, vaginal assisted delivery, cesarean section or massive blood loss during pregnancy ***(David et al., 2004).***

Methods for quantification of FMH:

Kleihauer–Betke test is the gold standard test for quantification of FMH ***(Maciuleviciene et al., 2008).***

The controversy appears in that Kleihaeur -Betke test is a test which requires a specific laboratory setting and a highly performing hematology specialist so it is not that easy to be conducted and to give reliable results ***(Agarwal et al., 2011).***

There are many disadvantages to the Kleihauer-Betke test, firstly it is subjected to the human error (in the microscopic manual method),

The time between sampling and testing, if prolonged, this may lead to clotting of the sample and consequently false interpretation (in both of the microscopic manual and the microscopic automated methods) ***(Lachman et al., 1977).***

There is flow cytometry method which is detecting fetal red cells in the maternal blood by using anti-fetal red cells antibodies ***(Pelikan et al., 2004).***

Another trial worked on detecting the genomic material of the nucleated fetal red cells using molecular biology techniques ***(Hiromi et al., 1995).***

Both methods showed promising results, but still more work is needed to accredit them as substitutes to the standard Kleihaeur –Betke test.

Alpha-fetoprotein (AFP) is found in both fetal serum and also amniotic fluid. This protein is produced early in gestation by the fetal yolk sac and then later in the liver and gastrointestinal tract. The true function of AFP is unknown ***(Johnson et al., 2012).***

It is considered to be one of the most important markers which are used nowadays in early screening and diagnosis of many of high risk conditions and fetal abnormalities and malformations during pregnancy ***(Dehghani-Firouzbadi et al., 2010).***

For example maternal serum level of the Alpha-Fetoprotein is found by evidence to be raised hugely if the fetus has nervous system malformations as neural tube defects (example Spina bifida and anencephaly) or Down syndrome ***(Wang et al., 2009).***