# Association between Maternal Serum Level of Alpha-Fetoprotein and Fetomaternal Hemorrhage in cases of fetal interventional procedures

## Thesis

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*Candidate*

**Mahmoud Dewair**

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# 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** | : Kleihauer-Betke test |
| **MCA** | : Middle cerebral artery |
| **MoM** | : Multiples of median |
| **MSAFP** | : Maternal serum alfa-feto protein |
| **NEQAS** | : National External Quality Assessment Service |
| **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 |

# List of Abbreviations *(Cont.)*

| Abbr. | Full-term |
|---|---|

**RAAP** : Routine antenatal anti-D prophylaxis
**RBCs** : Red blood cells
**Rh D** : Rhesus D
**ROC curve** : Receiver-operating characteristic curve
**VFEM** : Volume of fetal erythrocytes in maternal circulation

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# Introduction

Fetomaternal hemorrhage is considered to be a grave complication which may occur during pregnancy. And due to its graveness the fetomatenal hemorrhage renders the pregnancy as a high risk condition so it must be diagnosed, followed and managed properly in order to avoid any hazards on the mother and the fetus ***(Sebring et al., 1990)***.

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 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 ***(Bernstein et al., 1992),*** 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).***

Quantification of fetomaternal hemorrhage is done when severe FMH is suspected, and accordingly dose can be adjusted. Additional dose of antiD should be given for every increase in fetal RBCs in maternal circulation ***(White et al., 2006).***

**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 Kleihauer -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**,**both methods showed promising results, but still more work is needed to accredit them as substitutes to the standard Kleihauer –Betke test***(Hiromi et al., 1995)***.

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