

# **Tranexamic acid use in elective cesarean Section for women with placenta previa: A Randomised controlled trial**

*Thesis*

*Submitted for Partial Fulfillment of the Requirements  
Of Master degree in Obstetrics and Gynecology*

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**2017**



# *Acknowledgement*

*First of all, I thank ALLAH,*

*Then, I would like to express my deepest gratitude to **Prof. Alaa Eldin Hamed Abdelaziz Elfeky** Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University for dedicating so much of his precious time and effort to help me complete this work,*

*Indeed, words do fail me when I come to express my unlimited appreciation to **Dr. Ahmed Elsayed Hassan Elbohoty** Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University who was always there to help me, to encourage me and very kindly offer me his valuable remarks in every step of this work,*

*I am deeply indebted to **Dr. Mortada Elsayed Ahmed Abdelrahman** Lecturer in Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University for his guidance and unlimited assistance throughout this work,*

*I would like to thank **my family** and **my special one** for their huge support.*

*Finally, thanks to all **my patients** who supported me and gave a hand to the success of this work,*

*✍ Ahmed Abdelaziz Mohammed*

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## List of Abbreviations

<b>CRASH</b>	Clinical Randomization of an Antifibrinolytic in Significant Haemorrhage
<b>FDA</b>	Food and Drug Administration
<b>GM</b>	Grams
<b>ICU</b>	Intensive care unit
<b>LSCS</b>	Lower segment caesarean section
<b>PPH</b>	Postpartum Hemorrhage
<b>P</b>	Probability
<b>T</b>	T-test
<b>TAS</b>	Transabdominal sonography
<b>TVS</b>	Transvaginal sonography
<b>TXA</b>	Tranexamic acid
<b>WOMAN</b>	World Maternal Antifibrinolytic Trial
<b>X<sup>2</sup></b>	Chi square test

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## **Introduction**

Placenta previa is a considerable cause of maternal and fetal morbidity and mortality and is associated with high demands on health resources (*Knight, 2007*). The number of cases of placenta previa and its complications, including placenta accreta, is steadily increasing. This is due to the rising incidence of caesarean sections combined with increasing maternal age. The prevalence of placenta previa has been recently estimated to be approximately 0.5% of all pregnancies (*Silver et al., 2006*).

It is defined as when the placenta is completely, or in part, inserted into the lower segment of the uterus (*Yang et al., 2007*). It is classified by ultrasound imaging, according to what is relevant clinically: if the placenta covers the internal cervical os completely, it is considered a major previa; if the leading edge of the placenta is in the lower uterine segment, but not covering the cervical os, so is called minor or partial previa (*Knight et al., 2008*).

Placenta previa is associated with many complications, including massive antepartum and intrapartum hemorrhage. The ability to predict severe antepartum hemorrhage and emergency cesarean section is critical in the management of placenta previa. Also,

placenta previa is associated with preterm delivery, with the neonatal mortality increasing threefold as a result of prematurity (*Sekiguchi et al., 2013*).

Women with placenta previa often present with painless, bright red vaginal bleeding, commonly occurring around 32 weeks of gestation, but can be as early as late mid-trimester. This bleeding often starts mildly and may increase as the area of placental separation increases (*Callander et al., 2004*). So, clinical suspicion should be raised in all women with vaginal bleeding after 20 weeks of gestation (*Brinsden et al., 2006*). A low lying placenta may be also suspected with high presenting part or an abnormal lie. The definitive diagnosis usually relies on ultrasound imaging (*Paterson-Brown et al., 2010*).

Prior to delivery, very important discussion should be held with all women with placenta previa and their partners, clarifying mode of delivery, indications for blood transfusion and hysterectomy. Any concerns, queries or refusals of treatment should be dealt with effectively and documented clearly (*Ghourab, 2001*). Any woman giving consent for caesarean section should understand not only the general risks associated with caesarean section, but also the specific risks of placenta previa in terms of massive

obstetric hemorrhage, the need for blood transfusion and the chance of hysterectomy (*Paterson-Brown et al., 2010*).

There is no solid management, otherwise individual characteristics should be considered. For example, high-risk cases suspected of having placenta accreta are planned for delivery at around 36–37 weeks of gestation (with corticosteroid cover), while in those with uncomplicated placenta previa delivery can be delayed until 38–39 completed weeks of gestation (*RCOG, 2010*). The anticipation and planning of surgery for suspected placenta previa is extremely important (*RCOG, 2008*). It enables logical decisions to be made without the element of surprise and often without the urgency of massive hemorrhage (*RCOG, 2009*).

Maternal morbidity could be reduced by precise antenatal diagnosis and surgical avoidance of the placenta, and its separation. Advantages are conservative management of the placenta, reducing the risk of hysterectomy and of bleeding if the placenta is indeed found to be adherent (*Wong et al., 2008*).

Massive hemorrhage is a common complication in placenta previa cases. Successful control of bleeding can often be achieved medically using uterotonics including oxytocin, ergometrine, and 15-methyl prostaglandin F2 $\alpha$ . However, once these medical treatments fail, surgical intervention is often necessary (*Eller et al., 2009*). Surgical interventions described for massive bleeding include uterine and vaginal packing with gauze, balloon tamponade, B-Lynch suture, vertical compression sutures, suturing an inverted lip of cervix over the bleeding placenta bed, uterine or internal iliac ligation, interventional radiology methods or even hysterectomy (*Al-Harbi et al., 2009*).

Interventional radiology is an important means in the treatment of massive postpartum hemorrhage, and therefore having this facility available locally is desirable. Ligations of the uterine artery and internal iliac artery have been reported, but affecting subsequent access to intervention radiology techniques and embolisation, making them extremely difficult or impossible. Bimanual compression or even aortic compression can give extra time for help to arrive, or for the anaesthetist to ‘catch up’ haemodynamically in the unstable women (*Dawlatly et al., 2007*).

A recent American College of Obstetricians and Gynecologists practice bulletin suggests that uterine tamponade can be an effective way to decrease hemorrhage secondary to uterine atony, as a procedure used to obviate the need for hysterectomy. Furthermore, it is suggested that if hysterectomy is performed for uterine atony, there should be documentation of these therapies' attempts (*ACOG Practice Bulletin, 2006*).

Intra-operative estimation of blood loss is an important issue in this study. Various methods had been undertaken to estimate intra-operative blood loss (*Della et al., 2011*). Intra-operative blood loss could be estimated by 3 different methods. The first is the visual estimation by different operating room staff: the anesthetist, the obstetrician as well as the scrub nurse would estimate the loss by careful observation of the operative field during surgery and report it at the end (*New York State Department of Health, 2009*). The second is to weigh dry and wet surgical swabs before and at the end of surgery and the difference would be the blood absorbed by the swabs (*Toledo et al., 2012*). Another method is the application of Bourke and Smith equation which is one of the acceptable formulae to calculate the intra-operative blood loss utilizing preoperative and post-operative hematocrit values (*Stafford et al., 2008*).

Using Tranexamic acid in decreasing the blood loss during cesarean section in cases of placenta previa is a pilot study. Tranexamic acid was used in more than one study to decrease bleeding during postpartum hemorrhage and elective cesarean section (*Ducloy-Bouthors et al., 2011*). Tranexamic acid is a potent antifibrinolytic agent that exerts its effect by blocking lysine binding sites on plasminogen molecules and has the potential to enhance the effectiveness of the patient's own haemostatic mechanisms. Consequently, clot breakdown (fibrinolysis) is inhibited and excessive or recurrent bleeding is reduced (*Shakur et al., 2010*).