International Journal of Medicine
pISSN 1468-3814 | eISSN 2667-7008
https://theinternationalmedicine.com/

Case Report *DOI: 10.61336/im/26-2-12*

Perioperative Anticoagulation in C Section for IVF Pregnancy - A Case Report.

Dr. Reddyshetty Swetha[1], Dr. Naveen Prasath G.[2], Dr. Geetha J.[3]

[1]Postgraduate in Anesthesia, Department of Anaesthesia, Dhanalakshmi Srinivasan Medical College and Hospital, Siruvachur, Perambalur, Tamil Nadu, India.

[2]Postgraduate in Anesthesia, Department of Anaesthesia, Dhanalakshmi Srinivasan Medical College and Hospital, Siruvachur, Perambalur, Tamil Nadu, India.

[3]Professor, Department of Anaesthesia, Dhanalakshmi Srinivasan Medical College and Hospital, Siruvachur, Perambalur, Tamil Nadu, India.

Correspondence:
Dr. Geetha J.
Professor, Department of Anaesthesia, Dhanalakshmi Srinivasan Medical College and Hospital, Siruvachur, Perambalur, Tamil Nadu, India.

Received: 26-02-2026
Revised: 19-03-2026
Accepted: 09-04-2026
Published: 13-04-2026

Abstract

Background: ***Objective:*** To evaluate the safety and effectiveness of continuous anticoagulation therapy throughout pregnancy in an in vitro fertilization (IVF) conception, and to discuss anesthetic considerations, monitoring strategies, and maternal–fetal outcomes. ***Materials and Methods:*** A case of a 28-year-old woman with infertility due to bilateral tubal block who conceived through IVF is presented. Given the increased risk of venous thromboembolism (VTE), she was initiated on anticoagulation therapy starting with unfractionated heparin, later transitioned to low molecular weight heparin (enoxaparin 40 mg once daily), along with low-dose aspirin. She was evaluated preoperatively for an elective cesarean section. Anticoagulation was modified prior to surgery, and general anesthesia was administered considering bleeding risks. Clinical monitoring, coagulation profile, and perioperative precautions were undertaken. ***Results:*** The patient underwent elective cesarean section under general anesthesia without intraoperative or postoperative complications. There was no excessive bleeding, thromboembolic event, or adverse fetal outcome. A healthy neonate was delivered. Postoperative recovery was uneventful, and anticoagulation therapy was resumed along with thromboprophylactic measures. ***Conclusion:*** Pregnancy, particularly following IVF, is associated with a significantly increased thrombotic risk. Continuous anticoagulation with low molecular weight heparin from early pregnancy through the puerperium appears to be safe and effective, with minimal maternal and fetal complications. Careful perioperative planning, appropriate modification of anticoagulant therapy, and the use of general anesthesia can ensure favorable outcomes in such high-risk cases.

Keywords: Pregnancy, Invitrofertilization(IVF), Anticoagulation, Cesarean section, Puerperium.

INTRODUCTION

Human papillomavirus (HPV) is etiologically involved in most cervical cancers (CCs) and has been identified in The physiological changes in pregnancy favour always the wellbeing of fetus, fetal growth amnd delivery while compromising mothers health situations in many ways involving almost all the organ systems. The blood loss during delivery is supposed to be prepared to compensate in the antenatal period as increase in thrombogenicity. The risk of venous thrombosis during third trimester of pregnancy is six times higher and that during the first six weeks post-partum about 22 times[1] than in non-pregnant women. The thrombotic risk is higher in the first trimester of pregnancy conceived through invitro fertilization namely ovarian stimulation with estrogens, egg retrieval embryo transfer and tubal or fundal fetal growth involves increased thrombosis both due to increased coagulation and reduced endogenous anticoagulants.

In this case report we discuss the continued anti coagulation throughout an IVF conception, monitoring of anticoagulation, choice of anticoagulants in the antepartum and puerperium and anticipated pros and cons of usage of anticoagulants.

CASE REPORT

History

A 28 years old lady who was investigated for infertility was detected to have bilateral tubal block by hysterosalphingogram. She underwent invitrofertilization process for conception which was successful. In view of her precious pregnancy and possible venous thromboembolism she was started on anticoagulants early in pregnancy by specialists in reproductive

medicine initially on unfractionated heparin 5000 units subcutaneously twice daily and later switched over to enoxaparin 40mg SC once daily.
This lady presented to the pre anaesthetic clinic for assessment towards an elective C section. She was earlier on treatment elsewhere and presented for C section at our centre. She was also on Aspirin 75mg once daily. In view of the varied anticoagulant therapy it was decided to offer general anaesthesia for the elective section.

Clinical Features
The patient eas 70kgs with BMI of 28.6, term pregnancy, cephalic presentation and normal fetal heart. No bleeding tendencies, no purpuric spots or ecchymosis. Her pulse rate was 90 per minute and blood pressure was 110/60 mmhg. There was no pedal edema and her respiratory and cardiovascular systems were clinically normal.

Investigations
Hemoglobin 10.6gm% platelets 2lakhs/mm3. Bleeding time was 2minutes 20seconds, clotting time 5 minutes 30 seconds, prothrombin time 16 seconds , activated partial thromboplastin time 24 seconds and Internationalised normalised ratio was 1.2. Her blood group was O positive. Her ECG and ECHO cardiogram were within normal limits and urine albuminwas negative. Her blood sugar was 100mg%, urea and creatinine were 24 mg% and 1.1 mg% respectively. Venous Doppler of lower limbs was normal.

Anticipated Challenges in Anaesthesia
1. Maternal and fetal wellbeing on account of precious pregnancy.
2. Anticoagulant and antiplatelet therapy increasing risk of bleeding.
3. High degree of suspicion on occurrence of venous thromboembolism and deep vein thrombosis of legs.
4. Continuation of anticoagulation through 6 weeks of puerperium.
5. Risks of general anesthesia such as instrumentation of a reactive airway and acid aspiration syndrome.

Optimisation
Though the patient was initially on unfractionated heparin she had been stabilised on low molecular weight heparin 40mg subcutaneously once daily. It was recommended by physician to withhold enoxaparin 24 hours prior to proposed day of C section and administer half the dose of enoxaparin namely 20mg as the last dose prior to surgery.
She was continuously monitored for premature uterine contractions and fetal heart. A coagulation profile including bleeding and clotting times PT, APTT and INR, platelets were performed on the morning of the C section. Factor Xa levels were not available with our institution.

Plan
General Anaesthesia

Premedication
Antiacid and anti-reflux prophylaxis with Ranitidine 50mg and Metoclopramide 4mg were given.

Preparation
Two 18 G intravenous access, two laryngoscopes, two suction, two anaesthetists, difficult airway cart, drug and monitor check along with check of anaesthesia work station.

Monitors
Pulse oximeter, electrocardiogram, capnogram, noninvasive blood pressure, urine output.

Induction
Pre oxygenation, abdomen painted and drapped by obstetrician, rapid sequence induction, sellicks manoeurre offered by assistant, Thiopentone sodium 300mg, succinylcholine 100mg, Glycopyrrolate 0.2mg 7.00mm cuffed endotracheal tube used to intubate trachea, cuff inflated and secured. 50% O2/N2O and Isoflurane 0.6%/ IPPV/Incision / delivery time two minutes, well baby delivered Atracurium 25mg for NDMR, Pentazocine 30mg following delivery, oxytocin 20 units intravenous infusion as uterotonic, abdomen closed in layers after hemostasis, residual neuromuscular blockade was reversed TOF ¾ with neostigmine 2.5 mg and glycopyrrolate 0.6 mg.

Extubation was smooth and recovery was complete. There was no undue bleeding and the patient was shifted to post-operative care unit. Analgesia was achieved with Tramadol 50 mg and promethazine 12.5 mg intravenously. Stockings to prevent deep vein thrombosis and resumption of anticoagulation were executed.

DISCUSSION

This case is presented to highlight the need of anticoagulation throughout an invitro conception pregnancy, choice of low molecular weight heparin namely enoxaparin over unfractionated heparin, advantages and disadvantages of anticoagulation, its monitoring and management.

Discussion of this case embraces the following aspects namely pathophysiology of thrombogenicity in pregnancy and more so in invitro conceptions, indications and advantages of perinatal anticoagulation, comparing in detail the pharmacology of unfractionated heparin and low molecular weight heparin and our experience in administering anticoagulation in pregnancy.

Pathophysiology: In 1856, Rudolf Virchow postulated a triad which could predispose to venous thrombosis, stasis, local trauma to vessel wall and hypercoagulability form the major contributory factors for the development of venous thrombosis. The risk of each of these increases even in normal pregnancy. Enlarging uterus compresses the lower extremity venous system promoting stasis. From early third trimester to six weeks postpartum there is 50% reduction in venous flow velocity in the legs.

The risk factors associated with increased thromboembolism can be categorised as obstetric and general.

Obstetric Risk Factors Include

- C-section delivery
- Diabetes
- Hemorrhage and anemia
- Hyperemesis
- Immobility
- Multifetal gestation
- Multiparity
- Preeclampsia
- Puerperal infection
- Invitro fertilisation

General Risk Factors are

- Age more than 35y
- Malignancy
- Connective tissue disorder
- Dehydration
- Immobility
- Infection and inflammatory disease
- Myeloproliferative disorder
- Nephrotic syndrome
- Obesity
- Oral contraceptive usage
- Orthopedic surgery
- Paraplegia
- Prior thromboembolism
- Sickle cell disease
- Smoking
- Thrombophilia

Apart from the above risk factors an estimated 20–50 percent of women who develop a venous thrombosis during pregnancy or postpartum have an identifiable underlying genetic disorder according to American College of Obstetricians and Gynaecologists 2011.

The prevalence of venous thromboembolism in patient undergoing assisted reproduction is 0.1–0.2%[2] is ten times higher than the general population 2.2/10000.[3] This risk is increased to 100 fold in patients who develop ovarian hyperstimulation (1.7%).

The risk reduction strategies for VTE in IVF are use of mild ovarian stimulation and avoiding hyperstimulation, use of GnRH as a trigger and avoiding exposure to HCG, FET in a natural cycle, single embryo transfer and use of prophylactic or therapeutic anticoagulation.[4]

An increase in procoagulant factors and reduced natural anticoagulants both contribute to thrombogenicity in IVF. The hyperestrogenism that results from ovarian stimulation which is the first step in the process of assisted reproduction is the main thrombogenic agent increasing the risk of VTE in the first trimester of IVF conception while in a normal natural pregnancy the risk is high in third trimester. The increased risk of VTE in IVF pregnancies in the first trimester is due to a 5-10 fold risk in first trimester while an ovarian hyperstimulation syndrome increases the risk of thrombosis 100 fold. In patients with unsuccessful IVF this risk was not so high.

Mechanism of Thrombosis in Invitro Fertilisation

The hyperestrogenism resulting fom ovarian hyperstimulation causes increase in fibrinogen, vonwillebrand factor, factors Vlll and V and increases activated protein C resistance[5] reduced fibrinolysis due to decreased tissue plasminogen activatorinhibitor type 1. The natural anticoagulants antithrombin III and protein S are reduced. Protein S inactivates factor Va and Vllla controlling thrombin generation. Activated protein C leads to protein S formation. Antithrombin deficiency leads to reduced thrombin neutralisation which binds to thrombomodulin in endothelial cells causing activation of protein C.[6]

Ovarian stimulation is a critical step in IVF as it enables precise timing of insemination and retrieval of multiple oocytes. Hence, the risks have to be accepted and attempted to reduce to a minimum.

It has been hypothesised that homeostatic changes during controlled ovarian stimulation increase peritoneal fluid drained through the thoracic duct into the subclavian veins[7] leading to a local environment with increased risk of VTE in the upper body.

ACCP 2012, RCOG 2015, and British Fertility Society 2024 have recommended low molecular weight heparins as 2C evidence.[8]

Deep Vein Thrombosis

Women are up to 5 times more likely to develop DVT in pregnancy than when not pregnant.[9] The frequency of DVT is similar in all three trimesters and also increased in the first 6 weeks of the postpartum period.

Venous stasis results from hormonally induced decreased venous tone and obstruction of venous flow by the enlarged uterus. A reduction of venous flow velocity of approximately 50% occurs in the legs by 25–29 weeks of gestation and returns to normal after 6 weeks of puerperium.[10]

Compression of the left common iliac vein by the right common iliac artery is accentuated by the gravid uterus. Hence, DVT of the left lower limb is more common than the right lower limb.

Increased fibrin generation, decreased fibrinolysis, increased levels of factors II, VII, VIII, IX, X, and there is progressive fall in protein S levels.[11]

Thus, the physiological preparation for the haemostatic challenge during delivery is the basis of increased thrombogenicity in pregnancy, more so in IVF.

The haemostatic activation may be demonstrated by increased markers such as prothrombin fragment 1+2 and D-dimer.

The choice of anticoagulants is parenteral and is between enoxaparin and heparin.

The following discussion involves elaboration and comparison between unfractionated heparin and low molecular weight heparin.

Heparin

Heparin is a sulfated polysaccharide commercially derived from porcine intestinal mucosa and is a polymer of alternating D-glucuronic acid and N-acetyl-D-glucosamine residues.[12]

Mechanism of Action

The anticoagulant action of heparin is by activating antithrombin and accelerating the rate at which it inhibits thrombin and factor Xa.

Antithrombin is an obligatory plasma cofactor for heparin and belongs to the serine protease inhibitor (serpin) superfamily.

Heparin binds to serpin via a unique pentasaccharide sequence found in one-third of the chains of commercial heparin. Heparin chains lacking this pentasaccharide sequence have little or no anticoagulant activity.[13]

Once bound to antithrombin, heparin induces a conformational change in the reactive centre loop of antithrombin and renders it more readily accessible to target proteases.

This change enhances the rate at which antithrombin inhibits factor Xa by at least two orders of magnitude but has little effect on the rate of thrombin inhibition.

Heparin serves as a template that binds antithrombin and thrombin simultaneously. Formation of this ternary complex brings the enzyme in close apposition to the inhibitor, thereby promoting the formation of a stable covalent thrombin–antithrombin complex.

Only pentasaccharide-containing heparin chains composed of at least 18 saccharide units (molecular weight ~5400) have sufficient length to bind and bridge thrombin and antithrombin together.

With a mean molecular weight of 15,000 (5000–30,000 range), almost all chains of UFH are long enough to perform the bridging function. Heparin has equal capacity to promote inhibition of thrombin and factor Xa by antithrombin and has an anti-factor Xa to anti-factor IIa ratio of 1:1.Heparin causes release of TFPI (tissue factor pathway inhibitor) from endothelium. TFPI also contributes to the antithrombotic activity of heparin.

Pharmacology of Heparin

Heparin can be administered subcutaneously or intravenously, a higher dose is needed via the subcutaneous route to optimize bioavailability. There is dose-dependent clearance due to binding of heparin to endothelium. At low IV doses, the half-life is short, and at high doses, the half-life is longer as clearance becomes slower once the endothelium is saturated.

Clearance is mainly extrarenal. Heparin binds to macrophages, which internalise and depolymerise long heparin chains and secrete shorter chains back into circulation.Half-life: 30–60 minutes with IV bolus of 25–100 units/kg. Once heparin enters circulation, it binds to plasma proteins other than antithrombin such as platelet factor 4, von Willebrand factor, and acute phase reactants. This attenuates the properties of heparin as an anticoagulant.[14]

Monitoring of Heparin Therapy

1. Activated partial thromboplastin time (aPTT)
2. Anti-factor Xa levels
3. Therapeutic serum heparin levels: 0.3–0.7 units/ml

Dosage

- Prophylaxis: 5000 units SC BD/TDS
- Intravenous heparin: Bolus 70 units/kg followed by infusion 12–15 units/kg/hr.
- The limitations of heparin are both pharmacokinetic and biophysical limitations.

Table 1: Limitation of heparin

Limitations	Mechanism
Poor bioavailability	Limited absorption of long heparin chains
Dose – dependent clearance	Binds to endothelial cells
Variable anticoagulant response	Binds to plasma protein, levels vary from patient to patient
Reduced activity in the vicinity of platelet- rich thrombi	Neutralized by platelet factor 4 released from activated platelets
Limited activity against factor Xa incorporated into the prothrombinase complex and thrombin bound to fibrin	Reduced capacity of heparin- antithrombin complex to inhibit factor Xa bound to activated platelets and thrombin

Side Effects

- Bleeding, Thrombocytopenia, Osteoporosis, Elevated transaminases.
- Bleeding is neutralised by protamine sulfate (a basic polypeptide from salmon sperm).
- 1 mg IV protamine sulfate neutralises 100 units of heparin.
- Heparin-induced thrombocytopenia (HIT) is managed by stopping heparin and starting alternative drugs such as: direct thrombin inhibitors (lepirudin, argatroban, bivalirudin) ondaparinux or rivaroxaban.

Osteoporosis
Heparin causes bone resorption and affects both osteoclasts and osteoblasts, leading to symptomatic vertebral fractures in 2–3% of patients.

Low Molecular Weight Heparin (LMWH)
LMWH is prepared from UFH by controlled enzymatic or chemical depolymerisation.
The mean molecular weight is 5000 (about one-third of UFH).

Mechanism of Action
Anticoagulation by activating antithrombin. At least half of LMWH chains are too short to bridge thrombin and antithrombin. It inhibits factor Xa by antithrombin more than thrombin. Anti-factor Xa: Anti-factor IIa ratio = 2:1 to 4:1.

Pharmacology
- May be administered IV or SC .Reduced binding to endothelial cells and macrophages. Hence clearance is not dose dependent and plasma half-life is longer.
- Half-life: ~4 hours
- LMWH accumulates in renal insufficiency. It has 90% bioavailability with SC route

Monitoring of LMWH Therapy
- Monitoring is generally not needed as it is a safer drug. Therapeutic anti-factor Xa levels: 0.5–1.2 units/ml Prophylactic peak anti-factor Xa levels: 0.2–0.5 units/ml
- Monitoring is essential in: Obesity Renal failure pregnancy, mechanical heart valves situation.
- Dose150–200 units/kg for VTE
- Enoxaparin 40 mg OD SC

Side Effects
- Bleeding occurs mostly with concomitant use of antiplatelets and fibtinolytics.
- Thrombocytopenia: the risk 5 fold lower than heparin.
- Osteoporosis risk is also lower.

Heparin [UFH] Vs Low Molecular Weight Heparin [LMWH]

Table 2: Heparin [UFH] Vs Low Molecular Weight Heparin [LMWH]

Parameters	Heparin [UFH]	LMWH
1. Category	Parenteral anticoagulant	Parenteral anticoagulant
2. Source	Biological – Porcine intestine or Bovine lung	Biological – Chemical / enzymatic deploymerization of UFH [Eg -Enoxaparin, Dalteparin ,Nadroparin, Tinzaparin]
3. Average Molecular Mass	15 kDa	4.5 kDa
4. Average Molecular weight	15000 g/ mol	4500 g/mol
5. Basic structure	Long- chain polysaccharides	Short – chain polysaccharides
6. Mechanism of action	Inhibits Factor Xa and Thrombin [IIa]	Predominantly inhibits Factor Xa [Xa > IIa]
7. Monitoring	aPTT required	Usually no monitoring [Anti – Xa] in special cases
8. Routes of administration	IV & SC	SC
9. Bioavailability	30%	90%
10. Half life	1 hour	4 hours
11. Pharmacokinetic profile	Less predictable	More predictable
12. Anticoagulant effect	Less predictable	More predictable
13. Use in renal failure.	Can be administered	Contraindicated if GFR < 30ml/min
14. Self-administration	Not recommended	Safely administered in outpatient
15. Risk of bleeding	High	Low

Advantages of Low Molecular Weight Heparin and Fondaparinux over Heparin.

Table 3: Advantages of Low Molecular Weight Heparin and Fondaparinux over Heparin

Advantage	Disadvantage
Better bioavailability and longer half-life after subcutaneous injection	Can be given subcutaneously once or twice daily for both prophylaxis and treatment
Dose – independent clearance	Simplified dosing
Predictable anticoagulant response	Montoring of coagulation is unnecessary in most patients
Lowe risk for heparin- induced thrombocytopenia	Safer than heparin for short – or long term administration
Lower risk for osteoporosis	Safer than heparin for long term administration

CONCLUSION

Pregnancy is a thrombogenic environment. The Physiological changes in pregnancy augment thrombogenesis both by increasing coagulants and reducing endogenous anticoagulants. The Thrombogenic risk is 5–15 fold higher in IVF conception due to essential steps involved in the IVF procedure namely hyperestrogenism during ovarian stimulation.

The thromboembolic risk is high in normal pregnancy during last trimester & first 6 weeks of puerperium while in IVF conception it is high in first trimester itself extending into puerperium. Both heparin and enoxaparin do not cross the placenta and hence safe to fetus while all the other oral anticoagulants (warfarin, fondaparinux) cross the placenta to reach significant fetal levels. Considering the definitive indication, the use of short acting unfractionated Heparin seems advantageous towards stopping and restarting only at 6 hours with immediate therapeutic levels lest the fear of surgical bleeding risk during C-section and coagulopathy if regional anaesthesia is warranted.

In contrast a sustained stable level of anticoagulation seems essential for the successful outcome of the precious in vitro fertilization conception which is provided by enoxaparin 40 mg OD.

The case is presented to evidence the safety and advantages of the use of low molecular weight heparin right from 1st trimester to puerperium without any anticipated maternal and fetal complications against the conventional heparin therapy and safety of general anaesthesia for C – section.

REFERENCES

1. Sultan AA. Thromboembolic disorders. Chap 52. In: Corton M, Leveno K, Bloom S, et al, eds. Williams obstetrics. 24th edn. McGraw Hill 2014: p. 1628.
2. Rova K, Passmark H, Lindqvist PG. Venous thromboembolism in relation to in vitro fertilisation. Fertility and Sterility 2012;97(1):95-100.
3. Bates SM, Middeldorp S, Rodger M, et al. Guidance for the treatment and prevention of obstetric-associated VTE. Journal of Thrombosis and Thrombolysis 2016;41(1):92-128.
4. Nelson SM. Venous thrombosis during assisted reproduction: novel risk reduction strategies. Thrombosis Research 2013;131(Suppl 1):S1-3.
5. Curvers J, Nienhuis SJ, Nap AW, et al. Activated protein C resistance during IVF treatment. Eur J Obstet Gynecol Reprod Biol 2001;95(2):222-4.
6. Seligsohn U. Antithrombin deficiency. In: Corton M, Leveno K, Bloom S, et al, eds. Williams Obstetrics. 24th edn. McGraw Hill 2014.
7. Bauersachs RM, Manolopoulos K, Hoppe I, et al. More on: the 'ART' behind the clot: solving the mystery. Journal of Thrombosis and Haemostasis. 2007;5(2):438-9.
8. Grandone E, Bitsadze V, Khizroeva J, et al. Risk of thrombosis in women undergoing in vitro fertilization: a narrative review. J Clin Med 2025;14(4):1053.
9. Jeffrey I. Weitz. Hemostasis, fibrinolysis, thrombosis and cardiovascular disease. Chap- 98. In: Zipes DP, Libby P, Bonow RO, eds, et al. Braunwald's heart disease. 11th edn. Elsevier 2019:1835-7.
10. Marik PE, Plante LA. Venous thromboembolism in pregnancy. N Engl J Med 2008;359(19):2025-33.
11. Dunning K, Le Masters G, Bhattacharya A. A major public health issue: high incidence of falls during pregnancy. Maternal and Child Health Journal 2010;14(5):720-5.
12. Weintraub AY, Lerner F, Mazor M. The pathophysiology of trauma in pregnancy: a review. Journal of Maternal-Fetal and Neonatal Medicine 2006;19(10):601-5.
13. La Rosa M, Loaiza S, Zambrano MA, et al. Trauma in pregnancy. Clin Obstet Gynecol 2020;63(2):447-54.
14. Weiss HB, Songer TJ, Fabio A. Fetal deaths related to maternal injury. JAMA 2001;286(15):1863-8.